Gene	Disease	Summary	Description	Variants
ABCA4	Cone rod dystrophy	A rare genetic isolated inherited retinal disorder characterized by primary cone degeneration with significant secondary rod involvement, with a variable fundus appearance. Typical presentation includes decreased visual acuity, central scotoma, photophobia, color vision alteration, followed by night blindness and loss of peripheral visual field.	Cone rod dystrophy (CRD) is characterized by primary cone involvement or, occasionally, by concomitant loss of both cones and rods, explaining the predominant symptoms of CRDs: decreased visual acuity, color vision defects, photoaversion and decreased sensitivity in the central visual field, later followed by progressive loss in peripheral vision and night blindness. The fundus appearance is varaible ranging from normal in the early stages, with only subtle temporal optic nerve pallor, macular pigment migration and atrophy or a bull's-eye maculopathy, to peripheral retinal pigment epithelium atrophy, intra retinal pigmentation migration, arteriolar attenuation, and optic disc pallor as disease progresses. Cone-rod dystrophy (CRD) should be distinguished from rod-cone dystrophy (RCD), also known as retinitis pigmentosa. Unlike RCD, which typically start with night blindness and progressive visual field constriction while central vision is preserved until late stages, CRD is characterized by a primary decrease in central vision leading to earlier legal blindness. At end stage, however, CRDs do not differ from end stage RCDs. CRDs are most frequently nonsyndromic, however they may also be part of several syndromes, such as AlstrÃ¶m syndrome, Bardet-Biedl syndrome and Spinocerebellar Ataxia Type 7.	c.1755del ; NM_000350.2(ABCA4):c.1804C>T ; NM_000350.2(ABCA4):c.5819T>C ; NM_000350.2(ABCA4):c.52C>T ; c.5512del ; NM_000350.2(ABCA4):c.3106G>A ; c.6394G>T ; c.1771del ; NM_000350.2(ABCA4):c.4793C>A ; NM_000350.2(ABCA4):c.763C>T ; NM_000350.2(ABCA4):c.5882G>A ; NM_000350.2(ABCA4):c.4469G>A ; NM_000350.2(ABCA4):c.6118C>T ; NM_000350.2(ABCA4):c.2300T>A ; NM_000350.2(ABCA4):c.3210_3211dupGT ; NM_000350.2(ABCA4):c.1848del ; NM_000350.2(ABCA4):c.3322C>T ; NM_000350.2(ABCA4):c.1018T>G ; NM_000350.2(ABCA4):c.1222C>T ; NM_000350.2(ABCA4):c.634C>T ; NM_000350.2(ABCA4):c.6089G>A ; NM_000350.2(ABCA4):c.5461-10T>C ; NM_000350.2(ABCA4):c.4457C>T ; NM_000350.2(ABCA4):c.6449G>A ; NM_000350.2(ABCA4):c.3083C>T ; NM_000350.2(ABCA4):c.2616_2617delCT ; NM_000350.2(ABCA4):c.5881G>A ; NM_000350.2(ABCA4):c.4429C>T ; NM_000350.2(ABCA4):c.1938-1G>A ; NM_000350.2(ABCA4):c.2160+1G>T ; NM_000350.2(ABCA4):c.5912T>G ; NM_000350.2(ABCA4):c.5714+5G>A ; NM_000350.2(ABCA4):c.67-2A>G ; NM_000350.2(ABCA4):c.3539_3554del16 ; NM_000350.2(ABCA4):c.1225del ; NM_000350.2(ABCA4):c.3364G>A ; NM_000350.2(ABCA4):c.4139C>T ; NM_000350.2(ABCA4):c.1964T>G ; c.1755del ; NM_000350.2(ABCA4):c.1804C>T ; NM_000350.2(ABCA4):c.5819T>C ; NM_000350.2(ABCA4):c.52C>T ; c.5512del ; NM_000350.2(ABCA4):c.3106G>A ; c.6394G>T ; c.1771del ; NM_000350.2(ABCA4):c.4793C>A ; NM_000350.2(ABCA4):c.763C>T ; NM_000350.2(ABCA4):c.5882G>A ; NM_000350.2(ABCA4):c.4469G>A ; NM_000350.2(ABCA4):c.6118C>T ; NM_000350.2(ABCA4):c.2300T>A ; NM_000350.2(ABCA4):c.3210_3211dupGT ; NM_000350.2(ABCA4):c.1848del ; NM_000350.2(ABCA4):c.3322C>T ; NM_000350.2(ABCA4):c.1018T>G ; NM_000350.2(ABCA4):c.1222C>T ; NM_000350.2(ABCA4):c.634C>T ; NM_000350.2(ABCA4):c.6089G>A ; NM_000350.2(ABCA4):c.5461-10T>C ; NM_000350.2(ABCA4):c.4457C>T ; NM_000350.2(ABCA4):c.6449G>A ; NM_000350.2(ABCA4):c.3083C>T ; NM_000350.2(ABCA4):c.2616_2617delCT ; NM_000350.2(ABCA4):c.5881G>A ; NM_000350.2(ABCA4):c.4429C>T ; NM_000350.2(ABCA4):c.1938-1G>A ; NM_000350.2(ABCA4):c.2160+1G>T ; NM_000350.2(ABCA4):c.5912T>G ; NM_000350.2(ABCA4):c.5714+5G>A ; NM_000350.2(ABCA4):c.67-2A>G ; NM_000350.2(ABCA4):c.3539_3554del16 ; NM_000350.2(ABCA4):c.1225del ; NM_000350.2(ABCA4):c.3364G>A ; NM_000350.2(ABCA4):c.4139C>T ; NM_000350.2(ABCA4):c.1964T>G

ABCA4	NON RARE IN EUROPE: Age-related macular degeneration	Age-related macular degeneration-2 (ARMD2) is a complex disorder characterized by the accumulation of drusen in and under the retinal pigment epithelium (RPE) and the progressive atrophy of the macular RPE. These changes result in loss of photoreceptor function and vision impairment. Environmental risk factors include cigarette smoking, diet, and cholesterol level.		c.1755del ; NM_000350.2(ABCA4):c.1804C>T ; NM_000350.2(ABCA4):c.5819T>C ; NM_000350.2(ABCA4):c.52C>T ; c.5512del ; NM_000350.2(ABCA4):c.3106G>A ; c.6394G>T ; c.1771del ; NM_000350.2(ABCA4):c.4793C>A ; NM_000350.2(ABCA4):c.763C>T ; NM_000350.2(ABCA4):c.5882G>A ; NM_000350.2(ABCA4):c.4469G>A ; NM_000350.2(ABCA4):c.6118C>T ; NM_000350.2(ABCA4):c.2300T>A ; NM_000350.2(ABCA4):c.3210_3211dupGT ; NM_000350.2(ABCA4):c.1848del ; NM_000350.2(ABCA4):c.3322C>T ; NM_000350.2(ABCA4):c.1018T>G ; NM_000350.2(ABCA4):c.1222C>T ; NM_000350.2(ABCA4):c.634C>T ; NM_000350.2(ABCA4):c.6089G>A ; NM_000350.2(ABCA4):c.5461-10T>C ; NM_000350.2(ABCA4):c.4457C>T ; NM_000350.2(ABCA4):c.6449G>A ; NM_000350.2(ABCA4):c.3083C>T ; NM_000350.2(ABCA4):c.2616_2617delCT ; NM_000350.2(ABCA4):c.5881G>A ; NM_000350.2(ABCA4):c.4429C>T ; NM_000350.2(ABCA4):c.1938-1G>A ; NM_000350.2(ABCA4):c.2160+1G>T ; NM_000350.2(ABCA4):c.5912T>G ; NM_000350.2(ABCA4):c.5714+5G>A ; NM_000350.2(ABCA4):c.67-2A>G ; NM_000350.2(ABCA4):c.3539_3554del16 ; NM_000350.2(ABCA4):c.1225del ; NM_000350.2(ABCA4):c.3364G>A ; NM_000350.2(ABCA4):c.4139C>T ; NM_000350.2(ABCA4):c.1964T>G ; c.1755del ; NM_000350.2(ABCA4):c.1804C>T ; NM_000350.2(ABCA4):c.5819T>C ; NM_000350.2(ABCA4):c.52C>T ; c.5512del ; NM_000350.2(ABCA4):c.3106G>A ; c.6394G>T ; c.1771del ; NM_000350.2(ABCA4):c.4793C>A ; NM_000350.2(ABCA4):c.763C>T ; NM_000350.2(ABCA4):c.5882G>A ; NM_000350.2(ABCA4):c.4469G>A ; NM_000350.2(ABCA4):c.6118C>T ; NM_000350.2(ABCA4):c.2300T>A ; NM_000350.2(ABCA4):c.3210_3211dupGT ; NM_000350.2(ABCA4):c.1848del ; NM_000350.2(ABCA4):c.3322C>T ; NM_000350.2(ABCA4):c.1018T>G ; NM_000350.2(ABCA4):c.1222C>T ; NM_000350.2(ABCA4):c.634C>T ; NM_000350.2(ABCA4):c.6089G>A ; NM_000350.2(ABCA4):c.5461-10T>C ; NM_000350.2(ABCA4):c.4457C>T ; NM_000350.2(ABCA4):c.6449G>A ; NM_000350.2(ABCA4):c.3083C>T ; NM_000350.2(ABCA4):c.2616_2617delCT ; NM_000350.2(ABCA4):c.5881G>A ; NM_000350.2(ABCA4):c.4429C>T ; NM_000350.2(ABCA4):c.1938-1G>A ; NM_000350.2(ABCA4):c.2160+1G>T ; NM_000350.2(ABCA4):c.5912T>G ; NM_000350.2(ABCA4):c.5714+5G>A ; NM_000350.2(ABCA4):c.67-2A>G ; NM_000350.2(ABCA4):c.3539_3554del16 ; NM_000350.2(ABCA4):c.1225del ; NM_000350.2(ABCA4):c.3364G>A ; NM_000350.2(ABCA4):c.4139C>T ; NM_000350.2(ABCA4):c.1964T>G
ABCA4	Retinitis pigmentosa	Retinitis pigmentosa (RP) is an inherited retinal dystrophy leading to progressive loss of the photoreceptors and retinal pigment epithelium and resulting in blindness usually after several decades.	Retinitis pigmentosa is slowly progressive but relentless. There is however broad variability in age of onset, rate of progression and secondary clinical manifestations. Affected individuals generally first develop night blindness (nyctalopia) due to loss of rod function, often in adolescence or earlier. They then develop peripheral visual field impairment, and over time loss of central vision, usually at late stages, often around midlife. Central visual acuity loss may occur at any age as a result of cystoid macular edema or photoreceptor loss. Posterior subcapsular cataracts are common and severity is age dependent. Reduced color vision may also be found. Fundus examination reveals bone spicule pigment deposits, attenuated retinal vessels, retinal atrophy and waxy optic nerve pallor. Severity is partly correlated with the pattern of inheritance with X-linked cases having the most severe course, autosomal recessive and single occurrence cases having intermediate severity, and autosomal dominant the most favorable course.	c.1755del ; NM_000350.2(ABCA4):c.1804C>T ; NM_000350.2(ABCA4):c.5819T>C ; NM_000350.2(ABCA4):c.52C>T ; c.5512del ; NM_000350.2(ABCA4):c.3106G>A ; c.6394G>T ; c.1771del ; NM_000350.2(ABCA4):c.4793C>A ; NM_000350.2(ABCA4):c.763C>T ; NM_000350.2(ABCA4):c.5882G>A ; NM_000350.2(ABCA4):c.4469G>A ; NM_000350.2(ABCA4):c.6118C>T ; NM_000350.2(ABCA4):c.2300T>A ; NM_000350.2(ABCA4):c.3210_3211dupGT ; NM_000350.2(ABCA4):c.1848del ; NM_000350.2(ABCA4):c.3322C>T ; NM_000350.2(ABCA4):c.1018T>G ; NM_000350.2(ABCA4):c.1222C>T ; NM_000350.2(ABCA4):c.634C>T ; NM_000350.2(ABCA4):c.6089G>A ; NM_000350.2(ABCA4):c.5461-10T>C ; NM_000350.2(ABCA4):c.4457C>T ; NM_000350.2(ABCA4):c.6449G>A ; NM_000350.2(ABCA4):c.3083C>T ; NM_000350.2(ABCA4):c.2616_2617delCT ; NM_000350.2(ABCA4):c.5881G>A ; NM_000350.2(ABCA4):c.4429C>T ; NM_000350.2(ABCA4):c.1938-1G>A ; NM_000350.2(ABCA4):c.2160+1G>T ; NM_000350.2(ABCA4):c.5912T>G ; NM_000350.2(ABCA4):c.5714+5G>A ; NM_000350.2(ABCA4):c.67-2A>G ; NM_000350.2(ABCA4):c.3539_3554del16 ; NM_000350.2(ABCA4):c.1225del ; NM_000350.2(ABCA4):c.3364G>A ; NM_000350.2(ABCA4):c.4139C>T ; NM_000350.2(ABCA4):c.1964T>G ; c.1755del ; NM_000350.2(ABCA4):c.1804C>T ; NM_000350.2(ABCA4):c.5819T>C ; NM_000350.2(ABCA4):c.52C>T ; c.5512del ; NM_000350.2(ABCA4):c.3106G>A ; c.6394G>T ; c.1771del ; NM_000350.2(ABCA4):c.4793C>A ; NM_000350.2(ABCA4):c.763C>T ; NM_000350.2(ABCA4):c.5882G>A ; NM_000350.2(ABCA4):c.4469G>A ; NM_000350.2(ABCA4):c.6118C>T ; NM_000350.2(ABCA4):c.2300T>A ; NM_000350.2(ABCA4):c.3210_3211dupGT ; NM_000350.2(ABCA4):c.1848del ; NM_000350.2(ABCA4):c.3322C>T ; NM_000350.2(ABCA4):c.1018T>G ; NM_000350.2(ABCA4):c.1222C>T ; NM_000350.2(ABCA4):c.634C>T ; NM_000350.2(ABCA4):c.6089G>A ; NM_000350.2(ABCA4):c.5461-10T>C ; NM_000350.2(ABCA4):c.4457C>T ; NM_000350.2(ABCA4):c.6449G>A ; NM_000350.2(ABCA4):c.3083C>T ; NM_000350.2(ABCA4):c.2616_2617delCT ; NM_000350.2(ABCA4):c.5881G>A ; NM_000350.2(ABCA4):c.4429C>T ; NM_000350.2(ABCA4):c.1938-1G>A ; NM_000350.2(ABCA4):c.2160+1G>T ; NM_000350.2(ABCA4):c.5912T>G ; NM_000350.2(ABCA4):c.5714+5G>A ; NM_000350.2(ABCA4):c.67-2A>G ; NM_000350.2(ABCA4):c.3539_3554del16 ; NM_000350.2(ABCA4):c.1225del ; NM_000350.2(ABCA4):c.3364G>A ; NM_000350.2(ABCA4):c.4139C>T ; NM_000350.2(ABCA4):c.1964T>G

ABCA4	Stargardt disease	A rare ophthalmic disorder that is usually characterized by a progressive loss of central vision associated with irregular macular and perimacular yellow-white fundus flecks, and a so-called "beaten bronze" atrophic central macular lesion.	The disease typically presents within the first two decades of life, even though symptoms can also appear during adulthood and as late as the seventh decade. Although disease progression and severity varies widely, Stargardt disease (STGD1) is usually characterized by a progressive loss of central vision causing blurry vision and, occasionally, an increasing difficulty to adapt in the dark. Peripheral vision is usually normal. Most affected individuals also have impaired color vision. Photophobia may be present.	c.1755del ; NM_000350.2(ABCA4):c.1804C>T ; NM_000350.2(ABCA4):c.5819T>C ; NM_000350.2(ABCA4):c.52C>T ; c.5512del ; NM_000350.2(ABCA4):c.3106G>A ; c.6394G>T ; c.1771del ; NM_000350.2(ABCA4):c.4793C>A ; NM_000350.2(ABCA4):c.763C>T ; NM_000350.2(ABCA4):c.5882G>A ; NM_000350.2(ABCA4):c.4469G>A ; NM_000350.2(ABCA4):c.6118C>T ; NM_000350.2(ABCA4):c.2300T>A ; NM_000350.2(ABCA4):c.3210_3211dupGT ; NM_000350.2(ABCA4):c.1848del ; NM_000350.2(ABCA4):c.3322C>T ; NM_000350.2(ABCA4):c.1018T>G ; NM_000350.2(ABCA4):c.1222C>T ; NM_000350.2(ABCA4):c.634C>T ; NM_000350.2(ABCA4):c.6089G>A ; NM_000350.2(ABCA4):c.5461-10T>C ; NM_000350.2(ABCA4):c.4457C>T ; NM_000350.2(ABCA4):c.6449G>A ; NM_000350.2(ABCA4):c.3083C>T ; NM_000350.2(ABCA4):c.2616_2617delCT ; NM_000350.2(ABCA4):c.5881G>A ; NM_000350.2(ABCA4):c.4429C>T ; NM_000350.2(ABCA4):c.1938-1G>A ; NM_000350.2(ABCA4):c.2160+1G>T ; NM_000350.2(ABCA4):c.5912T>G ; NM_000350.2(ABCA4):c.5714+5G>A ; NM_000350.2(ABCA4):c.67-2A>G ; NM_000350.2(ABCA4):c.3539_3554del16 ; NM_000350.2(ABCA4):c.1225del ; NM_000350.2(ABCA4):c.3364G>A ; NM_000350.2(ABCA4):c.4139C>T ; NM_000350.2(ABCA4):c.1964T>G ; c.1755del ; NM_000350.2(ABCA4):c.1804C>T ; NM_000350.2(ABCA4):c.5819T>C ; NM_000350.2(ABCA4):c.52C>T ; c.5512del ; NM_000350.2(ABCA4):c.3106G>A ; c.6394G>T ; c.1771del ; NM_000350.2(ABCA4):c.4793C>A ; NM_000350.2(ABCA4):c.763C>T ; NM_000350.2(ABCA4):c.5882G>A ; NM_000350.2(ABCA4):c.4469G>A ; NM_000350.2(ABCA4):c.6118C>T ; NM_000350.2(ABCA4):c.2300T>A ; NM_000350.2(ABCA4):c.3210_3211dupGT ; NM_000350.2(ABCA4):c.1848del ; NM_000350.2(ABCA4):c.3322C>T ; NM_000350.2(ABCA4):c.1018T>G ; NM_000350.2(ABCA4):c.1222C>T ; NM_000350.2(ABCA4):c.634C>T ; NM_000350.2(ABCA4):c.6089G>A ; NM_000350.2(ABCA4):c.5461-10T>C ; NM_000350.2(ABCA4):c.4457C>T ; NM_000350.2(ABCA4):c.6449G>A ; NM_000350.2(ABCA4):c.3083C>T ; NM_000350.2(ABCA4):c.2616_2617delCT ; NM_000350.2(ABCA4):c.5881G>A ; NM_000350.2(ABCA4):c.4429C>T ; NM_000350.2(ABCA4):c.1938-1G>A ; NM_000350.2(ABCA4):c.2160+1G>T ; NM_000350.2(ABCA4):c.5912T>G ; NM_000350.2(ABCA4):c.5714+5G>A ; NM_000350.2(ABCA4):c.67-2A>G ; NM_000350.2(ABCA4):c.3539_3554del16 ; NM_000350.2(ABCA4):c.1225del ; NM_000350.2(ABCA4):c.3364G>A ; NM_000350.2(ABCA4):c.4139C>T ; NM_000350.2(ABCA4):c.1964T>G
ACAD9	Acyl-CoA dehydrogenase 9 deficiency	A rare disorder characterized by neurological dysfunction, hepatic failure and cardiomyopathy due to a deficiency of complex I of the respiratory chain.	Patients present predominantly with neurological, hepatic and /or cardiomyopathic disease with isolated NADH-CoQ reductase deficiency (see this term). Manifestations include failure to thrive, hypertrophic cardiomyopathy, exercise intolerance, liver disease and mild to severe neurological dysfunction.	c.453+1G>A ; NM_014049.4(ACAD9):c.1240C>T ; c.23del ; NM_014049.4(ACAD9):c.359delT ; NM_014049.4(ACAD9):c.797G>A ; NM_014049.4(ACAD9):c.130T>A ; NM_014049.4(ACAD9):c.1594C>T ; NM_014049.4(ACAD9):c.1249C>T ; NM_014049.4(ACAD9):c.976G>C ; c.453+1G>A ; NM_014049.4(ACAD9):c.1240C>T ; c.23del ; NM_014049.4(ACAD9):c.359delT ; NM_014049.4(ACAD9):c.797G>A ; NM_014049.4(ACAD9):c.130T>A ; NM_014049.4(ACAD9):c.1594C>T ; NM_014049.4(ACAD9):c.1249C>T ; NM_014049.4(ACAD9):c.976G>C

ACADM	Medium chain acyl-CoA dehydrogenase deficiency	Medium chain acyl-CoA dehydrogenase (MCAD) deficiency (MCADD) is an inborn error of mitochondrial fatty acid oxidation characterized by a rapidly progressive metabolic crisis, often presenting as hypoketotic hypoglycemia, lethargy, vomiting, seizures and coma, which can be fatal in the absence of emergency medical intervention.	MCADD usually presents 3 to 24 months after birth in previously healthy infants. However, neonatal presentations are well described as are those in adults, given sufficient metabolic stress (such as significant alcohol ingestion). Nevertheless, many affected individuals remain asymptomatic throughout life. Typically hypoketotic hypoglycemia, lethargy and vomiting are triggered by an infection, fasting or surgery. Some patients, however, can present with a progressive metabolic crisis despite ketosis and normal blood glucose. Rarely patients may present in crisis with "paradoxically" gross ketosis. During a crisis, a patient may manifest with lethargy, emesis, respiratory arrest, seizures, hepatomegaly and rapid progression to cardiac arrest unless emergency treatment is implemented. Potential brain injury occurring during these episodes can lead to an increased risk of long term neurological damage. Sudden unexplained death can sometimes be the first manifestation of this disease. Historically, about 25% of undiagnosed patients die during their first presentation of a crisis.	NM_000016.5(ACADM):c.250C>T ; NM_000016.5(ACADM):c.797A>G ; NM_000016.5(ACADM):c.449_452delCTGA ; NM_000016.5(ACADM):c.447G>A ; NM_000016.5(ACADM):c.799G>A ; NM_000016.5(ACADM):c.734C>T ; NM_000016.5(ACADM):c.616C>T ; NM_000016.5(ACADM):c.817_829del ; NM_000016.5(ACADM):c.984del ; NM_000016.5(ACADM):c.617G>A ; NM_000016.5(ACADM):c.287-2A>G ; NM_000016.5(ACADM):c.1102_1105delTTAG ; NM_000016.5(ACADM):c.250C>T ; NM_000016.5(ACADM):c.797A>G ; NM_000016.5(ACADM):c.449_452delCTGA ; NM_000016.5(ACADM):c.447G>A ; NM_000016.5(ACADM):c.799G>A ; NM_000016.5(ACADM):c.734C>T ; NM_000016.5(ACADM):c.616C>T ; NM_000016.5(ACADM):c.817_829del ; NM_000016.5(ACADM):c.984del ; NM_000016.5(ACADM):c.617G>A ; NM_000016.5(ACADM):c.287-2A>G ; NM_000016.5(ACADM):c.1102_1105delTTAG
ACADS	Short chain acyl-CoA dehydrogenase deficiency	Short-chain acyl-CoA dehydrogenase (SCAD) deficiency is a very rare inborn error of mitochondrial fatty acid oxidation characterized by variable manifestations ranging from asymptomatic individuals (in most cases) to those with failure to thrive, hypotonia, seizures, developmental delay and progressive myopathy.	Most infants with SCAD deficiency identified through newborn screening programs have been well at the time of diagnosis and most have remained asymptomatic. In affected individuals manifestations include seizures, developmental delay (delayed sitting/walking and/or speech/social interaction), failure to grow with poor feeding, and usually muscle weakness and hypotonia.	NM_000017.4(ACADS):c.417G>C ; c.561_568del ; NM_000017.4:c.319C>T ; NM_000017.3(ACADS):c.529T>C ; NM_000017.3(ACADS):c.1147C>T ; NM_000017.3(ACADS):c.136C>T ; NM_000017.4(ACADS):c.417G>C ; c.561_568del ; NM_000017.4:c.319C>T ; NM_000017.3(ACADS):c.529T>C ; NM_000017.3(ACADS):c.1147C>T ; NM_000017.3(ACADS):c.136C>T

ACADSB	2-methylbutyryl-CoA dehydrogenase deficiency	2-Methylbutyryl-CoA dehydrogenase deficiency is an autosomal recessive metabolic disorder of impaired isoleucine degradation. It is most often ascertained via newborn screening and is usually clinically asymptomatic, although some patients have been reported to have delayed development and neurologic signs. Therefore, the clinical relevance of the deficiency is unclear.	A rare organic aciduria characterized by impaired isoleucine degradation with increased plasma or whole blood C5 acylcarnitine levels (typically observed in newborn screening) and increased urinary excretion of N-methylbutyrylglycine. The condition is usually clinically asymptomatic, although patients with muscular hypotonia, developmental delay, and seizures (among others) have been reported.	NM_001609.3(ACADSB):c.303+1G>A ; NM_001609.3(ACADSB):c.763C>T ; NM_001609.3(ACADSB):c.303+1G>A ; NM_001609.3(ACADSB):c.763C>T
ACADVL	Very long chain acyl-CoA dehydrogenase deficiency	Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency (VLCADD) is an inherited disorder of mitochondrial long-chain fatty acid oxidation with a variable presentation including: cardiomyopathy, hypoketotic hypoglycemia, liver disease, exercise intolerance and rhabdomyolysis.	VLCADD is a clinically heterogeneous disease, with 3 major phenotypes. Severe infantile VLCADD has an early onset, usually within the first 3-12 months of life and as early as the neonatal period, with high mortality and a high incidence of hypoketotic hypoglycaemia, liver disease, cardiac arrhythmias and cardiomyopathy. Pericardial effusion is also reported. Moderately severe infantile/childhood VLCADD has a later onset (early neonatal period to early childhood) and usually presents with hypoketotic hypoglycemia, lower mortality and rarely cardiomyopathy. Late-onset myopathic VLCADD presents in older children and young adults (usually >10 years of age) with isolated skeletal muscle involvement, exercise intolerance, myalgia, rhabdomyolysis and myoglobinuria usually triggered by exercise, fasting, cold/heat and/or stress but viral infection can also precipitate/exacerbate this presentation. In rare cases it can lead to renal failure and can be fatal. Some patients presenting with myopathic disease may have a previous history of hypoglycemia in infancy/childhood.	NM_000018.3(ACADVL):c.1389dupG ; NM_000018.2(ACADVL):c.1182+1G>A ; c.1309dup ; NM_000018.4:c.1096C>T ; NM_000018.3(ACADVL):c.343delG ; NM_000018.3(ACADVL):c.1106T>C ; c.334C>T ; NM_000018.3(ACADVL):c.848T>C ; NM_000018.3(ACADVL):c.753-2A>C ; NM_000018.3(ACADVL):c.1406G>A ; c.411+1G>C ; NM_000018.3(ACADVL):c.298_299delCA ; NM_000018.3(ACADVL):c.1837C>T ; NM_000018.3(ACADVL):c.1843C>T ; c.212-1G>A ; NM_000018.3(ACADVL):c.1532+1G>A ; NM_000018.3(ACADVL):c.1357C>T ; NM_000018.3(ACADVL):c.685C>T ; NM_000018.4(ACADVL):c.1097G>A ; NM_000018.4(ACADVL):c.520G>A ; NM_000018.3(ACADVL):c.1141_1143delGAG ; c.1816del ; NM_000018.3(ACADVL):c.1389dupG ; NM_000018.2(ACADVL):c.1182+1G>A ; c.1309dup ; NM_000018.4:c.1096C>T ; NM_000018.3(ACADVL):c.343delG ; NM_000018.3(ACADVL):c.1106T>C ; c.334C>T ; NM_000018.3(ACADVL):c.848T>C ; NM_000018.3(ACADVL):c.753-2A>C ; NM_000018.3(ACADVL):c.1406G>A ; c.411+1G>C ; NM_000018.3(ACADVL):c.298_299delCA ; NM_000018.3(ACADVL):c.1837C>T ; NM_000018.3(ACADVL):c.1843C>T ; c.212-1G>A ; NM_000018.3(ACADVL):c.1532+1G>A ; NM_000018.3(ACADVL):c.1357C>T ; NM_000018.3(ACADVL):c.685C>T ; NM_000018.4(ACADVL):c.1097G>A ; NM_000018.4(ACADVL):c.520G>A ; NM_000018.3(ACADVL):c.1141_1143delGAG ; c.1816del

ACAT1	Beta-ketothiolase deficiency	A rare, genetic organic aciduria affecting ketone body metabolism and the catabolism of isoleucine and characterized by intermittent ketoacidotic episodes associated with vomiting, dyspnea, tachypnoea, hypotonia, lethargy and coma, with an onset during infancy and usually ceasing by adolescence.	Children often appear normal at birth with disease presentation typically between the ages of 5 months to 2 years; however, presentation may occur anywhere between birth and childhood. The onset of symptoms usually occurs in the form of a ketoacidotic crisis, most often brought on by stress, fasting, acute illness and/or infections (i.e. gastroenteritis), and rarely by increased dietary protein intake. An acetone or fruity odor on the breath often signals ketoacidosis. These episodes are associated with vomiting, dyspnea, lethargy and unconsciousness, and can lead to coma and death if not treated. Neurological sequelae (such as developmental delay) following severe episodes are common. Rarely, patients present with signs of metabolic encephalopathy (hypotonia, dysarthria, chorea, developmental delay). The occurrence of developmental delay or neurological manifestations before a first ketoacidotic crisis, however, is rare. The frequency of episodes decreases with age, eventually stopping before adolescence. In between episodes, patients are often asymptomatic.	NM_000019.3(ACAT1):c.1033_1035del ; c.412_419del ; NM_000019.3(ACAT1):c.2T>A ; NM_000019.3(ACAT1):c.547G>A ; NM_000019.3(ACAT1):c.622C>T ; NM_000019.3(ACAT1):c.1138G>A ; NM_000019.3(ACAT1):c.905delA ; NM_000019.4(ACAT1):c.1083dup ; NM_000019.3(ACAT1):c.1136G>T ; NM_000019.3(ACAT1):c.1033_1035del ; c.412_419del ; NM_000019.3(ACAT1):c.2T>A ; NM_000019.3(ACAT1):c.547G>A ; NM_000019.3(ACAT1):c.622C>T ; NM_000019.3(ACAT1):c.1138G>A ; NM_000019.3(ACAT1):c.905delA ; NM_000019.4(ACAT1):c.1083dup ; NM_000019.3(ACAT1):c.1136G>T
ACOX1	Peroxisomal acyl-CoA oxidase deficiency	Peroxisomal acyl-CoA oxidase deficiency is a rare neurodegenerative disorder that belongs to the group of inherited peroxisomal disorders and is characterized by hypotonia and seizures in the neonatal period and neurological regression in early infancy.	Peroxisomal acyl-CoA oxidase deficiency is a disorder of peroxisomal fatty acid beta-oxidation. See also D-bifunctional protein deficiency, caused by mutation in the HSD17B4 gene on chromosome 5q2. The clinical manifestations of these 2 deficiencies are similar to those of disorders of peroxisomal assembly, including Zellweger cerebrohepatorenal syndrome and neonatal adrenoleukodystrophy: neonatal hypotonia, seizures, apneic spells, delayed psychomotor development, and neurologic regression after age 2 years. Brain imaging shows progressive white-matter demyelination without cortical malformations. Biochemical analysis shows accumulation of very long chain fatty acids (VLCFA) resulting from an isolated deficiency of peroxisomal fatty acyl-CoA oxidase.	c.591del ; NM_004035.6(ACOX1):c.832A>G ; NM_004035.6(ACOX1):c.532G>T ; c.591del ; NM_004035.6(ACOX1):c.832A>G ; NM_004035.6(ACOX1):c.532G>T

ADA	Omenn syndrome	Omenn syndrome (OS) is an inflammatory condition characterized by erythroderma, desquamation, alopecia, chronic diarrhea, failure to thrive, lymphadenopathy, and hepatosplenomegaly, associated with severe combined immunodeficiency (SCID; see this term).	OS presents during the first year of life with features of SCID including chronic diarrhea, pneumonitis and failure to thrive. In addition, patients present with inflammatory symptoms including lymphadenopathy, hepatosplenomegaly and generalized erythroderma, which may often cause alopecia and loss of eyebrows and eyelashes; protein loss may lead to generalized edema and metabolic disturbances. The signs and symptoms of OS can evolve over time and may not appear simultaneously. Some patients present with some but not all of these symptoms and may be described as having atypical Omenn syndrome. OS may also be associated with syndromic disorders including cartilage-hair hypoplasia (CHH), adenosine deaminase (ADA) deficiency, monosomy 22q11, coloboma of the eye, CHARGE syndrome and ligase 4 deficiency (see these terms).	
ADA	Severe combined immunodeficiency due to adenosine deaminase deficiency	Severe combined immunodeficiency (SCID) due to adenosine deaminase (ADA) deficiency is a form of SCID characterized by profound lymphopenia and very low immunoglobulin levels of all isotypes resulting in severe and recurrent opportunistic infections.	SCID due to ADA deficiency has a variable clinical presentation. The most common form presents in infancy with severe and recurrent opportunistic infections (including respiratory tract infections and candidiasis), failure to thrive, and usually results in early death. Ten to 15% of patients have a delayed clinical onset by age 6-24 months, and a smaller percentage have a partial form of ADA deficiency with later onset between ages 4 years and adulthood, both types showing less severe infections and gradual immunologic deterioration. Patients may also present with extraimmune manifestations (including neurodevelopmental deficits, behavioral disorders, sensorineural deafness, and skeletal and hepatic abnormalities) as a result of the systemic nature of ADA expression.	NM_000022.3(ADA):c.890C>A ; NM_000022.2(ADA):c.986C>T ; NM_000022.2(ADA):c.632G>A ; NM_000022.3(ADA):c.872C>T ; NM_000022.2(ADA):c.956_960delAAGAG ; NM_000022.2(ADA):c.320T>C ; NM_000022.3(ADA):c.890C>A ; NM_000022.2(ADA):c.986C>T ; NM_000022.2(ADA):c.632G>A ; NM_000022.3(ADA):c.872C>T ; NM_000022.2(ADA):c.956_960delAAGAG ; NM_000022.2(ADA):c.320T>C

ADAMTS2	Dermatosparaxis Ehlers-Danlos syndrome	A form of Ehlers-Danlos syndrome (EDS) characterized by extreme skin fragility and laxity, a prominent facial gestalt, excessive bruising and, sometimes, major complications due to visceral and vascular fragility.		NM_014244.4(ADAMTS2):c.2384G>A
AGA	Aspartylglucosaminuria	An autosomal recessive lysosomal storage disease belonging to the oligosaccharidosis group (also called glycoproteinosis).	Urea cycle disorders are characterized by the triad of hyperammonemia, encephalopathy, and respiratory alkalosis. Five disorders involving different defects in the biosynthesis of the enzymes of the urea cycle have been described: ornithine transcarbamylase deficiency (311250), carbamyl phosphate synthetase deficiency (237300), argininosuccinate synthetase deficiency, or citrullinemia (215700), argininosuccinate lyase deficiency (207900), and arginase deficiency.	NM_000027.3(AGA):c.755G>A ; NM_000027.3(AGA):c.302C>T ; NM_000027.4(AGA):c.800dup ; NM_000027.3(AGA):c.904G>A ; NM_000027.3(AGA):c.488G>C ; NM_000027.3(AGA):c.214T>C ; NM_000027.3(AGA):c.755G>A ; NM_000027.3(AGA):c.302C>T ; NM_000027.4(AGA):c.800dup ; NM_000027.3(AGA):c.904G>A ; NM_000027.3(AGA):c.488G>C ; NM_000027.3(AGA):c.214T>C
AGL	Glycogen storage disease due to glycogen debranching enzyme deficiency	Glycogen debranching enzyme (GDE) deficiency, or glycogen storage disease type 3 (GSD 3), is a form of glycogen storage disease characterized by severe muscle weakness and hepatopathy.	GSD 3 commonly occurs in early childhood. Children present with hepatomegaly, growth retardation and occasional seizures related to hypoglycemia. Hepatomegaly may disappear with adulthood. Muscle weakness is slowly progressive. Other frequently associated signs include muscular hypotonia and hypertrophic cardiomyopathy. Symptoms often improve at puberty, except in the few cases where cirrhosis or myopathy appears. Biological findings include hypoglycemia without acidosis, hypertriglyceridemia, and hypertransaminasemia during childhood.	NM_000642.2(AGL):c.1222C>T ; NM_000642.2(AGL):c.1485delT ; NM_000642.2(AGL):c.3216_3217delGA ; NM_000642.2(AGL):c.4342G>C ; NM_000642.3:c.4456delT ; NM_000642.2(AGL):c.294-2A>T ; NM_000642.2(AGL):c.2590C>T ; NM_000642.2(AGL):c.4529dupA ; NM_000642.2(AGL):c.18_19delGA ; NM_000642.2(AGL):c.2039G>A ; NM_000642.2(AGL):c.16C>T ; NM_000642.2(AGL):c.4260-12A>G ; NM_000642.2(AGL):c.1999del ; NM_000642.2(AGL):c.3980G>A ; c.1783C>T ; c.4260-1G>T ; NM_000642.2(AGL):c.1222C>T ; NM_000642.2(AGL):c.1485delT ; NM_000642.2(AGL):c.3216_3217delGA ; NM_000642.2(AGL):c.4342G>C ; NM_000642.3:c.4456delT ; NM_000642.2(AGL):c.294-2A>T ; NM_000642.2(AGL):c.2590C>T ; NM_000642.2(AGL):c.4529dupA ; NM_000642.2(AGL):c.18_19delGA ; NM_000642.2(AGL):c.2039G>A ; NM_000642.2(AGL):c.16C>T ; NM_000642.2(AGL):c.4260-12A>G ; NM_000642.2(AGL):c.1999del ; NM_000642.2(AGL):c.3980G>A ; c.1783C>T ; c.4260-1G>T

AGPS	Rhizomelic chondrodysplasia punctata type 3	A rare, primary bone dysplasia characterized by rhizomelic limb shortening, punctate calcifications in cartilage with epiphyseal and metaphyseal abnormalities (chondrodysplasia punctata) and coronal cleft vertebrae associated with profound postnatal growth deficiency, early-onset cataracts, severe intellectual disability and seizures.	Presentation is at birth with severe joint contractures; cataracts may be present or appear in the first few months of life. Respiratory distress nd feeding difficulties are commonly observed after birth. Whilst birth parameters (weight, length, and head circumference) are in the lower range from normal, profound postnatal growth retardation ensues. Rhizomelic limb shortening is typically greater in the humerus than the femur. Other skeletal abnormalities include punctate calcifications in cartilage with epiphyseal and metaphyseal abnormalities (chondrodysplasia punctata) and coronal cleft vertebrae. Intellectual disability is severe, and the majority of children develop seizures.	NM_003659.3(AGPS):c.926C>T ; NM_003659.3(AGPS):c.1406T>C ; NM_003659.3(AGPS):c.1703C>T ; NM_003659.3(AGPS):c.1256G>A ; NM_003659.3(AGPS):c.926C>T ; NM_003659.3(AGPS):c.1406T>C ; NM_003659.3(AGPS):c.1703C>T ; NM_003659.3(AGPS):c.1256G>A
AGXT	Primary hyperoxaluria type 1	A disorder of glyoxylate metabolism characterized by an excess of oxalate resulting in kidney stones, nephrocalcinosis and ultimately renal failure and systemic oxalosis. There are 3 types of PH, types 1-3, all caused by liver-specific enzyme defects.	Hyperoxaluria may lead to kidney stones, nephrocalcinosis and ultimately renal failure and systemic oxalosis. Symptoms can appear at any age and may vary from infantile failure to thrive and cortical nephrocalcinosis with renal failure to hematuria, medullary nephrocalcinosis or sporadic stone disease, even within one family. PH1 is the most severe form; overall, more than 70% of PH1 patients develop end-stage kidney disease over time; this may even occur in patients with sporadic stone disease. Storage of oxalate occurs in severe renal failure and may affect bone, eyes, heart, arteries and peripheral nerves (systemic oxalosis). PH2 has a more benign course; no infantile oxalosis has been described and end-stage kidney disease occurs at relatively late age in about 20% of patients. PH3 is most benign with so far only a few reports of renal impairment and no end-stage kidney disease.	NM_000030.2(AGXT):c.454T>A ; NM_000030.2(AGXT):c.698G>A ; NM_000030.2(AGXT):c.33dupC ; NM_000030.2(AGXT):c.248A>G ; NM_000030.2(AGXT):c.322T>C ; NM_000030.2(AGXT):c.560C>T ; NM_000030.2(AGXT):c.245G>A ; NM_000030.2(AGXT):c.508G>A ; NM_000030.2(AGXT):c.613T>C ; NM_000030.2(AGXT):c.738G>A ; NM_000030.3:c.121G>A ; NM_000030.2(AGXT):c.731T>C ; NM_000030.2(AGXT):c.697C>T ; NM_000030.2(AGXT):c.466G>A ; c.166-2A>G ; NM_000030.2(AGXT):c.454T>A ; NM_000030.2(AGXT):c.698G>A ; NM_000030.2(AGXT):c.33dupC ; NM_000030.2(AGXT):c.248A>G ; NM_000030.2(AGXT):c.322T>C ; NM_000030.2(AGXT):c.560C>T ; NM_000030.2(AGXT):c.245G>A ; NM_000030.2(AGXT):c.508G>A ; NM_000030.2(AGXT):c.613T>C ; NM_000030.2(AGXT):c.738G>A ; NM_000030.3:c.121G>A ; NM_000030.2(AGXT):c.731T>C ; NM_000030.2(AGXT):c.697C>T ; NM_000030.2(AGXT):c.466G>A ; c.166-2A>G

ALDOB	Hereditary fructose intolerance	Hereditary fructose intolerance (HFI) is an autosomal recessive disorder of fructose metabolism (see this term), resulting from a deficiency of hepatic fructose-1-phosphate aldolase activity and leading to gastrointestinal disorders and postprandial hypoglycemia following fructose ingestion. HFI is a benign condition when treated, but it is life-threatening and potentially fatal if left untreated.	HFI usually presents in infancy at the time of weaning (when fructose is added to the diet), manifesting with hypoglycemia, lactic acidosis, ketosis with recurrent vomiting, abdominal pain and systemic manifestations following consumption of fructose-containing foods. Persistent ingestion of fructose and related sugars (such as sucrose and sorbitol) may lead to growth retardation, hepatomegaly, proximal tubular dysfunction, liver and renal failure, seizures, coma and risk of death. All patients achieve adulthood, develop a natural aversion to fruit/sweets and report a life long history of vomiting and hypoglycemia following fructose ingestion. Dental caries are absent in a significant proportion of adult population with HFI (which may give a clue to the diagnosis). Sometimes, the diagnosis may be made in an adult who has, owing to his aversion to fructose, excluded all fructose-containing food since childhood.	NM_000035.4(ALDOB):c.1013C>T ; NM_000035.4(ALDOB):c.720C>A ; NM_000035.4(ALDOB):c.442T>C ; c.1067C>A ; NM_000035.4(ALDOB):c.178C>T ; NM_000035.3(ALDOB):c.113-1_115delGGTA ; NM_000035.4(ALDOB):c.1005C>G ; NM_000035.4(ALDOB):c.10C>T ; NM_000035.3(ALDOB):c.360_363delCAAA ; NM_000035.4(ALDOB):c.448G>C ; NM_000035.4(ALDOB):c.524C>A ; c.2T>C ; NM_000035.4(ALDOB):c.612T>A ; NM_000035.4(ALDOB):c.1013C>T ; NM_000035.4(ALDOB):c.720C>A ; NM_000035.4(ALDOB):c.442T>C ; c.1067C>A ; NM_000035.4(ALDOB):c.178C>T ; NM_000035.3(ALDOB):c.113-1_115delGGTA ; NM_000035.4(ALDOB):c.1005C>G ; NM_000035.4(ALDOB):c.10C>T ; NM_000035.3(ALDOB):c.360_363delCAAA ; NM_000035.4(ALDOB):c.448G>C ; NM_000035.4(ALDOB):c.524C>A ; c.2T>C ; NM_000035.4(ALDOB):c.612T>A
ALG6	ALG6-CDG	Congenital disorders of glycosylation, previously called carbohydrate-deficient glycoprotein syndromes (CDGSs), are caused by defects in mannose addition during N-linked oligosaccharide assembly. CDGs can be divided into 2 types, depending on whether they impair lipid-linked oligosaccharide (LLO) assembly and transfer (CDG I), or affect trimming of the protein-bound oligosaccharide or the addition of sugars to it (CDG II).	A form of congenital disorders of N-linked glycosylation characterized by feeding problems, mild-to-moderate neurologic involvement with hypotonia, poor head control, developmental delay, ataxia, strabismus, and seizures, ranging from febrile convulsions to epilepsy. Retinal degeneration has also been reported. A minority of patients show other manifestations, particularly intestinal (such as protein-losing enteropathy) and liver involvement. The disease is caused by loss of function mutations of the gene ALG6 (1p31.3).	NM_013339.4(ALG6):c.1432T>C ; NM_013339.4(ALG6):c.998C>T ; NM_013339.3(ALG6):c.897_899del ; c.316C>T ; NM_013339.4(ALG6):c.1432T>C ; NM_013339.4(ALG6):c.998C>T ; NM_013339.3(ALG6):c.897_899del ; c.316C>T

ALMS1	AlstrÃ¶m syndrome	A rare multisystemic disorder characterized by cone-rod dystrophy, hearing loss, obesity, insulin resistance and hyperinsulinemia, type 2 diabetes mellitus, dilated cardiomyopathy (DCM), and progressive hepatic and renal dysfunction.	The clinical features, age of onset, and severity can vary greatly among and within families. Cone-rod retinal dystrophy usually develops within a few weeks after birth, with the first symptoms being nystagmus and extreme photodysphoria or light sensitivity. It is progressive and leads to blindness, usually by the second decade of life. Most patients develop mild-to-moderate slowly progressive bilateral sensorineural hearing loss. There is evidence of multi-organ fibrosis in AS. DCM manifests in approximately 2/3 of patients, either as infants or as adolescents. Patients are at risk of sudden congestive heart failure at any age. Obesity with hyperphagia, insulin resistance and hyperinsulinemia are early and consistent features. Liver dysfunction usually begins in childhood with steatosis (fatty liver). In some cases, cirrhosis, portal hypertension and liver failure can occur. Chronic respiratory illness (bronchitis/pneumonia), pulmonary hypertension, recurrent otitis media, and hypertriglyceridemia are frequent. Slowly progressive nephropathy can lead to end stage renal failure. Patients have distinctive facial characteristics (thin hair, premature frontal balding, deep-set eyes with a rounded face and thick ears,). Most children have characteristic wide, thick, flat feet, and short stubby fingers and toes with no polydactyly or syndactyly. Hypogonadism in males/hyperandrogenism in females is also reported. Most patients have normal intelligence, although some reports have indicated delayed global development and intellectual disability. As some phenotypes develop slowly over time, non-classical presentations have also been reported.	ENST00000613296.5:c.888_904del ; NM_015120.4(ALMS1):c.11618_11619delCT ; NM_015120.4(ALMS1):c.8383C>T ; ENST00000613296.5:c.11608_11609del ; ENST00000613296.5:c.11449dup ; NM_015120.4(ALMS1):c.11316_11319delAGAG ; NM_015120.4(ALMS1):c.11449C>T ; ENST00000613296.5:c.1571_1573delinsT ; ENST00000613296.5:c.10576_10577del ; NM_015120.4(ALMS1):c.8164C>T ; NM_015120.4(ALMS1):c.10775delC ; ENST00000613296.5:c.9908-1G>A ; ENST00000613296.5:c.888_904del ; NM_015120.4(ALMS1):c.11618_11619delCT ; NM_015120.4(ALMS1):c.8383C>T ; ENST00000613296.5:c.11608_11609del ; ENST00000613296.5:c.11449dup ; NM_015120.4(ALMS1):c.11316_11319delAGAG ; NM_015120.4(ALMS1):c.11449C>T ; ENST00000613296.5:c.1571_1573delinsT ; ENST00000613296.5:c.10576_10577del ; NM_015120.4(ALMS1):c.8164C>T ; NM_015120.4(ALMS1):c.10775delC ; ENST00000613296.5:c.9908-1G>A

ALPL	Adult hypophosphatasia	A moderate form of hypophosphatasia (HPP) characterized by adult onset osteomalacia, chondrocalcinosis, osteoarthropathy, stress fractures and dental anomalies.	Adult HPP is clinically very heterogeneous. In its mildest form it is the least severe form of hypophosphatasia (HPP), characterized by non-specific symptoms in later age, such as osteoporosis, musculoskeletal pain, chondrocalcinosis. Most patients present features during middle age but some may have had a history of mild rickets or other musculoskeletal manifestations in childhood. Cardinal features include stress fractures and pseudo-fractures of the lower limbs, along with foot, thigh, and hip pain. The most common fracture types are metatarsal and tibial and femoral pseudofractures. Osteomalacia, chondrocalcinosis, and osteoarthropathy may develop with age. Some patients report history of early loss of primary dentition. Loss of permanent dentition is also common and some cases of enamel hypoplasia and tooth mobility are described. Patients with the adult form of HPP may have had some manifestations in early life between the prenatal period and childhood (prenatal benign HPP or childhood HPP). The presence of bone symptoms (osteomalacia, fractures) distinguish adult HPP from odontohypophosphatasia.	NM_000478.5(ALPL):c.211C>T ; NM_000478.5(ALPL):c.814C>T ; NM_000478.5(ALPL):c.98C>T ; NM_000478.4(ALPL):c.571G>A ; NM_000478.6(ALPL):c.407G>A ; NM_000478.5(ALPL):c.1366G>A ; NM_000478.5(ALPL):c.1250A>G ; NM_000478.4(ALPL):c.1133A>T ; NM_000478.5(ALPL):c.1001G>A ; NM_000478.5(ALPL):c.620A>C ; NM_000478.5(ALPL):c.881A>C ; NM_000478.5(ALPL):c.535G>A ; NM_000478.5(ALPL):c.526G>A ; NM_000478.5(ALPL):c.1306T>C ; NM_000478.5(ALPL):c.892G>A ; NM_000478.5(ALPL):c.212G>C ; NM_000478.5(ALPL):c.323C>T ; NM_000478.4(ALPL):c.346G>A ; NM_000478.5(ALPL):c.211C>T ; NM_000478.5(ALPL):c.814C>T ; NM_000478.5(ALPL):c.98C>T ; NM_000478.4(ALPL):c.571G>A ; NM_000478.6(ALPL):c.407G>A ; NM_000478.5(ALPL):c.1366G>A ; NM_000478.5(ALPL):c.1250A>G ; NM_000478.4(ALPL):c.1133A>T ; NM_000478.5(ALPL):c.1001G>A ; NM_000478.5(ALPL):c.620A>C ; NM_000478.5(ALPL):c.881A>C ; NM_000478.5(ALPL):c.535G>A ; NM_000478.5(ALPL):c.526G>A ; NM_000478.5(ALPL):c.1306T>C ; NM_000478.5(ALPL):c.892G>A ; NM_000478.5(ALPL):c.212G>C ; NM_000478.5(ALPL):c.323C>T ; NM_000478.4(ALPL):c.346G>A

ALPL	Childhood-onset hypophosphatasia	A rare, moderate form of hypophosphatasia (HPP) characterized by onset after six months of age and widely variable clinical features from low bone mineral density for age, to unexplained fractures, skeletal deformities, and rickets with short stature and waddling gait.	Patients develop manifestations after six months of age and generally before five years of age. Clinical manifestations cover a wide spectrum. Commonly, patients have rickets leading to short stature, with delay in walking and a waddling gait, and bone and joint pain. Skeletal deformities may include dolichocephalic skull and enlarged joints. Other common features are signs of intracranial hypertension and failure to thrive. Diaphyseal and metaphyseal fractures are common. Some affected children have premature loss of deciduous teeth, starting with incisors and then loss of other teeth with intact roots, before five years of age. The disease may follow an intermittent course with remission and recurrence in later life. There may be some clinical overlap between childhood-onset HPP and moderately severe infantile HPP.	NM_000478.5(ALPL):c.211C>T ; NM_000478.5(ALPL):c.814C>T ; NM_000478.5(ALPL):c.98C>T ; NM_000478.4(ALPL):c.571G>A ; NM_000478.6(ALPL):c.407G>A ; NM_000478.5(ALPL):c.1366G>A ; NM_000478.5(ALPL):c.1250A>G ; NM_000478.4(ALPL):c.1133A>T ; NM_000478.5(ALPL):c.1001G>A ; NM_000478.5(ALPL):c.620A>C ; NM_000478.5(ALPL):c.881A>C ; NM_000478.5(ALPL):c.535G>A ; NM_000478.5(ALPL):c.526G>A ; NM_000478.5(ALPL):c.1306T>C ; NM_000478.5(ALPL):c.892G>A ; NM_000478.5(ALPL):c.212G>C ; NM_000478.5(ALPL):c.323C>T ; NM_000478.4(ALPL):c.346G>A ; NM_000478.5(ALPL):c.211C>T ; NM_000478.5(ALPL):c.814C>T ; NM_000478.5(ALPL):c.98C>T ; NM_000478.4(ALPL):c.571G>A ; NM_000478.6(ALPL):c.407G>A ; NM_000478.5(ALPL):c.1366G>A ; NM_000478.5(ALPL):c.1250A>G ; NM_000478.4(ALPL):c.1133A>T ; NM_000478.5(ALPL):c.1001G>A ; NM_000478.5(ALPL):c.620A>C ; NM_000478.5(ALPL):c.881A>C ; NM_000478.5(ALPL):c.535G>A ; NM_000478.5(ALPL):c.526G>A ; NM_000478.5(ALPL):c.1306T>C ; NM_000478.5(ALPL):c.892G>A ; NM_000478.5(ALPL):c.212G>C ; NM_000478.5(ALPL):c.323C>T ; NM_000478.4(ALPL):c.346G>A
ALPL	Infantile hypophosphatasia	A rare, severe, genetic form of hypophosphatasia (HPP) characterized by infantile rickets without elevated serum alkaline phosphatase (ALP) activity and a wide range of clinical manifestations due to hypomineralization.	Individuals with infantile-HPP may be normal at birth. Clinical signs resembling rickets are generally found between birth and six months of age. Initial manifestations may include irritability, poor feeding, failure to thrive, hypotonia, and more rarely seizures. Other clinical features include growth failure, short stature, blue sclerae, bone hypomineralization (softening or thinning of the skull, rachitic ribs, scoliosis, thickening of wrists and ankles and bowing of long bones), craniosynostosis (possibly with increased intracranial pressure), lax ligaments, and hypercalciuria/hypercalcemia. Some patients have premature loss of deciduous teeth. Kidney damage (nephrocalcinosis due to hypercalciuria) is reported in some older infants. Severity is variable but many affected patients are at risk of respiratory failure due to rachitic deformities of the chest within the first year of life. There may be some clinical overlap with the moderate form, classed as childhood-onset HPP.	NM_000478.5(ALPL):c.211C>T ; NM_000478.5(ALPL):c.814C>T ; NM_000478.5(ALPL):c.98C>T ; NM_000478.4(ALPL):c.571G>A ; NM_000478.6(ALPL):c.407G>A ; NM_000478.5(ALPL):c.1366G>A ; NM_000478.5(ALPL):c.1250A>G ; NM_000478.4(ALPL):c.1133A>T ; NM_000478.5(ALPL):c.1001G>A ; NM_000478.5(ALPL):c.620A>C ; NM_000478.5(ALPL):c.881A>C ; NM_000478.5(ALPL):c.535G>A ; NM_000478.5(ALPL):c.526G>A ; NM_000478.5(ALPL):c.1306T>C ; NM_000478.5(ALPL):c.892G>A ; NM_000478.5(ALPL):c.212G>C ; NM_000478.5(ALPL):c.323C>T ; NM_000478.4(ALPL):c.346G>A ; NM_000478.5(ALPL):c.211C>T ; NM_000478.5(ALPL):c.814C>T ; NM_000478.5(ALPL):c.98C>T ; NM_000478.4(ALPL):c.571G>A ; NM_000478.6(ALPL):c.407G>A ; NM_000478.5(ALPL):c.1366G>A ; NM_000478.5(ALPL):c.1250A>G ; NM_000478.4(ALPL):c.1133A>T ; NM_000478.5(ALPL):c.1001G>A ; NM_000478.5(ALPL):c.620A>C ; NM_000478.5(ALPL):c.881A>C ; NM_000478.5(ALPL):c.535G>A ; NM_000478.5(ALPL):c.526G>A ; NM_000478.5(ALPL):c.1306T>C ; NM_000478.5(ALPL):c.892G>A ; NM_000478.5(ALPL):c.212G>C ; NM_000478.5(ALPL):c.323C>T ; NM_000478.4(ALPL):c.346G>A

ALPL	Odontohypophosphatasia	A particular form of hypophosphatasia (HPP) characterized by reduced activity of unfractionated serum alkaline phosphatase, premature exfoliation of primary and/or permanent teeth and/or severe dental caries, in the absence of skeletal system abnormalities.	The main feature of odontohypophosphatasia is premature exfoliation of fully rooted primary teeth and/or severe dental caries. The anterior deciduous teeth are most commonly affected along with the incisors. X-rays reveal reduced alveolar bone, reduced thickness of dentin, and enlarged pulp chambers and root canals. Patients with other forms of HPP often have dental manifestations but these are always associated with skeletal abnormalities and other manifestations.	NM_000478.5(ALPL):c.211C>T ; NM_000478.5(ALPL):c.814C>T ; NM_000478.5(ALPL):c.98C>T ; NM_000478.4(ALPL):c.571G>A ; NM_000478.6(ALPL):c.407G>A ; NM_000478.5(ALPL):c.1366G>A ; NM_000478.5(ALPL):c.1250A>G ; NM_000478.4(ALPL):c.1133A>T ; NM_000478.5(ALPL):c.1001G>A ; NM_000478.5(ALPL):c.620A>C ; NM_000478.5(ALPL):c.881A>C ; NM_000478.5(ALPL):c.535G>A ; NM_000478.5(ALPL):c.526G>A ; NM_000478.5(ALPL):c.1306T>C ; NM_000478.5(ALPL):c.892G>A ; NM_000478.5(ALPL):c.212G>C ; NM_000478.5(ALPL):c.323C>T ; NM_000478.4(ALPL):c.346G>A ; NM_000478.5(ALPL):c.211C>T ; NM_000478.5(ALPL):c.814C>T ; NM_000478.5(ALPL):c.98C>T ; NM_000478.4(ALPL):c.571G>A ; NM_000478.6(ALPL):c.407G>A ; NM_000478.5(ALPL):c.1366G>A ; NM_000478.5(ALPL):c.1250A>G ; NM_000478.4(ALPL):c.1133A>T ; NM_000478.5(ALPL):c.1001G>A ; NM_000478.5(ALPL):c.620A>C ; NM_000478.5(ALPL):c.881A>C ; NM_000478.5(ALPL):c.535G>A ; NM_000478.5(ALPL):c.526G>A ; NM_000478.5(ALPL):c.1306T>C ; NM_000478.5(ALPL):c.892G>A ; NM_000478.5(ALPL):c.212G>C ; NM_000478.5(ALPL):c.323C>T ; NM_000478.4(ALPL):c.346G>A
ALPL	Perinatal lethal hypophosphatasia	A rare, genetic form of hypophosphatasia (HPP) characterized by markedly impaired bone mineralization in utero due to reduced activity of serum alkaline phosphatase (ALP) and causing stillbirth or respiratory failure within days of birth.	Affected infants may have characteristic skin-covered osteochondral spurs protruding from the forearms or legs and often a small thoracic cavity. They may have hypercalcemia associated with apnea or seizures, and marked shortening of the long bones. Patients rarely survive for more than a few days due to inadequate chest size, hypoplastic lungs and rachitic deformities, leading to respiratory failure.	NM_000478.5(ALPL):c.211C>T ; NM_000478.5(ALPL):c.814C>T ; NM_000478.5(ALPL):c.98C>T ; NM_000478.4(ALPL):c.571G>A ; NM_000478.6(ALPL):c.407G>A ; NM_000478.5(ALPL):c.1366G>A ; NM_000478.5(ALPL):c.1250A>G ; NM_000478.4(ALPL):c.1133A>T ; NM_000478.5(ALPL):c.1001G>A ; NM_000478.5(ALPL):c.620A>C ; NM_000478.5(ALPL):c.881A>C ; NM_000478.5(ALPL):c.535G>A ; NM_000478.5(ALPL):c.526G>A ; NM_000478.5(ALPL):c.1306T>C ; NM_000478.5(ALPL):c.892G>A ; NM_000478.5(ALPL):c.212G>C ; NM_000478.5(ALPL):c.323C>T ; NM_000478.4(ALPL):c.346G>A ; NM_000478.5(ALPL):c.211C>T ; NM_000478.5(ALPL):c.814C>T ; NM_000478.5(ALPL):c.98C>T ; NM_000478.4(ALPL):c.571G>A ; NM_000478.6(ALPL):c.407G>A ; NM_000478.5(ALPL):c.1366G>A ; NM_000478.5(ALPL):c.1250A>G ; NM_000478.4(ALPL):c.1133A>T ; NM_000478.5(ALPL):c.1001G>A ; NM_000478.5(ALPL):c.620A>C ; NM_000478.5(ALPL):c.881A>C ; NM_000478.5(ALPL):c.535G>A ; NM_000478.5(ALPL):c.526G>A ; NM_000478.5(ALPL):c.1306T>C ; NM_000478.5(ALPL):c.892G>A ; NM_000478.5(ALPL):c.212G>C ; NM_000478.5(ALPL):c.323C>T ; NM_000478.4(ALPL):c.346G>A
ALPL	Prenatal benign hypophosphatasia	A very rare form of hypophosphatasia characterized by prenatal skeletal manifestations (limb shortening and bowing) that slowly resolve spontaneously and later may develop into the moderate childhood or adult forms of the disease.	PB-HPP may be identified on prenatal ultrasound examination. Patients manifest variable limb shortening and bowing and often have dimples overlaying long bones deformities. Postnatally, skeletal manifestations slowly resolve and patients eventually develop manifestations corresponding to other, non-lethal forms of HPP (either childhood-onset, adult hypophosphatasia or odontohypophosphatasia). Patients display progressive improvement of the skeletal anomalies and mineralization during the third trimester of pregnancy and after birth. Mothers of affected infants generally have biochemical evidence of hypophosphatasia but no clinical manifestations.	NM_000478.5(ALPL):c.211C>T ; NM_000478.5(ALPL):c.814C>T ; NM_000478.5(ALPL):c.98C>T ; NM_000478.4(ALPL):c.571G>A ; NM_000478.6(ALPL):c.407G>A ; NM_000478.5(ALPL):c.1366G>A ; NM_000478.5(ALPL):c.1250A>G ; NM_000478.4(ALPL):c.1133A>T ; NM_000478.5(ALPL):c.1001G>A ; NM_000478.5(ALPL):c.620A>C ; NM_000478.5(ALPL):c.881A>C ; NM_000478.5(ALPL):c.535G>A ; NM_000478.5(ALPL):c.526G>A ; NM_000478.5(ALPL):c.1306T>C ; NM_000478.5(ALPL):c.892G>A ; NM_000478.5(ALPL):c.212G>C ; NM_000478.5(ALPL):c.323C>T ; NM_000478.4(ALPL):c.346G>A ; NM_000478.5(ALPL):c.211C>T ; NM_000478.5(ALPL):c.814C>T ; NM_000478.5(ALPL):c.98C>T ; NM_000478.4(ALPL):c.571G>A ; NM_000478.6(ALPL):c.407G>A ; NM_000478.5(ALPL):c.1366G>A ; NM_000478.5(ALPL):c.1250A>G ; NM_000478.4(ALPL):c.1133A>T ; NM_000478.5(ALPL):c.1001G>A ; NM_000478.5(ALPL):c.620A>C ; NM_000478.5(ALPL):c.881A>C ; NM_000478.5(ALPL):c.535G>A ; NM_000478.5(ALPL):c.526G>A ; NM_000478.5(ALPL):c.1306T>C ; NM_000478.5(ALPL):c.892G>A ; NM_000478.5(ALPL):c.212G>C ; NM_000478.5(ALPL):c.323C>T ; NM_000478.4(ALPL):c.346G>A

AMT	Atypical glycine encephalopathy	A rare form of glycine encephalopathy presenting disease onset or clinical manifestations that differ from neonatal or infantile glycine encephalopathy.	Symptoms are mostly non-specific and are not similar to the severe neurological symptoms observed in neonatal and infantile GE (see these terms). Some patients have milder disease with onset from late infancy to adulthood, while others have rapidly progressive severe disease often of late onset. It also includes patients with transient hyperglycinemia, whose symptoms in neonatal period resemble those of neonatal form. Manifestations include cognitive decline, behavioral disorders, ataxia, peripheral neuropathy and optic atrophy.	NM_000481.3(AMT):c.259-1G>C ; NM_000481.3(AMT):c.574C>T ; NM_000481.3(AMT):c.959G>A ; NM_000481.3(AMT):c.826G>C ; NM_000481.3(AMT):c.806G>A ; NM_000481.4:c.125A>G ; NM_000481.3(AMT):c.259-1G>C ; NM_000481.3(AMT):c.574C>T ; NM_000481.3(AMT):c.959G>A ; NM_000481.3(AMT):c.826G>C ; NM_000481.3(AMT):c.806G>A ; NM_000481.4:c.125A>G
AMT	Infantile glycine encephalopathy	Infantile glycine encephalopathy is a mild to severe form of glycine encephalopathy (GE; see this term), characterized by early hypotonia, developmental delay and seizures.	Patients present with infantile-onset seizures and variable psychomotor delay after initially normal development, and often have a relatively long history of hypotonia. Seizures of any type are found in less than half of patients and some develop choreoathetosis. Developmental delay mostly affects language and behavioral problems are sometimes found including temper tantrums, irritability, aggressiveness and rage. Attention deficit-hyperactivity disorder (AD-HD) is also sometimes found. Patients do not have lethargy or coma in the neonatal period, unlike those with neonatal GE. The course may be mild or severe (50% of patients in each case).	NM_000481.3(AMT):c.259-1G>C ; NM_000481.3(AMT):c.574C>T ; NM_000481.3(AMT):c.959G>A ; NM_000481.3(AMT):c.826G>C ; NM_000481.3(AMT):c.806G>A ; NM_000481.4:c.125A>G ; NM_000481.3(AMT):c.259-1G>C ; NM_000481.3(AMT):c.574C>T ; NM_000481.3(AMT):c.959G>A ; NM_000481.3(AMT):c.826G>C ; NM_000481.3(AMT):c.806G>A ; NM_000481.4:c.125A>G

AMT	Neonatal glycine encephalopathy	Neonatal glycine encephalopathy is a frequent, usually severe form of glycine encephalopathy (GE; see this term) characterized by coma, apnea, hypotonia, seizure and myoclonic jerks in the neonatal period, and subsequent developmental delay.	Patients develop disease manifestations within the first hours or days of life. Symptoms include progressive lethargy, hypotonia, myoclonic jerks leading to apnea. In the absence of intubation and ventilation, apnea may be fatal. With supportive measures, most patients regain spontaneous respiration and some show improvement in alertness over time. Subsequently, they have profound intellectual deficit and increasingly intractable seizures over the first year of life, which often require multiple anticonvulsants. In the vast majority of cases (85%), the course is severe, but some patients have a milder course and less severe clinical outcome. In severe cases, patients make little developmental progress and have limited interaction with their environment. Early spasticity, scoliosis and club feet have also been reported. In milder cases, developmental progress is considerably greater with patients learning to walk and interact, and seizures are generally easier to treat.	NM_000481.3(AMT):c.259-1G>C ; NM_000481.3(AMT):c.574C>T ; NM_000481.3(AMT):c.959G>A ; NM_000481.3(AMT):c.826G>C ; NM_000481.3(AMT):c.806G>A ; NM_000481.4:c.125A>G ; NM_000481.3(AMT):c.259-1G>C ; NM_000481.3(AMT):c.574C>T ; NM_000481.3(AMT):c.959G>A ; NM_000481.3(AMT):c.826G>C ; NM_000481.3(AMT):c.806G>A ; NM_000481.4:c.125A>G
AR	Complete androgen insensitivity syndrome	Complete androgen insensitivity syndrome (CAIS) is a form of androgen insensitivity syndrome (AIS; see this term), a disorder of sex development (DSD), characterized by the presence of female external genitalia in a 46,XY individual with normal testis development but undescended testes and unresponsiveness to age-appropriate levels of androgens.	The typical presentation is primary amenorrhea in an adolescent female. CAIS may also present in infancy or childhood with an inguinal hernia or labial swelling containing a testis. Breast development at puberty is normal, but pubic and axillary hair is absent or scanty. The external genitalia are normal female but internal female genitalia are absent. Adult patients are tall. Other presentations may be serendipitous from a mismatch in prenatal sexing (XY) and birth female phenotype, history of an inguinal hernia repair in an older sister, or development of a pelvic tumor in later adult life.	NM_000044.4(AR):c.2567G>A ; NM_000044.4(AR):c.2395C>G ; NM_000044.4(AR):c.1771A>T ; NM_000044.4(AR):c.2391G>A ; c.340C>T ; NM_000044.4(AR):c.2650A>T ; NM_000044.4(AR):c.2323C>T ; NM_000044.4(AR):c.2567G>A ; NM_000044.4(AR):c.2395C>G ; NM_000044.4(AR):c.1771A>T ; NM_000044.4(AR):c.2391G>A ; c.340C>T ; NM_000044.4(AR):c.2650A>T ; NM_000044.4(AR):c.2323C>T

AR	Kennedy disease	Kennedy's disease, also known as bulbospinal muscular atrophy (BSMA), is a rare X-linked recessive motor neuron disease characterized by proximal and bulbar muscle wasting.	Disease onset occurs between 30-60 years of age. Initial clinical manifestations include tremor, muscle cramps, muscle twitching, fatigue and slurred speech. With disease progression patients additionally develop weakness and wasting of the limb and bulbar muscles, manifesting as dysarthria, dysphonia, hanging jaw, tongue wasting, chewing difficulty and impaired mobility. Intellectual decline is minimal to none. In the terminal stages of the disease some patients may be unable to swallow or breathe. Non-neurological manifestations include gynecomastia, hypogonadism (leading to infertility and impotence) and in rare cases Dupuytren's contracture, or groin hernia.	NM_000044.4(AR):c.2567G>A ; NM_000044.4(AR):c.2395C>G ; NM_000044.4(AR):c.1771A>T ; NM_000044.4(AR):c.2391G>A ; c.340C>T ; NM_000044.4(AR):c.2650A>T ; NM_000044.4(AR):c.2323C>T ; NM_000044.4(AR):c.2567G>A ; NM_000044.4(AR):c.2395C>G ; NM_000044.4(AR):c.1771A>T ; NM_000044.4(AR):c.2391G>A ; c.340C>T ; NM_000044.4(AR):c.2650A>T ; NM_000044.4(AR):c.2323C>T
AR	Partial androgen insensitivity syndrome	A disorder of sex development (DSD) distinct from complete AIS (CAIS) characterized by the presence of abnormal genital development in a 46,XY individual with normal testis development and partial responsiveness to age-appropriate levels of androgens.	Patients have a highly variable genital appearance. The prototypic form of presentation is severe hypospadias, micropenis, and bifid scrotum in which the testes may or may not be descended. In the more severe form of PAIS, patients have female external genitalia with clitoromegaly, partial labial fusion and labial swellings comprising testes. A mild end of the spectrum, labeled MAIS (mild or minimal AIS), is a male with gynecomastia at puberty or an adult presenting with male factor infertility.	NM_000044.4(AR):c.2567G>A ; NM_000044.4(AR):c.2395C>G ; NM_000044.4(AR):c.1771A>T ; NM_000044.4(AR):c.2391G>A ; c.340C>T ; NM_000044.4(AR):c.2650A>T ; NM_000044.4(AR):c.2323C>T ; NM_000044.4(AR):c.2567G>A ; NM_000044.4(AR):c.2395C>G ; NM_000044.4(AR):c.1771A>T ; NM_000044.4(AR):c.2391G>A ; c.340C>T ; NM_000044.4(AR):c.2650A>T ; NM_000044.4(AR):c.2323C>T
AR	Posterior hypospadias	A rare, non-syndromic, congenital, urogenital tract malformation affecting males and characterized by penoscrotal, scrotal or perineal displacement of the urethral meatus, and commonly associated with curvation of the penis. The scrotum might appear bifid in severe cases, and the boy can also have a micropenis.	The consequences of hypospadias, apart from the appearance, include spraying of the urinary stream, inability to urinate in standing position, and later in life curvature, unless corrected, leads to difficulties during intercourse. Fertility problems and decreased satisfaction with genital appearance are more common. Severe hypospadias and concomitant undescended testis, is regarded as a disorder of sex development (DSD) and should be referred to special multidisciplinary teams for molecular and hormonal evaluation.	NM_000044.4(AR):c.2567G>A ; NM_000044.4(AR):c.2395C>G ; NM_000044.4(AR):c.1771A>T ; NM_000044.4(AR):c.2391G>A ; c.340C>T ; NM_000044.4(AR):c.2650A>T ; NM_000044.4(AR):c.2323C>T ; NM_000044.4(AR):c.2567G>A ; NM_000044.4(AR):c.2395C>G ; NM_000044.4(AR):c.1771A>T ; NM_000044.4(AR):c.2391G>A ; c.340C>T ; NM_000044.4(AR):c.2650A>T ; NM_000044.4(AR):c.2323C>T

ARG1	Argininemia	A rare autosomal recessive amino acid metabolism disorder characterized clinically by variable degrees of hyperammonemia, developing from about 3 years of age, and leading to progressive loss of developmental milestones and spasticity in the absence of treatment.	Arginase deficiency is an autosomal recessive inborn error of metabolism caused by a defect in the final step in the urea cycle, the hydrolysis of arginine to urea and ornithine.	NM_000045.3(ARG1):c.869C>G ; NM_000045.3(ARG1):c.32T>C ; NM_000045.3(ARG1):c.703G>C ; NM_000045.3(ARG1):c.365G>A ; NM_000045.3(ARG1):c.413G>T ; NM_000045.3(ARG1):c.61C>T ; NM_000045.3(ARG1):c.871C>T ; NM_000045.3(ARG1):c.869C>G ; NM_000045.3(ARG1):c.32T>C ; NM_000045.3(ARG1):c.703G>C ; NM_000045.3(ARG1):c.365G>A ; NM_000045.3(ARG1):c.413G>T ; NM_000045.3(ARG1):c.61C>T ; NM_000045.3(ARG1):c.871C>T
ARSA	Metachromatic leukodystrophy, adult form	The metachromatic leukodystrophies comprise several allelic disorders.Â 7 forms are recognized: 5 allelic forms of MLD: late infantile, juvenile, and adult forms, partial cerebroside sulfate deficiency, and pseudoarylsulfatase A deficiency; and 2 nonallelic forms: metachromatic leukodystrophy due to saposin B deficiency and multiple sulfatase deficiency or juvenile sulfatidosis, a disorder that combines features of a mucopolysaccharidosis with those of metachromatic leukodystrophy.	A subtype of Metachromatic leukodystrophy characterized by progressive psychomotor regression with an insidious onset after the age of 16 years, most often beginning with intellectual and behavioral changes, such as memory deficits or emotional instability. The clinical picture is dominated by gradual cognitive, later also motor, decline, taking a protracted course with periods of waxing and waning. Decerebration and death occur within decades after disease onset.	NM_000487.5(ARSA):c.1108-2A>G ; NM_000487.5(ARSA):c.991G>T ; NM_000487.5(ARSA):c.763G>A ; NM_000487.5(ARSA):c.542T>G ; NM_000487.5(ARSA):c.979G>A ; NM_000487.5(ARSA):c.302G>A ; NM_000487.5(ARSA):c.257G>A ; NM_000487.5(ARSA):c.293C>T ; NM_000487.5(ARSA):c.1125_1126delCT ; NM_000487.5(ARSA):c.346C>T ; NM_000487.5(ARSA):c.1210+1G>A ; c.1401_1411del ; NM_000487.5(ARSA):c.883G>A ; NM_000487.5(ARSA):c.465+1G>A ; NM_000487.5(ARSA):c.739G>A ; c.854+1G>A ; NM_000487.5(ARSA):c.827C>T ; NM_000487.5(ARSA):c.937C>T ; NM_000487.5(ARSA):c.583delT ; NM_000487.5(ARSA):c.737G>A ; NM_000487.5(ARSA):c.1150G>A ; NM_000487.5(ARSA):c.542dup ; NM_000487.5(ARSA):c.1408_1418del11 ; NM_000487.5(ARSA):c.641C>T ; NM_000487.5(ARSA):c.938G>A ; NM_000487.5(ARSA):c.195delC ; c.1241del ; NM_000487.5(ARSA):c.899T>C ; c.582del ; NM_000487.5(ARSA):c.1283C>T ; NM_000487.5(ARSA):c.869G>A ; NM_000487.5(ARSA):c.986C>T ; NM_000487.5(ARSA):c.34delG ; NM_000487.5(ARSA):c.1232C>T ; NM_000487.5(ARSA):c.1108-2A>G ; NM_000487.5(ARSA):c.991G>T ; NM_000487.5(ARSA):c.763G>A ; NM_000487.5(ARSA):c.542T>G ; NM_000487.5(ARSA):c.979G>A ; NM_000487.5(ARSA):c.302G>A ; NM_000487.5(ARSA):c.257G>A ; NM_000487.5(ARSA):c.293C>T ; NM_000487.5(ARSA):c.1125_1126delCT ; NM_000487.5(ARSA):c.346C>T ; NM_000487.5(ARSA):c.1210+1G>A ; c.1401_1411del ; NM_000487.5(ARSA):c.883G>A ; NM_000487.5(ARSA):c.465+1G>A ; NM_000487.5(ARSA):c.739G>A ; c.854+1G>A ; NM_000487.5(ARSA):c.827C>T ; NM_000487.5(ARSA):c.937C>T ; NM_000487.5(ARSA):c.583delT ; NM_000487.5(ARSA):c.737G>A ; NM_000487.5(ARSA):c.1150G>A ; NM_000487.5(ARSA):c.542dup ; NM_000487.5(ARSA):c.1408_1418del11 ; NM_000487.5(ARSA):c.641C>T ; NM_000487.5(ARSA):c.938G>A ; NM_000487.5(ARSA):c.195delC ; c.1241del ; NM_000487.5(ARSA):c.899T>C ; c.582del ; NM_000487.5(ARSA):c.1283C>T ; NM_000487.5(ARSA):c.869G>A ; NM_000487.5(ARSA):c.986C>T ; NM_000487.5(ARSA):c.34delG ; NM_000487.5(ARSA):c.1232C>T

ARSA	Metachromatic leukodystrophy, juvenile form	The metachromatic leukodystrophies comprise several allelic disorders.Â 7 forms are recognized: 5 allelic forms of MLD: late infantile, juvenile, and adult forms, partial cerebroside sulfate deficiency, and pseudoarylsulfatase A deficiency; and 2 nonallelic forms: metachromatic leukodystrophy due to saposin B deficiency and multiple sulfatase deficiency or juvenile sulfatidosis, a disorder that combines features of a mucopolysaccharidosis with those of metachromatic leukodystrophy.	A subtype of Metachromatic leukodystrophy characterized by progressive psychomotor regression with an onset between 30 months and 16 years of age, often beginning with behavioral abnormalities or deterioration of school performance. Further manifestations are ataxia, gait disturbances, reduced deep tendon reflexes, spasticity, seizures, paralysis, dementia, and loss of speech, vision, and hearing, eventually resulting in complete loss of motor and cognitive skills, and decerebration. The rate of deterioration is variable with possible survival up to the third decade of life.	NM_000487.5(ARSA):c.1108-2A>G ; NM_000487.5(ARSA):c.991G>T ; NM_000487.5(ARSA):c.763G>A ; NM_000487.5(ARSA):c.542T>G ; NM_000487.5(ARSA):c.979G>A ; NM_000487.5(ARSA):c.302G>A ; NM_000487.5(ARSA):c.257G>A ; NM_000487.5(ARSA):c.293C>T ; NM_000487.5(ARSA):c.1125_1126delCT ; NM_000487.5(ARSA):c.346C>T ; NM_000487.5(ARSA):c.1210+1G>A ; c.1401_1411del ; NM_000487.5(ARSA):c.883G>A ; NM_000487.5(ARSA):c.465+1G>A ; NM_000487.5(ARSA):c.739G>A ; c.854+1G>A ; NM_000487.5(ARSA):c.827C>T ; NM_000487.5(ARSA):c.937C>T ; NM_000487.5(ARSA):c.583delT ; NM_000487.5(ARSA):c.737G>A ; NM_000487.5(ARSA):c.1150G>A ; NM_000487.5(ARSA):c.542dup ; NM_000487.5(ARSA):c.1408_1418del11 ; NM_000487.5(ARSA):c.641C>T ; NM_000487.5(ARSA):c.938G>A ; NM_000487.5(ARSA):c.195delC ; c.1241del ; NM_000487.5(ARSA):c.899T>C ; c.582del ; NM_000487.5(ARSA):c.1283C>T ; NM_000487.5(ARSA):c.869G>A ; NM_000487.5(ARSA):c.986C>T ; NM_000487.5(ARSA):c.34delG ; NM_000487.5(ARSA):c.1232C>T ; NM_000487.5(ARSA):c.1108-2A>G ; NM_000487.5(ARSA):c.991G>T ; NM_000487.5(ARSA):c.763G>A ; NM_000487.5(ARSA):c.542T>G ; NM_000487.5(ARSA):c.979G>A ; NM_000487.5(ARSA):c.302G>A ; NM_000487.5(ARSA):c.257G>A ; NM_000487.5(ARSA):c.293C>T ; NM_000487.5(ARSA):c.1125_1126delCT ; NM_000487.5(ARSA):c.346C>T ; NM_000487.5(ARSA):c.1210+1G>A ; c.1401_1411del ; NM_000487.5(ARSA):c.883G>A ; NM_000487.5(ARSA):c.465+1G>A ; NM_000487.5(ARSA):c.739G>A ; c.854+1G>A ; NM_000487.5(ARSA):c.827C>T ; NM_000487.5(ARSA):c.937C>T ; NM_000487.5(ARSA):c.583delT ; NM_000487.5(ARSA):c.737G>A ; NM_000487.5(ARSA):c.1150G>A ; NM_000487.5(ARSA):c.542dup ; NM_000487.5(ARSA):c.1408_1418del11 ; NM_000487.5(ARSA):c.641C>T ; NM_000487.5(ARSA):c.938G>A ; NM_000487.5(ARSA):c.195delC ; c.1241del ; NM_000487.5(ARSA):c.899T>C ; c.582del ; NM_000487.5(ARSA):c.1283C>T ; NM_000487.5(ARSA):c.869G>A ; NM_000487.5(ARSA):c.986C>T ; NM_000487.5(ARSA):c.34delG ; NM_000487.5(ARSA):c.1232C>T
ARSA	Metachromatic leukodystrophy, late infantile form	The metachromatic leukodystrophies comprise several allelic disorders.Â 7 forms are recognized: 5 allelic forms of MLD: late infantile, juvenile, and adult forms, partial cerebroside sulfate deficiency, and pseudoarylsulfatase A deficiency; and 2 nonallelic forms: metachromatic leukodystrophy due to saposin B deficiency and multiple sulfatase deficiency or juvenile sulfatidosis, a disorder that combines features of a mucopolysaccharidosis with those of metachromatic leukodystrophy.	A subtype of Metachromatic leukodystrophy characterized by rapidly progressive psychomotor regression with an onset before 30 months of age after a period of apparently normal development. Manifestations developing during the course of the disease are impaired feeding and swallowing due to pseudobulbar palsies, seizures, painful spasms, muscle weakness, ataxia, paralysis, dementia, and loss of speech, vision, and hearing, quickly resulting in complete loss of motor and cognitive skills, and decerebration. Death occurs within the first decade of life.	NM_000487.5(ARSA):c.1108-2A>G ; NM_000487.5(ARSA):c.991G>T ; NM_000487.5(ARSA):c.763G>A ; NM_000487.5(ARSA):c.542T>G ; NM_000487.5(ARSA):c.979G>A ; NM_000487.5(ARSA):c.302G>A ; NM_000487.5(ARSA):c.257G>A ; NM_000487.5(ARSA):c.293C>T ; NM_000487.5(ARSA):c.1125_1126delCT ; NM_000487.5(ARSA):c.346C>T ; NM_000487.5(ARSA):c.1210+1G>A ; c.1401_1411del ; NM_000487.5(ARSA):c.883G>A ; NM_000487.5(ARSA):c.465+1G>A ; NM_000487.5(ARSA):c.739G>A ; c.854+1G>A ; NM_000487.5(ARSA):c.827C>T ; NM_000487.5(ARSA):c.937C>T ; NM_000487.5(ARSA):c.583delT ; NM_000487.5(ARSA):c.737G>A ; NM_000487.5(ARSA):c.1150G>A ; NM_000487.5(ARSA):c.542dup ; NM_000487.5(ARSA):c.1408_1418del11 ; NM_000487.5(ARSA):c.641C>T ; NM_000487.5(ARSA):c.938G>A ; NM_000487.5(ARSA):c.195delC ; c.1241del ; NM_000487.5(ARSA):c.899T>C ; c.582del ; NM_000487.5(ARSA):c.1283C>T ; NM_000487.5(ARSA):c.869G>A ; NM_000487.5(ARSA):c.986C>T ; NM_000487.5(ARSA):c.34delG ; NM_000487.5(ARSA):c.1232C>T

ARSA	NON RARE IN EUROPE: Pseudoarylsulfatase A deficiency	The metachromatic leukodystrophies comprise several allelic disorders.Â Kihara (1982)Â recognized 5 allelic forms of MLD: late infantile, juvenile, and adult forms, partial cerebroside sulfate deficiency, and pseudoarylsulfatase A deficiency; and 2 nonallelic forms: metachromatic leukodystrophy due to saposin B deficiency and multiple sulfatase deficiency or juvenile sulfatidosis, a disorder that combines features of a mucopolysaccharidosis with those of metachromatic leukodystrophy.	Pseudoarylsulfatase A deficiency refers to a condition of apparent ARSA enzyme deficiency in persons without neurologic abnormalities.Â Dubois et al. (1977)Â described very low arylsulfatase A and cerebroside sulfatase activities in leukocytes of healthy members of a metachromatic leukodystrophy family.Â Langenbeck et al. (1977)Â proposed a one locus, multiple allele hypothesis to explain the peculiar findings in that kindred	NM_000487.5(ARSA):c.1108-2A>G ; NM_000487.5(ARSA):c.991G>T ; NM_000487.5(ARSA):c.763G>A ; NM_000487.5(ARSA):c.542T>G ; NM_000487.5(ARSA):c.979G>A ; NM_000487.5(ARSA):c.302G>A ; NM_000487.5(ARSA):c.257G>A ; NM_000487.5(ARSA):c.293C>T ; NM_000487.5(ARSA):c.1125_1126delCT ; NM_000487.5(ARSA):c.346C>T ; NM_000487.5(ARSA):c.1210+1G>A ; c.1401_1411del ; NM_000487.5(ARSA):c.883G>A ; NM_000487.5(ARSA):c.465+1G>A ; NM_000487.5(ARSA):c.739G>A ; c.854+1G>A ; NM_000487.5(ARSA):c.827C>T ; NM_000487.5(ARSA):c.937C>T ; NM_000487.5(ARSA):c.583delT ; NM_000487.5(ARSA):c.737G>A ; NM_000487.5(ARSA):c.1150G>A ; NM_000487.5(ARSA):c.542dup ; NM_000487.5(ARSA):c.1408_1418del11 ; NM_000487.5(ARSA):c.641C>T ; NM_000487.5(ARSA):c.938G>A ; NM_000487.5(ARSA):c.195delC ; c.1241del ; NM_000487.5(ARSA):c.899T>C ; c.582del ; NM_000487.5(ARSA):c.1283C>T ; NM_000487.5(ARSA):c.869G>A ; NM_000487.5(ARSA):c.986C>T ; NM_000487.5(ARSA):c.34delG ; NM_000487.5(ARSA):c.1232C>T ; NM_000487.5(ARSA):c.1108-2A>G ; NM_000487.5(ARSA):c.991G>T ; NM_000487.5(ARSA):c.763G>A ; NM_000487.5(ARSA):c.542T>G ; NM_000487.5(ARSA):c.979G>A ; NM_000487.5(ARSA):c.302G>A ; NM_000487.5(ARSA):c.257G>A ; NM_000487.5(ARSA):c.293C>T ; NM_000487.5(ARSA):c.1125_1126delCT ; NM_000487.5(ARSA):c.346C>T ; NM_000487.5(ARSA):c.1210+1G>A ; c.1401_1411del ; NM_000487.5(ARSA):c.883G>A ; NM_000487.5(ARSA):c.465+1G>A ; NM_000487.5(ARSA):c.739G>A ; c.854+1G>A ; NM_000487.5(ARSA):c.827C>T ; NM_000487.5(ARSA):c.937C>T ; NM_000487.5(ARSA):c.583delT ; NM_000487.5(ARSA):c.737G>A ; NM_000487.5(ARSA):c.1150G>A ; NM_000487.5(ARSA):c.542dup ; NM_000487.5(ARSA):c.1408_1418del11 ; NM_000487.5(ARSA):c.641C>T ; NM_000487.5(ARSA):c.938G>A ; NM_000487.5(ARSA):c.195delC ; c.1241del ; NM_000487.5(ARSA):c.899T>C ; c.582del ; NM_000487.5(ARSA):c.1283C>T ; NM_000487.5(ARSA):c.869G>A ; NM_000487.5(ARSA):c.986C>T ; NM_000487.5(ARSA):c.34delG ; NM_000487.5(ARSA):c.1232C>T

ARSB	Mucopolysaccharidosis type 6, rapidly progressing	Mucopolysaccharidosis type 6 (MPS 6) is a lysosomal storage disease with progressive multisystem involvement, associated with a deficiency of arylsulfatase B (ASB) leading to the accumulation of dermatan sulfate.	The disorder shows a wide spectrum of symptoms from slowly to rapidly progressing forms. The characteristic skeletal dysplasia includes short stature, dysostosis multiplex and degenerative joint disease. Rapidly progressing forms may have onset from birth, elevated urinary glycosaminoglycans (GAG, generally >100 microgram/mg creatinine), severe dysostosis multiplex, short stature, and death before the 2nd or 3rd decades. A more slowly progressing form has been described as having later onset, mildly elevated glycosaminoglycans (generally <100 microgram/mg creatinine), mild dysostosis multiplex, with death in the 4th or 5th decades. Other clinical findings may include cardiac valve disease, reduced pulmonary function, hepatosplenomegaly, sinusitis, otitis media, hearing loss, sleep apnea, corneal clouding, carpal tunnel disease, and inguinal or umbilical hernia. Although intellectual deficit is generally absent in MPS 6, central nervous system findings may include cervical cord compression caused by cervical spinal instability, meningeal thickening and/or bony stenosis, communicating hydrocephalus, optic nerve atrophy and blindness.	c.921del ; NM_000046.4(ARSB):c.629A>G ; NM_000046.5(ARSB):c.979C>T ; NC_000005.10:g.78780563dup ; NM_000046.5(ARSB):c.427del ; NM_000046.4(ARSB):c.753C>G ; NM_000046.4(ARSB):c.944G>A ; NM_000046.4(ARSB):c.589C>T ; NM_000046.4(ARSB):c.937C>G ; NM_000046.4(ARSB):c.1143-1G>C ; NM_000046.4(ARSB):c.1161dup ; NM_000046.4(ARSB):c.349T>C ; NM_000046.4(ARSB):c.971G>T ; NM_000046.4(ARSB):c.1366C>T ; NM_000046.4(ARSB):c.1143-8T>G ; NM_000046.4(ARSB):c.571C>T ; c.921del ; NM_000046.4(ARSB):c.629A>G ; NM_000046.5(ARSB):c.979C>T ; NC_000005.10:g.78780563dup ; NM_000046.5(ARSB):c.427del ; NM_000046.4(ARSB):c.753C>G ; NM_000046.4(ARSB):c.944G>A ; NM_000046.4(ARSB):c.589C>T ; NM_000046.4(ARSB):c.937C>G ; NM_000046.4(ARSB):c.1143-1G>C ; NM_000046.4(ARSB):c.1161dup ; NM_000046.4(ARSB):c.349T>C ; NM_000046.4(ARSB):c.971G>T ; NM_000046.4(ARSB):c.1366C>T ; NM_000046.4(ARSB):c.1143-8T>G ; NM_000046.4(ARSB):c.571C>T

ARSB	Mucopolysaccharidosis type 6, slowly progressing	Mucopolysaccharidosis type 6 (MPS 6) is a lysosomal storage disease with progressive multisystem involvement, associated with a deficiency of arylsulfatase B (ASB) leading to the accumulation of dermatan sulfate.	The disorder shows a wide spectrum of symptoms from slowly to rapidly progressing forms. The characteristic skeletal dysplasia includes short stature, dysostosis multiplex and degenerative joint disease. Rapidly progressing forms may have onset from birth, elevated urinary glycosaminoglycans (GAG, generally >100 microgram/mg creatinine), severe dysostosis multiplex, short stature, and death before the 2nd or 3rd decades. A more slowly progressing form has been described as having later onset, mildly elevated glycosaminoglycans (generally <100 microgram/mg creatinine), mild dysostosis multiplex, with death in the 4th or 5th decades. Other clinical findings may include cardiac valve disease, reduced pulmonary function, hepatosplenomegaly, sinusitis, otitis media, hearing loss, sleep apnea, corneal clouding, carpal tunnel disease, and inguinal or umbilical hernia. Although intellectual deficit is generally absent in MPS 6, central nervous system findings may include cervical cord compression caused by cervical spinal instability, meningeal thickening and/or bony stenosis, communicating hydrocephalus, optic nerve atrophy and blindness.	c.921del ; NM_000046.4(ARSB):c.629A>G ; NM_000046.5(ARSB):c.979C>T ; NC_000005.10:g.78780563dup ; NM_000046.5(ARSB):c.427del ; NM_000046.4(ARSB):c.753C>G ; NM_000046.4(ARSB):c.944G>A ; NM_000046.4(ARSB):c.589C>T ; NM_000046.4(ARSB):c.937C>G ; NM_000046.4(ARSB):c.1143-1G>C ; NM_000046.4(ARSB):c.1161dup ; NM_000046.4(ARSB):c.349T>C ; NM_000046.4(ARSB):c.971G>T ; NM_000046.4(ARSB):c.1366C>T ; NM_000046.4(ARSB):c.1143-8T>G ; NM_000046.4(ARSB):c.571C>T ; c.921del ; NM_000046.4(ARSB):c.629A>G ; NM_000046.5(ARSB):c.979C>T ; NC_000005.10:g.78780563dup ; NM_000046.5(ARSB):c.427del ; NM_000046.4(ARSB):c.753C>G ; NM_000046.4(ARSB):c.944G>A ; NM_000046.4(ARSB):c.589C>T ; NM_000046.4(ARSB):c.937C>G ; NM_000046.4(ARSB):c.1143-1G>C ; NM_000046.4(ARSB):c.1161dup ; NM_000046.4(ARSB):c.349T>C ; NM_000046.4(ARSB):c.971G>T ; NM_000046.4(ARSB):c.1366C>T ; NM_000046.4(ARSB):c.1143-8T>G ; NM_000046.4(ARSB):c.571C>T

ASL	Argininosuccinic aciduria	A rare, genetic disorder of urea cycle metabolism typically characterized by either a severe, neonatal-onset form that manifests with hyperammonemia accompanied with vomiting, hypothermia, lethargy and poor feeding in the first few days of life, or late-onset forms that manifest with stress- or infection-induced episodic hyperammonemia or, in some, behavioral abnormalities and/or learning disabilities, or chronic liver disease. Patients often manifest liver dysfunction.	ASA can have a variable clinical picture with either a neonatal-onset or a late-onset (at any age outside the newborn period). Neonates with severe neonatal-onset ASA usually appear normal during the first 24-48 hours after birth but within a few days present with severe hyperammonemia manifesting with lethargy, somnolence, refusal to feed, vomiting, tachypnea and respiratory alkalosis. If untreated, worsening lethargy, seizures, coma and death may occur. Late-onset ASA is usually triggered by an acute infection, stress or after high protein intake. A presentation of late-onset cognitive impairment or learning disabilities in the absence of hyperammonemic episodes has also been reported. Some patients can be clinically asymptomatic despite showing clear biochemical signs of the disease. Long-term complications associated with both forms of ASA include chronic hepatomegaly, liver dysfunction (fibrosis or cirrhosis), neurocognitive deficits (i.e. cognitive impairment, seizures, and developmental delay), brittle hair (i.e. trichorrhexis nodosa), hypokalemia and arterial hypertension.	NC_000007.14:g.66092883C>T ; NM_000048.3(ASL):c.1135C>T ; c.1369dup ; NM_001024943.1(ASL):c.337C>T ; NM_000048.3(ASL):c.544C>T ; NM_000048.3(ASL):c.1045_1057delGTCATCTCTACGC ; c.1144-2A>G ; NM_000048.3(ASL):c.1060C>T ; NM_001024943.2:c.346C>T ; NM_001024943.1(ASL):c.602+1G>A ; NM_000048.3(ASL):c.857A>G ; NM_000048.3(ASL):c.446+1G>A ; NM_000048.3(ASL):c.578G>A ; NM_001024943.1(ASL):c.1255_1256delCT ; c.525-2A>T ; NM_000048.3(ASL):c.532G>A ; NM_000048.3(ASL):c.539T>G ; NM_000048.3(ASL):c.35G>A ; NM_001024943.1(ASL):c.1153C>T ; NC_000007.14:g.66092883C>T ; NM_000048.3(ASL):c.1135C>T ; c.1369dup ; NM_001024943.1(ASL):c.337C>T ; NM_000048.3(ASL):c.544C>T ; NM_000048.3(ASL):c.1045_1057delGTCATCTCTACGC ; c.1144-2A>G ; NM_000048.3(ASL):c.1060C>T ; NM_001024943.2:c.346C>T ; NM_001024943.1(ASL):c.602+1G>A ; NM_000048.3(ASL):c.857A>G ; NM_000048.3(ASL):c.446+1G>A ; NM_000048.3(ASL):c.578G>A ; NM_001024943.1(ASL):c.1255_1256delCT ; c.525-2A>T ; NM_000048.3(ASL):c.532G>A ; NM_000048.3(ASL):c.539T>G ; NM_000048.3(ASL):c.35G>A ; NM_001024943.1(ASL):c.1153C>T
ASPA	Mild Canavan disease	Mild Canavan disease (CD) is a neurodegenerative disorder characterized by mild speech delay or motor development.	Mild CD usually presents in childhood with mild developmental delay or problems with speech or motor development. Head circumference is usually normal. Retinitis pigmentosa (see this term) may be present. .	NM_000049.4:c.854A>C ; NM_000049.4:c.693C>A ; NM_001128085.1(ASPA):c.433-2A>G ; NM_001128085.1(ASPA):c.654C>A ; NM_000049.2(ASPA):c.914C>A ; NM_000049.2(ASPA):c.212G>A ; NM_000049.4:c.854A>C ; NM_000049.4:c.693C>A ; NM_001128085.1(ASPA):c.433-2A>G ; NM_001128085.1(ASPA):c.654C>A ; NM_000049.2(ASPA):c.914C>A ; NM_000049.2(ASPA):c.212G>A

ASPA	Severe Canavan disease	Severe Canavan disease (CD) is a rapidly progressing neurodegenerative disorder characterized by leukodystrophy with macrocephaly, severe developmental delay and hypotonia.	Onset of severe CD is in infancy. Patients have hypotonia, head lag, and macrocephaly. Developmental delay is most frequently noticed between the 3rd and 5th months of life: patients fail to achieve independent sitting, ambulation and speech. The head circumference increases after the age of 6 months and is usually above the 90th percentile by one year of age. With age, hypotonia progresses to spasticity, seizures may occur and optic atrophy is apparent. Children are often irritable and exhibit sleep disturbance. Gastro-esophageal reflux leads to feeding difficulties, requiring nasogastric feeding or permanent feeding gastrostomy.	NM_000049.4:c.854A>C ; NM_000049.4:c.693C>A ; NM_001128085.1(ASPA):c.433-2A>G ; NM_001128085.1(ASPA):c.654C>A ; NM_000049.2(ASPA):c.914C>A ; NM_000049.2(ASPA):c.212G>A ; NM_000049.4:c.854A>C ; NM_000049.4:c.693C>A ; NM_001128085.1(ASPA):c.433-2A>G ; NM_001128085.1(ASPA):c.654C>A ; NM_000049.2(ASPA):c.914C>A ; NM_000049.2(ASPA):c.212G>A
ASS1	Acute neonatal citrullinemia type I	A severe form of citrullinemia type 1 characterized biologically by hyperammonemia and clinically by progressive lethargy, poor feeding and vomiting, seizures and possible loss of consciousness, within one to a few days of birth, with variable signs of increased intracranial pressure. The condition can lead to significant neurologic deficits.		NM_000050.4(ASS1):c.1087C>T ; NM_000050.4(ASS1):c.421-2A>G ; NM_000050.4(ASS1):c.1194-1G>C ; NM_000050.4(ASS1):c.257G>A ; NM_000050.4(ASS1):c.814C>T ; NM_000050.4(ASS1):c.794G>A ; NM_000050.4(ASS1):c.40G>A ; NM_000050.4(ASS1):c.1085G>T ; NM_000050.4(ASS1):c.535T>C ; NM_000050.4(ASS1):c.787G>A ; NM_000050.4(ASS1):c.1168G>A ; NM_000050.4(ASS1):c.910C>T ; NM_000050.4(ASS1):c.970+5G>A ; NM_000050.4(ASS1):c.836G>A ; NM_000050.4(ASS1):c.349G>A ; NM_000050.4(ASS1):c.793C>T ; NM_000050.4(ASS1):c.496-2A>G ; NM_000050.4(ASS1):c.835C>T ; NM_000050.4(ASS1):c.571G>A ; NM_000050.4(ASS1):c.970G>A ; NM_000050.4(ASS1):c.256C>T ; NM_000050.4(ASS1):c.539G>A ; NM_000050.4(ASS1):c.1087C>T ; NM_000050.4(ASS1):c.421-2A>G ; NM_000050.4(ASS1):c.1194-1G>C ; NM_000050.4(ASS1):c.257G>A ; NM_000050.4(ASS1):c.814C>T ; NM_000050.4(ASS1):c.794G>A ; NM_000050.4(ASS1):c.40G>A ; NM_000050.4(ASS1):c.1085G>T ; NM_000050.4(ASS1):c.535T>C ; NM_000050.4(ASS1):c.787G>A ; NM_000050.4(ASS1):c.1168G>A ; NM_000050.4(ASS1):c.910C>T ; NM_000050.4(ASS1):c.970+5G>A ; NM_000050.4(ASS1):c.836G>A ; NM_000050.4(ASS1):c.349G>A ; NM_000050.4(ASS1):c.793C>T ; NM_000050.4(ASS1):c.496-2A>G ; NM_000050.4(ASS1):c.835C>T ; NM_000050.4(ASS1):c.571G>A ; NM_000050.4(ASS1):c.970G>A ; NM_000050.4(ASS1):c.256C>T ; NM_000050.4(ASS1):c.539G>A

ASS1	Adult-onset citrullinemia type I	A form of citrullinemia type I characterized clinically by adult onset of symptoms including variable hyperammonemia and less striking neurological findings which may include intense headache, scotomas, migraine-like episodes, ataxia, slurred speech, lethargy and drowsiness. Serious increased intracranial pressure may occur.		NM_000050.4(ASS1):c.1087C>T ; NM_000050.4(ASS1):c.421-2A>G ; NM_000050.4(ASS1):c.1194-1G>C ; NM_000050.4(ASS1):c.257G>A ; NM_000050.4(ASS1):c.814C>T ; NM_000050.4(ASS1):c.794G>A ; NM_000050.4(ASS1):c.40G>A ; NM_000050.4(ASS1):c.1085G>T ; NM_000050.4(ASS1):c.535T>C ; NM_000050.4(ASS1):c.787G>A ; NM_000050.4(ASS1):c.1168G>A ; NM_000050.4(ASS1):c.910C>T ; NM_000050.4(ASS1):c.970+5G>A ; NM_000050.4(ASS1):c.836G>A ; NM_000050.4(ASS1):c.349G>A ; NM_000050.4(ASS1):c.793C>T ; NM_000050.4(ASS1):c.496-2A>G ; NM_000050.4(ASS1):c.835C>T ; NM_000050.4(ASS1):c.571G>A ; NM_000050.4(ASS1):c.970G>A ; NM_000050.4(ASS1):c.256C>T ; NM_000050.4(ASS1):c.539G>A ; NM_000050.4(ASS1):c.1087C>T ; NM_000050.4(ASS1):c.421-2A>G ; NM_000050.4(ASS1):c.1194-1G>C ; NM_000050.4(ASS1):c.257G>A ; NM_000050.4(ASS1):c.814C>T ; NM_000050.4(ASS1):c.794G>A ; NM_000050.4(ASS1):c.40G>A ; NM_000050.4(ASS1):c.1085G>T ; NM_000050.4(ASS1):c.535T>C ; NM_000050.4(ASS1):c.787G>A ; NM_000050.4(ASS1):c.1168G>A ; NM_000050.4(ASS1):c.910C>T ; NM_000050.4(ASS1):c.970+5G>A ; NM_000050.4(ASS1):c.836G>A ; NM_000050.4(ASS1):c.349G>A ; NM_000050.4(ASS1):c.793C>T ; NM_000050.4(ASS1):c.496-2A>G ; NM_000050.4(ASS1):c.835C>T ; NM_000050.4(ASS1):c.571G>A ; NM_000050.4(ASS1):c.970G>A ; NM_000050.4(ASS1):c.256C>T ; NM_000050.4(ASS1):c.539G>A
ATP7A	Menkes disease	A rare congenital disorder of copper metabolism with severe multisystemic manifestations that are primarily characterized by progressive neurodegeneration and marked connective tissue anomalies. A pathognomonic feature is the typical sparse, abnormal steely hair.	Menkes disease (MD) manifests in the neonatal period. Most patients are born at term with appropriate birth measurements. Cephalohematomas and spontaneous fractures are occasionally observed at birth. In the early neonatal period, patients may present with prolonged jaundice, hypothermia, hypoglycemia and feeding difficulties. Pectus excavatum and umbilical and inguinal hernias have also been reported. Unusual sparse and dull scalp hair is often the initial observation at the age of 1-2 months. Characteristically, the hair appears hypopigmented/depigmented, resembles steel wool and is friable, especially in the areas of the scalp subjected to friction. Additional symptoms are failure to thrive, poor eating, vomiting, and diarrhea. The appearance of pale skin, frontal or occipital bossing, micrognathia and pudgy cheeks may be observed. Patients develop gradual motor dysfunction and seizures. Muscular hypotonia in early life is replaced later-on by spasticity and weakness of the extremities. The clinical course is usually severe. Variable forms exist with occipital horn syndrome (OHS) being the mildest recognized form, which further presents with prominent bony exostoses and bladder diverticula.	NM_000052.6(ATP7A):c.3915_3921delCTCCCCA ; c.3257_3258del ; NM_000052.6(ATP7A):c.1974_1977dupGTTT ; NM_000052.6(ATP7A):c.1639C>T ; c.3294+2T>G ; NM_000052.6(ATP7A):c.3911A>G ; NM_000052.6(ATP7A):c.2938C>T ; NM_000052.6(ATP7A):c.3915_3921delCTCCCCA ; c.3257_3258del ; NM_000052.6(ATP7A):c.1974_1977dupGTTT ; NM_000052.6(ATP7A):c.1639C>T ; c.3294+2T>G ; NM_000052.6(ATP7A):c.3911A>G ; NM_000052.6(ATP7A):c.2938C>T

ATP7A	Occipital horn syndrome	A rare congenital disorder of copper metabolism that is principally characterized by bony exostoses (including the pathognomonic occipital horns), and connective tissue manifestations with cutis laxa and bladder diverticula. Central nervous system involvement is variable.	Age of onset ranges from infancy to childhood. Observations at birth may include cephalhematoma (12% of cases), loose and wrinkled skin, and umbilical or inguinal hernias. About one third of all patients primarily present with central nervous system involvement (hypotonia, developmental delay and/or seizures). Initial clinical presentation may occur later with bladder diverticula or skeletal manifestations. Bladder diverticula affects the majority of patients (>80%) and may manifest through recurrent urinary tract infections or pollakisuria. The most typical skeletal manifestation (present in 96% of all patients) is an exostosis on the occiput at the insertion of the trapezoid muscle (occipital horn), but exostoses may also occur on the tibia and radius. Other, more variable, skeletal features are hammer-shaped claviculae, scoliosis, pectus deformity, coxa valga, genua valga as well as dislocations of the radial head. Less frequently reported skeletal manifestations include bowing of the long bones, mid-diaphyseal broadening, metaphyseal spurring, rounding of the iliac wings and, rarely, osteopenia. Facial features become distinctive with age and includes a long face (46%), large ears (38%), sagging cheeks (45%) and coarse hair (74%). Trichoscopy may show pili torti. The skin is often hyperextensible and soft with fine wrinkling on the hands and feet. Skin redundancy is remarkable on the belly. Vascular tortuosity is common in the intracranial arteries (65%), but may also affect the cervical, splenic and splanchnic circulation and imposes a risk for aneurysm formation. Aortic root dilatation and dissection may rarely occur. Dysautonomia with postural orthostatic hypotension, temperature instability and chronic diarrhea is present in most patients (>90%). About half of all patients show a delayed motor development due to muscle hypotonia and joint hypermobility, and may report unusual clumsiness. Distal motor neuropathy has been recorded in at least one patient. About half of all patients have intellectual disability (ID) which is usually mild, but moderate to severe impairment may occur.	NM_000052.6(ATP7A):c.3915_3921delCTCCCCA ; c.3257_3258del ; NM_000052.6(ATP7A):c.1974_1977dupGTTT ; NM_000052.6(ATP7A):c.1639C>T ; c.3294+2T>G ; NM_000052.6(ATP7A):c.3911A>G ; NM_000052.6(ATP7A):c.2938C>T ; NM_000052.6(ATP7A):c.3915_3921delCTCCCCA ; c.3257_3258del ; NM_000052.6(ATP7A):c.1974_1977dupGTTT ; NM_000052.6(ATP7A):c.1639C>T ; c.3294+2T>G ; NM_000052.6(ATP7A):c.3911A>G ; NM_000052.6(ATP7A):c.2938C>T

ATP7A	X-linked distal spinal muscular atrophy type 3	X-linked distal spinal muscular atrophy type 3 is a rare distal hereditary motor neuropathy characterized by slowly progressive atrophy and weakness of distal muscles of hands and feet with normal deep tendon reflexes or absent ankle reflexes and minimal or no sensory loss, sometimes mild proximal weakness in the legs and feet and hand deformities in males.	The disorder was transmitted in an X-linked recessive pattern of inheritance. In 6 of 9 patients who were examined, age at onset ranged from 1 to 10 years, and the first detected symptom was foot deformity (pes cavus or pes varus); gait instability was reported in 2 other individuals. Subsequently, distal lower limb weakness and atrophy were observed, and finally, the hands were affected. Despite the large clinical variability, the disease progression was very slow and independent gait was maintained even late in life. There was no cognitive, pyramidal, or sensory impairment. EMG showed chronic denervation, muscle biopsy showed a neurogenic pattern, and sural nerve biopsy was normal.	NM_000052.6(ATP7A):c.3915_3921delCTCCCCA ; c.3257_3258del ; NM_000052.6(ATP7A):c.1974_1977dupGTTT ; NM_000052.6(ATP7A):c.1639C>T ; c.3294+2T>G ; NM_000052.6(ATP7A):c.3911A>G ; NM_000052.6(ATP7A):c.2938C>T ; NM_000052.6(ATP7A):c.3915_3921delCTCCCCA ; c.3257_3258del ; NM_000052.6(ATP7A):c.1974_1977dupGTTT ; NM_000052.6(ATP7A):c.1639C>T ; c.3294+2T>G ; NM_000052.6(ATP7A):c.3911A>G ; NM_000052.6(ATP7A):c.2938C>T

ATP7B	Wilson disease	A rare genetic disorder of copper metabolism presenting with non-specific hepatic, neurologic, psychiatric or ophthalmologic manifestations due to impaired biliary copper excretion and consecutive excessive copper deposition in the body.	The clinical spectrum is very wide, even within affected families. Likewise, age of onset is highly variable. Some patients remain asymptomatic for decades while few present symptoms before age 3 to 5. The disease can be observed in children after 3 years and most cases develop by 40 years of age. Late-onset cases after the fifth decade of life have also been described. Clinical presentation depends on gender and age. In children, at an average age of 10 years, hepatic manifestations typically prevail, most often commencing with liver damage. In general, hepatic manifestations (hepatomegaly, subacute or chronic hepatitis, acute liver failure or cirrhosis with portal hypertension) commonly precedes neurologic symptoms. Neurological manifestations (dystonia, intention tremor, dysarthria, coordination difficulties, chorea, choreoathetosis, and gait disorders) can be found in conjunction with hepatic symptoms or might also be the first clinical symptoms. Isolated psychiatric disorders (depression, phobias, compulsive behavior, personality changes, aggressiveness, or emotional instability) are rare and more commonly observed in conjunction with hepatic or neurologic disease. A wide range of other manifestations may also be present in affected patients: acute hemolytic episodes, delayed puberty, amenorrhea, repetitive miscarriage, Kayser-Fleischer rings due to copper deposits in the Descemet membrane, bone pain, arthralgia and osteoporosis, arrythmia, myocardiopathy, hematuria, nephrotic syndrome and renal lithiasis. Hepatocellular carcinoma has been reported in rare cases.	NM_000053.3(ATP7B):c.2532delA ; NM_000053.3(ATP7B):c.2906G>A ; NM_000053.3(ATP7B):c.2930C>T ; c.2807T>A ; NM_000053.4:c.3207C>A ; c.2356-2A>G ; NM_000053.3(ATP7B):c.2305A>G ; NM_000053.3(ATP7B):c.1745_1746delTA ; NM_000053.3(ATP7B):c.915T>A ; NM_001005918.2:c.3369_3372delTTAT ; NM_000053.3(ATP7B):c.2804C>T ; NM_000053.3(ATP7B):c.562C>T ; NM_000053.3(ATP7B):c.1145_1151delCCCAACT ; NM_000053.3(ATP7B):c.1512dupT ; NM_000053.3(ATP7B):c.3809A>G ; NM_000053.3(ATP7B):c.2297C>G ; NM_000053.3(ATP7B):c.2975C>T ; NM_000053.3(ATP7B):c.2795C>A ; NM_000053.3(ATP7B):c.3694A>C ; NM_000053.3(ATP7B):c.4088C>T ; c.3083del ; NM_000053.3(ATP7B):c.2071G>A ; NM_000053.3(ATP7B):c.3955C>T ; NM_000053.3(ATP7B):c.4058G>A ; NM_000053.3(ATP7B):c.3796G>A ; NM_000053.3(ATP7B):c.2755C>G ; NM_000053.3(ATP7B):c.2123T>C ; c.3359T>A ; NM_000053.3(ATP7B):c.2532delA ; NM_000053.3(ATP7B):c.2906G>A ; NM_000053.3(ATP7B):c.2930C>T ; c.2807T>A ; NM_000053.4:c.3207C>A ; c.2356-2A>G ; NM_000053.3(ATP7B):c.2305A>G ; NM_000053.3(ATP7B):c.1745_1746delTA ; NM_000053.3(ATP7B):c.915T>A ; NM_001005918.2:c.3369_3372delTTAT ; NM_000053.3(ATP7B):c.2804C>T ; NM_000053.3(ATP7B):c.562C>T ; NM_000053.3(ATP7B):c.1145_1151delCCCAACT ; NM_000053.3(ATP7B):c.1512dupT ; NM_000053.3(ATP7B):c.3809A>G ; NM_000053.3(ATP7B):c.2297C>G ; NM_000053.3(ATP7B):c.2975C>T ; NM_000053.3(ATP7B):c.2795C>A ; NM_000053.3(ATP7B):c.3694A>C ; NM_000053.3(ATP7B):c.4088C>T ; c.3083del ; NM_000053.3(ATP7B):c.2071G>A ; NM_000053.3(ATP7B):c.3955C>T ; NM_000053.3(ATP7B):c.4058G>A ; NM_000053.3(ATP7B):c.3796G>A ; NM_000053.3(ATP7B):c.2755C>G ; NM_000053.3(ATP7B):c.2123T>C ; c.3359T>A

BCKDHA	Classic maple syrup urine disease	Classic maple syrup urine disease (classic MSUD) is the most severe and probably common form of MSUD (see this term) characterized by a maple syrup odor in the cerumen at birth, poor feeding, lethargy and focal dystonia, followed by progressive encephalopathy and central respiratory failure if untreated.	Onset of classic MSUD occurs in the neonatal period (usually 12 hours after birth) with the presence of a maple syrup odor in the cerumen and later in urine, poor feeding and drowsiness. Progressive encephalopathy with lethargy, intermittent apnea, stereotyped movements (described as "fencing" and bicycling") and opisthotonus occur in the first few days of life. Without treatment, coma and central respiratory failure occur by days 7 to 10. Later, catabolic stress, infection or injury may cause acute, potentially fatal, leucine intoxication with vomiting, altered consciousness, ataxia and acute dystonia in toddlers and hallucinations, hyperactivity, focal dystonia, ataxia and choreoathetosis in children and adults.	NM_000709.3(BCKDHA):c.659C>T ; NM_000709.3(BCKDHA):c.964C>T ; c.797del ; NM_000709.3(BCKDHA):c.917delT ; NM_000709.3(BCKDHA):c.14delT ; NM_000709.3(BCKDHA):c.929C>G ; NM_000709.3(BCKDHA):c.1234G>A ; NM_000709.3(BCKDHA):c.740_741insT ; NM_000709.3(BCKDHA):c.632C>T ; NM_000709.3(BCKDHA):c.853G>C ; NM_000709.3(BCKDHA):c.909_910delGT ; NM_000709.3(BCKDHA):c.868G>A ; NM_000709.3(BCKDHA):c.979G>A ; NM_000709.3(BCKDHA):c.905A>C ; NM_000709.3(BCKDHA):c.1036C>T ; NM_000709.3(BCKDHA):c.659C>T ; NM_000709.3(BCKDHA):c.964C>T ; c.797del ; NM_000709.3(BCKDHA):c.917delT ; NM_000709.3(BCKDHA):c.14delT ; NM_000709.3(BCKDHA):c.929C>G ; NM_000709.3(BCKDHA):c.1234G>A ; NM_000709.3(BCKDHA):c.740_741insT ; NM_000709.3(BCKDHA):c.632C>T ; NM_000709.3(BCKDHA):c.853G>C ; NM_000709.3(BCKDHA):c.909_910delGT ; NM_000709.3(BCKDHA):c.868G>A ; NM_000709.3(BCKDHA):c.979G>A ; NM_000709.3(BCKDHA):c.905A>C ; NM_000709.3(BCKDHA):c.1036C>T
BCKDHA	Intermediate maple syrup urine disease	Intermediate maple syrup urine disease (intermediate MSUD) is a milder form of MSUD (see this term) characterized by persistently raised branched-chain amino acids (BCAAs) and ketoacids, but fewer or no acute episodes of decompensation.	Symptom onset of intermediate MSUD varies between the early months and the early years of childhood. Infants may have feeding problems, poor growth, maple syrup odor in urine and developmental delay. Older children usually present with learning difficulties. Like classic MSUD (see this term), catabolic stress can result in acute decompensation with anorexia, vomiting, ataxia (in infants/toddlers), cognitive impairment, sleep disturbances, hallucinations, hyperactivity, mood swings, acute dystonia, choreoathetosis (in adults), stupor, coma and cerebral edema, if untreated.	NM_000709.3(BCKDHA):c.659C>T ; NM_000709.3(BCKDHA):c.964C>T ; c.797del ; NM_000709.3(BCKDHA):c.917delT ; NM_000709.3(BCKDHA):c.14delT ; NM_000709.3(BCKDHA):c.929C>G ; NM_000709.3(BCKDHA):c.1234G>A ; NM_000709.3(BCKDHA):c.740_741insT ; NM_000709.3(BCKDHA):c.632C>T ; NM_000709.3(BCKDHA):c.853G>C ; NM_000709.3(BCKDHA):c.909_910delGT ; NM_000709.3(BCKDHA):c.868G>A ; NM_000709.3(BCKDHA):c.979G>A ; NM_000709.3(BCKDHA):c.905A>C ; NM_000709.3(BCKDHA):c.1036C>T ; NM_000709.3(BCKDHA):c.659C>T ; NM_000709.3(BCKDHA):c.964C>T ; c.797del ; NM_000709.3(BCKDHA):c.917delT ; NM_000709.3(BCKDHA):c.14delT ; NM_000709.3(BCKDHA):c.929C>G ; NM_000709.3(BCKDHA):c.1234G>A ; NM_000709.3(BCKDHA):c.740_741insT ; NM_000709.3(BCKDHA):c.632C>T ; NM_000709.3(BCKDHA):c.853G>C ; NM_000709.3(BCKDHA):c.909_910delGT ; NM_000709.3(BCKDHA):c.868G>A ; NM_000709.3(BCKDHA):c.979G>A ; NM_000709.3(BCKDHA):c.905A>C ; NM_000709.3(BCKDHA):c.1036C>T

BCKDHA	Intermittent maple syrup urine disease	Intermittent maple syrup urine disease (intermittent MSUD) is a mild form of MSUD (see this term) where patients (when well) are asymptomatic with normal levels of branched-chain amino acids (BCAAs) but with catabolic stress are at risk of acute decompensation with ketoacidosis, which can lead to cerebral edema and coma if untreated.	Unlike classic MSUD (see this term), patients with intermittent MSUD show normal growth and intellectual development during infancy and childhood. They may develop symptoms (mainly in childhood) with any catabolic stress (i.e. fasting, dehydration, fever, infections or pregnancy (in adults)). These precipitating factors can lead to a potentially fatal episode of acute decompensation with anorexia, nausea, vomiting, lethargy, ataxia (in infants/toddlers), cognitive impairment, sleep disturbances, hallucinations, hyperactivity, mood swings, acute dystonia, and choreoathetosis (in adults), that can progress to stupor, coma and cerebral edema. Intelligence and development are not usually affected by these episodes.	NM_000709.3(BCKDHA):c.659C>T ; NM_000709.3(BCKDHA):c.964C>T ; c.797del ; NM_000709.3(BCKDHA):c.917delT ; NM_000709.3(BCKDHA):c.14delT ; NM_000709.3(BCKDHA):c.929C>G ; NM_000709.3(BCKDHA):c.1234G>A ; NM_000709.3(BCKDHA):c.740_741insT ; NM_000709.3(BCKDHA):c.632C>T ; NM_000709.3(BCKDHA):c.853G>C ; NM_000709.3(BCKDHA):c.909_910delGT ; NM_000709.3(BCKDHA):c.868G>A ; NM_000709.3(BCKDHA):c.979G>A ; NM_000709.3(BCKDHA):c.905A>C ; NM_000709.3(BCKDHA):c.1036C>T ; NM_000709.3(BCKDHA):c.659C>T ; NM_000709.3(BCKDHA):c.964C>T ; c.797del ; NM_000709.3(BCKDHA):c.917delT ; NM_000709.3(BCKDHA):c.14delT ; NM_000709.3(BCKDHA):c.929C>G ; NM_000709.3(BCKDHA):c.1234G>A ; NM_000709.3(BCKDHA):c.740_741insT ; NM_000709.3(BCKDHA):c.632C>T ; NM_000709.3(BCKDHA):c.853G>C ; NM_000709.3(BCKDHA):c.909_910delGT ; NM_000709.3(BCKDHA):c.868G>A ; NM_000709.3(BCKDHA):c.979G>A ; NM_000709.3(BCKDHA):c.905A>C ; NM_000709.3(BCKDHA):c.1036C>T
BCKDHA	Thiamine-responsive maple syrup urine disease	Thiamine-responsive maple syrup urine disease (thiamine-responsive MSUD) is a less severe variant of MSUD (see this term) that manifests with a phenotype similar to intermediate MSUD (see this term) but that responds positively to treatment with thiamine.	Thiamine-responsive MSUD is poorly characterized. It appears to usually present after infancy with a phenotype very similar to that seen in intermediate MSUD (see this term). Manifestations include feeding problems, poor growth, maple syrup odor in urine and developmental delay. Older children usually present with learning difficulties. Like classic MSUD (see this term), physiological stress can result in acute decompensation with anorexia, nausea, vomiting (at all ages), ataxia (in infants/toddlers), cognitive impairment, sleep disturbances, hallucinations, hyperactivity, mood swings, acute / focal dystonia and choreoathetosis (in adults) that can progress to stupor, coma and cerebral edema, if untreated. Thiamine (doses of 10-1000 mg per day) has improved the leucine tolerance in the few reported cases of this MSUD subtype, but some dietary branched-chain amino-acid (BCAA) restriction remains necessary.	NM_000709.3(BCKDHA):c.659C>T ; NM_000709.3(BCKDHA):c.964C>T ; c.797del ; NM_000709.3(BCKDHA):c.917delT ; NM_000709.3(BCKDHA):c.14delT ; NM_000709.3(BCKDHA):c.929C>G ; NM_000709.3(BCKDHA):c.1234G>A ; NM_000709.3(BCKDHA):c.740_741insT ; NM_000709.3(BCKDHA):c.632C>T ; NM_000709.3(BCKDHA):c.853G>C ; NM_000709.3(BCKDHA):c.909_910delGT ; NM_000709.3(BCKDHA):c.868G>A ; NM_000709.3(BCKDHA):c.979G>A ; NM_000709.3(BCKDHA):c.905A>C ; NM_000709.3(BCKDHA):c.1036C>T ; NM_000709.3(BCKDHA):c.659C>T ; NM_000709.3(BCKDHA):c.964C>T ; c.797del ; NM_000709.3(BCKDHA):c.917delT ; NM_000709.3(BCKDHA):c.14delT ; NM_000709.3(BCKDHA):c.929C>G ; NM_000709.3(BCKDHA):c.1234G>A ; NM_000709.3(BCKDHA):c.740_741insT ; NM_000709.3(BCKDHA):c.632C>T ; NM_000709.3(BCKDHA):c.853G>C ; NM_000709.3(BCKDHA):c.909_910delGT ; NM_000709.3(BCKDHA):c.868G>A ; NM_000709.3(BCKDHA):c.979G>A ; NM_000709.3(BCKDHA):c.905A>C ; NM_000709.3(BCKDHA):c.1036C>T

BCKDHB	Classic maple syrup urine disease	Classic maple syrup urine disease (classic MSUD) is the most severe and probably common form of MSUD (see this term) characterized by a maple syrup odor in the cerumen at birth, poor feeding, lethargy and focal dystonia, followed by progressive encephalopathy and central respiratory failure if untreated.	Onset of classic MSUD occurs in the neonatal period (usually 12 hours after birth) with the presence of a maple syrup odor in the cerumen and later in urine, poor feeding and drowsiness. Progressive encephalopathy with lethargy, intermittent apnea, stereotyped movements (described as "fencing" and bicycling") and opisthotonus occur in the first few days of life. Without treatment, coma and central respiratory failure occur by days 7 to 10. Later, catabolic stress, infection or injury may cause acute, potentially fatal, leucine intoxication with vomiting, altered consciousness, ataxia and acute dystonia in toddlers and hallucinations, hyperactivity, focal dystonia, ataxia and choreoathetosis in children and adults.	NM_183050.3(BCKDHB):c.752T>C ; NM_183050.3(BCKDHB):c.508C>T ; NM_000056.4(BCKDHB):c.488A>T ; NM_000056.4(BCKDHB):c.508C>A ; NM_000056.4(BCKDHB):c.952-1G>A ; NM_000056.4(BCKDHB):c.356T>G ; NM_183050.2(BCKDHB):c.547C>T ; NM_000056.4(BCKDHB):c.344-1G>A ; NM_183050.3(BCKDHB):c.799C>T ; NM_183050.3(BCKDHB):c.1114G>T ; NM_183050.3(BCKDHB):c.832G>A ; NM_183050.2(BCKDHB):c.970C>T ; NM_000056.4(BCKDHB):c.526A>T ; NM_000056.4(BCKDHB):c.302G>A ; NM_000056.4(BCKDHB):c.508C>G ; NM_000056.4(BCKDHB):c.479T>G ; NM_183050.3(BCKDHB):c.342T>G ; NM_000056.4(BCKDHB):c.748G>T ; NM_183050.4:c.548G>C ; NM_183050.3(BCKDHB):c.752T>C ; NM_183050.3(BCKDHB):c.508C>T ; NM_000056.4(BCKDHB):c.488A>T ; NM_000056.4(BCKDHB):c.508C>A ; NM_000056.4(BCKDHB):c.952-1G>A ; NM_000056.4(BCKDHB):c.356T>G ; NM_183050.2(BCKDHB):c.547C>T ; NM_000056.4(BCKDHB):c.344-1G>A ; NM_183050.3(BCKDHB):c.799C>T ; NM_183050.3(BCKDHB):c.1114G>T ; NM_183050.3(BCKDHB):c.832G>A ; NM_183050.2(BCKDHB):c.970C>T ; NM_000056.4(BCKDHB):c.526A>T ; NM_000056.4(BCKDHB):c.302G>A ; NM_000056.4(BCKDHB):c.508C>G ; NM_000056.4(BCKDHB):c.479T>G ; NM_183050.3(BCKDHB):c.342T>G ; NM_000056.4(BCKDHB):c.748G>T ; NM_183050.4:c.548G>C
BCKDHB	Intermediate maple syrup urine disease	Intermediate maple syrup urine disease (intermediate MSUD) is a milder form of MSUD (see this term) characterized by persistently raised branched-chain amino acids (BCAAs) and ketoacids, but fewer or no acute episodes of decompensation.	Symptom onset of intermediate MSUD varies between the early months and the early years of childhood. Infants may have feeding problems, poor growth, maple syrup odor in urine and developmental delay. Older children usually present with learning difficulties. Like classic MSUD (see this term), catabolic stress can result in acute decompensation with anorexia, vomiting, ataxia (in infants/toddlers), cognitive impairment, sleep disturbances, hallucinations, hyperactivity, mood swings, acute dystonia, choreoathetosis (in adults), stupor, coma and cerebral edema, if untreated.	NM_183050.3(BCKDHB):c.752T>C ; NM_183050.3(BCKDHB):c.508C>T ; NM_000056.4(BCKDHB):c.488A>T ; NM_000056.4(BCKDHB):c.508C>A ; NM_000056.4(BCKDHB):c.952-1G>A ; NM_000056.4(BCKDHB):c.356T>G ; NM_183050.2(BCKDHB):c.547C>T ; NM_000056.4(BCKDHB):c.344-1G>A ; NM_183050.3(BCKDHB):c.799C>T ; NM_183050.3(BCKDHB):c.1114G>T ; NM_183050.3(BCKDHB):c.832G>A ; NM_183050.2(BCKDHB):c.970C>T ; NM_000056.4(BCKDHB):c.526A>T ; NM_000056.4(BCKDHB):c.302G>A ; NM_000056.4(BCKDHB):c.508C>G ; NM_000056.4(BCKDHB):c.479T>G ; NM_183050.3(BCKDHB):c.342T>G ; NM_000056.4(BCKDHB):c.748G>T ; NM_183050.4:c.548G>C ; NM_183050.3(BCKDHB):c.752T>C ; NM_183050.3(BCKDHB):c.508C>T ; NM_000056.4(BCKDHB):c.488A>T ; NM_000056.4(BCKDHB):c.508C>A ; NM_000056.4(BCKDHB):c.952-1G>A ; NM_000056.4(BCKDHB):c.356T>G ; NM_183050.2(BCKDHB):c.547C>T ; NM_000056.4(BCKDHB):c.344-1G>A ; NM_183050.3(BCKDHB):c.799C>T ; NM_183050.3(BCKDHB):c.1114G>T ; NM_183050.3(BCKDHB):c.832G>A ; NM_183050.2(BCKDHB):c.970C>T ; NM_000056.4(BCKDHB):c.526A>T ; NM_000056.4(BCKDHB):c.302G>A ; NM_000056.4(BCKDHB):c.508C>G ; NM_000056.4(BCKDHB):c.479T>G ; NM_183050.3(BCKDHB):c.342T>G ; NM_000056.4(BCKDHB):c.748G>T ; NM_183050.4:c.548G>C

BCKDHB	Intermittent maple syrup urine disease	Intermittent maple syrup urine disease (intermittent MSUD) is a mild form of MSUD (see this term) where patients (when well) are asymptomatic with normal levels of branched-chain amino acids (BCAAs) but with catabolic stress are at risk of acute decompensation with ketoacidosis, which can lead to cerebral edema and coma if untreated.	Unlike classic MSUD (see this term), patients with intermittent MSUD show normal growth and intellectual development during infancy and childhood. They may develop symptoms (mainly in childhood) with any catabolic stress (i.e. fasting, dehydration, fever, infections or pregnancy (in adults)). These precipitating factors can lead to a potentially fatal episode of acute decompensation with anorexia, nausea, vomiting, lethargy, ataxia (in infants/toddlers), cognitive impairment, sleep disturbances, hallucinations, hyperactivity, mood swings, acute dystonia, and choreoathetosis (in adults), that can progress to stupor, coma and cerebral edema. Intelligence and development are not usually affected by these episodes.	NM_183050.3(BCKDHB):c.752T>C ; NM_183050.3(BCKDHB):c.508C>T ; NM_000056.4(BCKDHB):c.488A>T ; NM_000056.4(BCKDHB):c.508C>A ; NM_000056.4(BCKDHB):c.952-1G>A ; NM_000056.4(BCKDHB):c.356T>G ; NM_183050.2(BCKDHB):c.547C>T ; NM_000056.4(BCKDHB):c.344-1G>A ; NM_183050.3(BCKDHB):c.799C>T ; NM_183050.3(BCKDHB):c.1114G>T ; NM_183050.3(BCKDHB):c.832G>A ; NM_183050.2(BCKDHB):c.970C>T ; NM_000056.4(BCKDHB):c.526A>T ; NM_000056.4(BCKDHB):c.302G>A ; NM_000056.4(BCKDHB):c.508C>G ; NM_000056.4(BCKDHB):c.479T>G ; NM_183050.3(BCKDHB):c.342T>G ; NM_000056.4(BCKDHB):c.748G>T ; NM_183050.4:c.548G>C ; NM_183050.3(BCKDHB):c.752T>C ; NM_183050.3(BCKDHB):c.508C>T ; NM_000056.4(BCKDHB):c.488A>T ; NM_000056.4(BCKDHB):c.508C>A ; NM_000056.4(BCKDHB):c.952-1G>A ; NM_000056.4(BCKDHB):c.356T>G ; NM_183050.2(BCKDHB):c.547C>T ; NM_000056.4(BCKDHB):c.344-1G>A ; NM_183050.3(BCKDHB):c.799C>T ; NM_183050.3(BCKDHB):c.1114G>T ; NM_183050.3(BCKDHB):c.832G>A ; NM_183050.2(BCKDHB):c.970C>T ; NM_000056.4(BCKDHB):c.526A>T ; NM_000056.4(BCKDHB):c.302G>A ; NM_000056.4(BCKDHB):c.508C>G ; NM_000056.4(BCKDHB):c.479T>G ; NM_183050.3(BCKDHB):c.342T>G ; NM_000056.4(BCKDHB):c.748G>T ; NM_183050.4:c.548G>C
BCKDHB	Thiamine-responsive maple syrup urine disease	Thiamine-responsive maple syrup urine disease (thiamine-responsive MSUD) is a less severe variant of MSUD (see this term) that manifests with a phenotype similar to intermediate MSUD (see this term) but that responds positively to treatment with thiamine.	Thiamine-responsive MSUD is poorly characterized. It appears to usually present after infancy with a phenotype very similar to that seen in intermediate MSUD (see this term). Manifestations include feeding problems, poor growth, maple syrup odor in urine and developmental delay. Older children usually present with learning difficulties. Like classic MSUD (see this term), physiological stress can result in acute decompensation with anorexia, nausea, vomiting (at all ages), ataxia (in infants/toddlers), cognitive impairment, sleep disturbances, hallucinations, hyperactivity, mood swings, acute / focal dystonia and choreoathetosis (in adults) that can progress to stupor, coma and cerebral edema, if untreated. Thiamine (doses of 10-1000 mg per day) has improved the leucine tolerance in the few reported cases of this MSUD subtype, but some dietary branched-chain amino-acid (BCAA) restriction remains necessary.	NM_183050.3(BCKDHB):c.752T>C ; NM_183050.3(BCKDHB):c.508C>T ; NM_000056.4(BCKDHB):c.488A>T ; NM_000056.4(BCKDHB):c.508C>A ; NM_000056.4(BCKDHB):c.952-1G>A ; NM_000056.4(BCKDHB):c.356T>G ; NM_183050.2(BCKDHB):c.547C>T ; NM_000056.4(BCKDHB):c.344-1G>A ; NM_183050.3(BCKDHB):c.799C>T ; NM_183050.3(BCKDHB):c.1114G>T ; NM_183050.3(BCKDHB):c.832G>A ; NM_183050.2(BCKDHB):c.970C>T ; NM_000056.4(BCKDHB):c.526A>T ; NM_000056.4(BCKDHB):c.302G>A ; NM_000056.4(BCKDHB):c.508C>G ; NM_000056.4(BCKDHB):c.479T>G ; NM_183050.3(BCKDHB):c.342T>G ; NM_000056.4(BCKDHB):c.748G>T ; NM_183050.4:c.548G>C
BCS1L	BjÃ¶rnstad syndrome	BjÃ¶rnstad syndrome is characterized by congenital sensorineural hearing loss and pili torti.	The hearing loss usually becomes evident very early in life, often in the first year. Pili torti, a condition in which the hair shaft is flattened and twisted, makes the hair very brittle and patients develop hair loss in the first two years of life.	NM_004328.4(BCS1L):c.1057G>A ; NM_004328.4(BCS1L):c.103G>C ; NM_001257342.1(BCS1L):c.232A>G ; NM_004328.4(BCS1L):c.148A>G ; NM_004328.4(BCS1L):c.548G>A ; NM_004328.4(BCS1L):c.830G>A ; NM_004328.4(BCS1L):c.133C>T ; c.696del ; NM_004328.4(BCS1L):c.166C>T ; NM_004328.4(BCS1L):c.1057G>A ; NM_004328.4(BCS1L):c.103G>C ; NM_001257342.1(BCS1L):c.232A>G ; NM_004328.4(BCS1L):c.148A>G ; NM_004328.4(BCS1L):c.548G>A ; NM_004328.4(BCS1L):c.830G>A ; NM_004328.4(BCS1L):c.133C>T ; c.696del ; NM_004328.4(BCS1L):c.166C>T

BCS1L	GRACILE syndrome	An inherited lethal mitochondrial disorder characterized by fetal growth restriction (GR), aminoaciduria (A), cholestasis (C), iron overload (I), lactacidosis (L), and early death (E).	Fetal growth restriction appears early during the pregnancy without signs of chronic hypoxia. Because of small fetal size, the pregnancies are usually interrupted a few weeks before the estimated due date (median 38 gestational weeks). The newborn infant is small for gestational age (birth weight approximately 1,700 g) and develops fulminant lactic acidosis (median pH 7.02, lactate 12.8 mmol/l) during the first day of life. In metabolic screening, marked aminoaciduria is found due to renal proximal tubulopathy of Fanconi type. Iron overload is illustrated by increased plasma ferritin and decreased transferrin concentrations and accumulation of iron in the liver. Further signs of hepatopathy are cholestasis with steatosis, fibrosis and cirrhosis. No dysmorphic features are noted. No distinct cerebral abnormalities have so far been found, however in some infants, EEG has been abnormal, maybe as a result of severe metabolic acidosis. The hearing response assessed with BAEP has been abnormal.	NM_004328.4(BCS1L):c.1057G>A ; NM_004328.4(BCS1L):c.103G>C ; NM_001257342.1(BCS1L):c.232A>G ; NM_004328.4(BCS1L):c.148A>G ; NM_004328.4(BCS1L):c.548G>A ; NM_004328.4(BCS1L):c.830G>A ; NM_004328.4(BCS1L):c.133C>T ; c.696del ; NM_004328.4(BCS1L):c.166C>T ; NM_004328.4(BCS1L):c.1057G>A ; NM_004328.4(BCS1L):c.103G>C ; NM_001257342.1(BCS1L):c.232A>G ; NM_004328.4(BCS1L):c.148A>G ; NM_004328.4(BCS1L):c.548G>A ; NM_004328.4(BCS1L):c.830G>A ; NM_004328.4(BCS1L):c.133C>T ; c.696del ; NM_004328.4(BCS1L):c.166C>T
BCS1L	Isolated complex III deficiency	Isolated complex III deficiency is a rare, genetic, mitochondrial oxidative phosphorylation disorder characterized by a wide spectrum of clinical manifestations ranging from isolated myopathy or transient hepatopathy to severe multisystem disorder (that may include hypotonia, failure to thrive, psychomotor delay, cardiomyopathy, encephalopathy, renal tubulopathy, hearing impairment, lactic acidosis, hypoglycemia and other signs and symptoms).	Autosomal recessive mitochondrial complex III deficiency is a severe multisystem disorder with onset at birth of lactic acidosis, hypotonia, hypoglycemia, failure to thrive, encephalopathy, and delayed psychomotor development. Visceral involvement, including hepatopathy and renal tubulopathy, may also occur. Many patients die in early childhood, but some may show longer survival.Ã	NM_004328.4(BCS1L):c.1057G>A ; NM_004328.4(BCS1L):c.103G>C ; NM_001257342.1(BCS1L):c.232A>G ; NM_004328.4(BCS1L):c.148A>G ; NM_004328.4(BCS1L):c.548G>A ; NM_004328.4(BCS1L):c.830G>A ; NM_004328.4(BCS1L):c.133C>T ; c.696del ; NM_004328.4(BCS1L):c.166C>T ; NM_004328.4(BCS1L):c.1057G>A ; NM_004328.4(BCS1L):c.103G>C ; NM_001257342.1(BCS1L):c.232A>G ; NM_004328.4(BCS1L):c.148A>G ; NM_004328.4(BCS1L):c.548G>A ; NM_004328.4(BCS1L):c.830G>A ; NM_004328.4(BCS1L):c.133C>T ; c.696del ; NM_004328.4(BCS1L):c.166C>T

BCS1L	Renal tubulopathy-encephalopathy-liver failure syndrome	Renal tubulopathy - encephalopathy - liver failure describes a spectrum of phenotypes with manifestations similar but milder than those seen in GRACILE syndrome (see this term) and that can be associated with encephalopathy and psychiatric disorders.	Disease presentation is variable. Most of the characteristics of GRACILE syndrome are present (fetal growth restriction, proximal tubulopathy and hepatopathy, as well as lactic acidosis) but they are often less severe. Signs of disturbances in iron metabolism have been described, such as increased serum ferritin levels, but it is unclear whether severe liver iron overload is present. Most infants die during the neonatal period. In those who survive, encephalopathy and psychiatric disorders have been described.	NM_004328.4(BCS1L):c.1057G>A ; NM_004328.4(BCS1L):c.103G>C ; NM_001257342.1(BCS1L):c.232A>G ; NM_004328.4(BCS1L):c.148A>G ; NM_004328.4(BCS1L):c.548G>A ; NM_004328.4(BCS1L):c.830G>A ; NM_004328.4(BCS1L):c.133C>T ; c.696del ; NM_004328.4(BCS1L):c.166C>T ; NM_004328.4(BCS1L):c.1057G>A ; NM_004328.4(BCS1L):c.103G>C ; NM_001257342.1(BCS1L):c.232A>G ; NM_004328.4(BCS1L):c.148A>G ; NM_004328.4(BCS1L):c.548G>A ; NM_004328.4(BCS1L):c.830G>A ; NM_004328.4(BCS1L):c.133C>T ; c.696del ; NM_004328.4(BCS1L):c.166C>T
BRIP1	Fanconi anemia	A rare genetic multisystem disorder characterized by progressive pancytopenia with bone marrow failure, variable congenital malformations and predisposition to develop hematological or solid tumors.	The first signs of Fanconi anemia (FA) are typically non-hematological features. Limb anomalies typically affect the extremities, are unilateral or (usually asymmetric) bilateral. Minor anomalies can also be present such as low birth length and weight, microcephaly and/or microphthalmia. Skin pigmentation abnormalities (cafÃ©-au-lait spots) and hypoplastic thenar eminence are frequent. Almost 20% of patients have ear malformations with or without hearing loss. Congenital malformations may involve other organ systems and vary within families. Short stature is syndromic and/or associated to endocrinopathies. Fertility is frequently impaired in males, and is highly disturbed in half of females. When congenital malformations are not prominent, diagnosis may be delayed until the onset of hematological anomalies. Bone marrow failure (BMF) occurs at a median age of 7 years, developing in 90% of patients by 40 years of age. The first manifestations are macrocytosis (very early) and thrombocytopenia. In patients with somatic mosaÃ¯cism, blood counts may stay normal until occurrence of hematological malignancy. In general, patients are highly predisposed to solid tumors (most frequently head and neck or anogenital regions).	c.502C>T ; NM_032043.2(BRIP1):c.2237_2240delTCAA ; NM_032043.2(BRIP1):c.1045G>C ; NM_032043.2(BRIP1):c.1702_1703delAA ; NM_032043.2(BRIP1):c.2990_2993delCAAA ; c.502C>T ; NM_032043.2(BRIP1):c.2237_2240delTCAA ; NM_032043.2(BRIP1):c.1045G>C ; NM_032043.2(BRIP1):c.1702_1703delAA ; NM_032043.2(BRIP1):c.2990_2993delCAAA

BRIP1	Hereditary breast and ovarian cancer syndrome	Breast cancer (BC) is the most common cancer in women, accounting for 25% of all new cases of cancer. Most BC cases are sporadic, while 5-10% are estimated to be due to an inherited predisposition.	HBC is not associated with specific phenotypic features.	c.502C>T ; NM_032043.2(BRIP1):c.2237_2240delTCAA ; NM_032043.2(BRIP1):c.1045G>C ; NM_032043.2(BRIP1):c.1702_1703delAA ; NM_032043.2(BRIP1):c.2990_2993delCAAA ; c.502C>T ; NM_032043.2(BRIP1):c.2237_2240delTCAA ; NM_032043.2(BRIP1):c.1045G>C ; NM_032043.2(BRIP1):c.1702_1703delAA ; NM_032043.2(BRIP1):c.2990_2993delCAAA
BSND	Autosomal recessive non-syndromic sensorineural deafness type DFNB	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	NM_057176.3(BSND):c.23G>T ; NM_057176.3(BSND):c.1A>T ; NM_057176.3(BSND):c.139G>A ; NM_057176.3(BSND):c.3G>A ; NM_057176.3(BSND):c.22C>T ; NM_057176.3(BSND):c.10G>T ; NM_057176.3(BSND):c.23G>T ; NM_057176.3(BSND):c.1A>T ; NM_057176.3(BSND):c.139G>A ; NM_057176.3(BSND):c.3G>A ; NM_057176.3(BSND):c.22C>T ; NM_057176.3(BSND):c.10G>T

BSND	Infantile Bartter syndrome with sensorineural deafness	Infantile Bartter syndrome with deafness, a phenotypic variant of Bartter syndrome (see this term) is characterized by maternal polyhydramnios, premature delivery, polyuria and sensorineural deafness and is associated with hypokalemic alkalosis, increased levels of plasma renin and aldosterone, low blood pressure, and vascular resistance to angiotensin II.	Infantile Bartter syndrome with deafness is a severe type of Bartter syndrome manifesting prenatally with maternal polyhydramnios (due to fetal polyuria) usually evident by the end of 2nd trimester, often leading to preterm labour and prematurity. Postnatally patients present with polyuria, isosthenuria/hyposthenuria and are at high risk of dehydration, hypovolemic hypotension and shock. Patients are found to have complete sensorineural deafness. Recurrent vomiting, muscle cramps, spasms and failure to thrive are observed. Progression to renal failure is frequent. Hypokalemic alkalosis, hypomagnesemia, hyperprostaglandin E-uria and hypochloremia are noted (hypercalciuria is only transient).	NM_057176.3(BSND):c.23G>T ; NM_057176.3(BSND):c.1A>T ; NM_057176.3(BSND):c.139G>A ; NM_057176.3(BSND):c.3G>A ; NM_057176.3(BSND):c.22C>T ; NM_057176.3(BSND):c.10G>T ; NM_057176.3(BSND):c.23G>T ; NM_057176.3(BSND):c.1A>T ; NM_057176.3(BSND):c.139G>A ; NM_057176.3(BSND):c.3G>A ; NM_057176.3(BSND):c.22C>T ; NM_057176.3(BSND):c.10G>T
BTD	Biotinidase deficiency	A late-onset form of multiple carboxylase deficiency, an inborn error of biotin metabolism that, if untreated, is characterized by seizures, breathing difficulties, hypotonia, skin rash, alopecia, hearing loss and delayed development.	Symptoms of BD deficiency typically appear within the first few months of life, but later onset has also been reported. Individuals with untreated profound deficiency (less than 10 % of mean normal serum biotinidase activity) have variable clinical findings including seizures, hypotonia, eczematoid rash, alopecia, ataxia, hearing loss, fungal infections, and developmental delay. Metabolically, untreated children can exhibit ketolactic acidosis, organic acidemia (-uria) and mild hyperammonemia. Individuals with untreated partial BD (10% to 30% of mean normal biotinidase activity) may be asymptomatic, but during periods of stress, such as illness, fever or fasting, may develop symptoms similar to those of individuals with profound BD. Multiple adults with optic neuropathy and/or peripheral neuropathy, that is often mistakenly diagnosed as multiple sclerosis, have been shown to have profound biotinidase deficiency.	NM_001281725.2(BTD):c.1279C>T ; NM_001281723.2(BTD):c.241C>T ; NM_001281723.2(BTD):c.1601C>T ; NM_001281723.2(BTD):c.635A>G ; NM_001281723.2(BTD):c.449G>A ; NM_001281723.2(BTD):c.190G>A ; NM_001281725.2(BTD):c.1292G>A ; NM_000060.4(BTD):c.1324del ; NM_001281723.2(BTD):c.761A>G ; NM_001281723.2(BTD):c.340G>C ; NM_001281723.2(BTD):c.1618C>T ; NM_001281723.2(BTD):c.1495C>T ; NM_000060.4(BTD):c.1508_1512delGGATG ; NM_001281723.2(BTD):c.649C>T ; NM_001281723.2(BTD):c.601G>A ; NM_001281723.2(BTD):c.637C>T ; NM_001281723.2(BTD):c.534G>T ; NM_001281723.2(BTD):c.563G>A ; NM_000060.2(BTD):c.933delT ; NM_001281724.2(BTD):c.1374A>C ; NM_001281723.2(BTD):c.800A>T ; NM_001281725.2(BTD):c.1279C>T ; NM_001281723.2(BTD):c.241C>T ; NM_001281723.2(BTD):c.1601C>T ; NM_001281723.2(BTD):c.635A>G ; NM_001281723.2(BTD):c.449G>A ; NM_001281723.2(BTD):c.190G>A ; NM_001281725.2(BTD):c.1292G>A ; NM_000060.4(BTD):c.1324del ; NM_001281723.2(BTD):c.761A>G ; NM_001281723.2(BTD):c.340G>C ; NM_001281723.2(BTD):c.1618C>T ; NM_001281723.2(BTD):c.1495C>T ; NM_000060.4(BTD):c.1508_1512delGGATG ; NM_001281723.2(BTD):c.649C>T ; NM_001281723.2(BTD):c.601G>A ; NM_001281723.2(BTD):c.637C>T ; NM_001281723.2(BTD):c.534G>T ; NM_001281723.2(BTD):c.563G>A ; NM_000060.2(BTD):c.933delT ; NM_001281724.2(BTD):c.1374A>C ; NM_001281723.2(BTD):c.800A>T

BTK	Short stature due to isolated growth hormone deficiency with X-linked hypogammaglobulinemia	IGHD3 is characterized by agammaglobulinemia and markedly reduced numbers of B cells, short stature, delayed bone age, and good response to treatment with growth hormone.	X-linked agammaglobulinemia is an immunodeficiency characterized by failure to produce mature B lymphocytes and associated with a failure of Ig heavy chain rearrangement. The defect in this disorder resides in BTK, also known as BPK or ATK, a key regulator in B-cell development. The X-linked form accounts for approximately 85 to 90% of cases of the disorder.	NM_000061.2(BTK):c.763C>T ; NM_000061.2(BTK):c.1766A>G ; NM_000061.2(BTK):c.919A>G ; NM_000061.2(BTK):c.1906G>T ; NM_000061.2(BTK):c.718G>T ; NM_000061.2(BTK):c.755G>A ; NM_000061.2(BTK):c.862C>T ; NM_000061.2(BTK):c.1559G>A ; NM_000061.2(BTK):c.1516T>C ; NM_000061.2(BTK):c.1082A>G ; NM_000061.2(BTK):c.1838G>A ; NM_000061.2(BTK):c.1773C>A ; NM_000061.2(BTK):c.1125T>G ; NM_000061.2(BTK):c.1288A>G ; NM_000061.2(BTK):c.338T>A ; NM_000061.2(BTK):c.1889T>A ; NM_000061.2(BTK):c.1558C>T ; NM_000061.2(BTK):c.1001A>C ; NM_000061.2(BTK):c.1820C>A ; NM_000061.2(BTK):c.1506C>A ; NM_000061.2(BTK):c.1275C>A ; NM_000061.2(BTK):c.1223T>C ; NM_000061.2(BTK):c.763C>T ; NM_000061.2(BTK):c.1766A>G ; NM_000061.2(BTK):c.919A>G ; NM_000061.2(BTK):c.1906G>T ; NM_000061.2(BTK):c.718G>T ; NM_000061.2(BTK):c.755G>A ; NM_000061.2(BTK):c.862C>T ; NM_000061.2(BTK):c.1559G>A ; NM_000061.2(BTK):c.1516T>C ; NM_000061.2(BTK):c.1082A>G ; NM_000061.2(BTK):c.1838G>A ; NM_000061.2(BTK):c.1773C>A ; NM_000061.2(BTK):c.1125T>G ; NM_000061.2(BTK):c.1288A>G ; NM_000061.2(BTK):c.338T>A ; NM_000061.2(BTK):c.1889T>A ; NM_000061.2(BTK):c.1558C>T ; NM_000061.2(BTK):c.1001A>C ; NM_000061.2(BTK):c.1820C>A ; NM_000061.2(BTK):c.1506C>A ; NM_000061.2(BTK):c.1275C>A ; NM_000061.2(BTK):c.1223T>C
BTK	X-linked agammaglobulinemia	A clinically variable form of isolated agammaglobulinemia, an inherited immunodeficiency disorder, characterized in affected males by recurrent bacterial infections during infancy.	Affected individuals are usually healthy in the first few months of life due to residual maternal immunoglobulins. The majority of patients develop recurrent or persistent bacterial infections, most commonly caused by S. pneumoniae and H. influenzae, within the first two years of life,: otitis media, conjunctivitis, sinusitis, respiratory infections, diarrhea and skin infections (impetigo, cellulitis, abscesses, and furuncles). Other severe infections may include empyema, meningitis, sepsis, or septic arthritis. Pyoderma or cellulitis (associated with neutropenia) and pseudomonas or staphylococcal sepsis are frequent presenting findings, particularly in patients less than 12 months of age. Lymph nodes, tonsils, and other lymphoid tissues are unusually small or absent. Rare patients are reported to have vitiligo, erythematous rash, or alopecia totalis. Infections tend to persist throughout adulthood. Affected patients are reported to have a higher susceptibility to severe and chronic enteroviral infections. Growth and development are usually normal. Some patients have a less severe clinical presentation and are not recognized as immunodeficient until 10 years of age or later. Complications of X-linked agammaglobulinemia (XLA) include progressive lung disease, chronic sinusitis, inflammatory bowel disease, arthritis , as well as neurological changes.	NM_000061.2(BTK):c.763C>T ; NM_000061.2(BTK):c.1766A>G ; NM_000061.2(BTK):c.919A>G ; NM_000061.2(BTK):c.1906G>T ; NM_000061.2(BTK):c.718G>T ; NM_000061.2(BTK):c.755G>A ; NM_000061.2(BTK):c.862C>T ; NM_000061.2(BTK):c.1559G>A ; NM_000061.2(BTK):c.1516T>C ; NM_000061.2(BTK):c.1082A>G ; NM_000061.2(BTK):c.1838G>A ; NM_000061.2(BTK):c.1773C>A ; NM_000061.2(BTK):c.1125T>G ; NM_000061.2(BTK):c.1288A>G ; NM_000061.2(BTK):c.338T>A ; NM_000061.2(BTK):c.1889T>A ; NM_000061.2(BTK):c.1558C>T ; NM_000061.2(BTK):c.1001A>C ; NM_000061.2(BTK):c.1820C>A ; NM_000061.2(BTK):c.1506C>A ; NM_000061.2(BTK):c.1275C>A ; NM_000061.2(BTK):c.1223T>C ; NM_000061.2(BTK):c.763C>T ; NM_000061.2(BTK):c.1766A>G ; NM_000061.2(BTK):c.919A>G ; NM_000061.2(BTK):c.1906G>T ; NM_000061.2(BTK):c.718G>T ; NM_000061.2(BTK):c.755G>A ; NM_000061.2(BTK):c.862C>T ; NM_000061.2(BTK):c.1559G>A ; NM_000061.2(BTK):c.1516T>C ; NM_000061.2(BTK):c.1082A>G ; NM_000061.2(BTK):c.1838G>A ; NM_000061.2(BTK):c.1773C>A ; NM_000061.2(BTK):c.1125T>G ; NM_000061.2(BTK):c.1288A>G ; NM_000061.2(BTK):c.338T>A ; NM_000061.2(BTK):c.1889T>A ; NM_000061.2(BTK):c.1558C>T ; NM_000061.2(BTK):c.1001A>C ; NM_000061.2(BTK):c.1820C>A ; NM_000061.2(BTK):c.1506C>A ; NM_000061.2(BTK):c.1275C>A ; NM_000061.2(BTK):c.1223T>C

CAPN3	Calpain-3-related limb-girdle muscular dystrophy R1	A subtype of autosomal recessive limb girdle muscular dystrophy characterized by a variable age of onset of progressive, typically symmetrical and selective weakness and atrophy of proximal shoulder- and pelvic-girdle muscles (gluteus maximus, thigh adductors, and muscles of the posterior compartment of the limbs are most commonly affected) without cardiac or facial involvement. Clinical manifestations include exercise intolerance, a waddling gait, scapular winging and calf pseudo-hypertrophy.	Autosomal recessive limb-girdle muscular dystrophy-1 affects primarily the proximal muscles, resulting in difficulty walking. The age at onset varies, but most patients show onset in childhood, and the disorder is progressive. Other features may include scapular winging, calf pseudohypertrophy, and contractures.	NM_000070.2(CAPN3):c.2251_2254dupGTCA ; NM_000070.2(CAPN3):c.1715G>A ; NM_000070.2(CAPN3):c.1468C>T ; c.217C>T ; NM_000070.2(CAPN3):c.580delT ; NM_000070.2(CAPN3):c.2362_2363delAGinsTCATCT ; NM_000070.2(CAPN3):c.223dupT ; NM_000070.2(CAPN3):c.1466G>A ; NM_000070.2(CAPN3):c.2120A>G ; NM_000070.2(CAPN3):c.855_864dupGTTGATTGCA ; c.1455_1458del ; NM_000070.2(CAPN3):c.2306G>A ; NM_000070.2(CAPN3):c.1469G>A ; NM_000070.2(CAPN3):c.598_612delTTCTGGAGTGCTCTG ; NM_000070.2(CAPN3):c.1795dupA ; NM_000070.3(CAPN3):c.549delA ; NM_000070.2(CAPN3):c.133G>A ; NM_000070.2(CAPN3):c.1838delA ; NM_000070.2(CAPN3):c.257C>T ; NM_000070.2(CAPN3):c.2243G>A ; NM_000070.2(CAPN3):c.328C>T ; NM_000070.2(CAPN3):c.1322delG ; c.367_368delinsTCATCT ; NM_000070.2(CAPN3):c.2251_2254dupGTCA ; NM_000070.2(CAPN3):c.1715G>A ; NM_000070.2(CAPN3):c.1468C>T ; c.217C>T ; NM_000070.2(CAPN3):c.580delT ; NM_000070.2(CAPN3):c.2362_2363delAGinsTCATCT ; NM_000070.2(CAPN3):c.223dupT ; NM_000070.2(CAPN3):c.1466G>A ; NM_000070.2(CAPN3):c.2120A>G ; NM_000070.2(CAPN3):c.855_864dupGTTGATTGCA ; c.1455_1458del ; NM_000070.2(CAPN3):c.2306G>A ; NM_000070.2(CAPN3):c.1469G>A ; NM_000070.2(CAPN3):c.598_612delTTCTGGAGTGCTCTG ; NM_000070.2(CAPN3):c.1795dupA ; NM_000070.3(CAPN3):c.549delA ; NM_000070.2(CAPN3):c.133G>A ; NM_000070.2(CAPN3):c.1838delA ; NM_000070.2(CAPN3):c.257C>T ; NM_000070.2(CAPN3):c.2243G>A ; NM_000070.2(CAPN3):c.328C>T ; NM_000070.2(CAPN3):c.1322delG ; c.367_368delinsTCATCT
CBS	Classic homocystinuria	Classical homocystinuria due to cystathionine beta-synthase (CbS) deficiency is characterized by the multiple involvement of the eye, skeleton, central nervous system, and vascular system.	Patients are normal at birth and, if left untreated, the disease course is progressive. Eye anomalies include ectopia lentis (85% of the cases), with high myopia. Skeletal changes include genu valgum and pes cavus, followed by dolichostenomelia, pectus excavatum or carinatum and kyphosis, or scoliosis and osteoporosis. Thromboembolism, affecting both large and small arteries and veins, is the most striking cause of morbidity and mortality. Intellectual deficiency rarely manifests before the first to second year of life. Clinically significant psychiatric illness is found in 51% of cases. Involvement of the liver, hair, and skin has also been reported.	NM_000071.2(CBS):c.374G>A ; NM_000071.2(CBS):c.146C>T ; NM_000071.2(CBS):c.415G>A ; c.526G>T ; NM_000071.2(CBS):c.1058C>T ; NM_000071.2(CBS):c.969G>A ; NM_000071.2(CBS):c.797G>A ; NM_000071.2(CBS):c.1330G>A ; NM_000071.2(CBS):c.1136G>A ; NM_000071.2(CBS):c.1150A>G ; NM_000071.2(CBS):c.1006C>T ; NM_000071.2(CBS):c.325T>C ; NM_000071.2(CBS):c.572C>T ; NM_000071.2(CBS):c.992C>A ; NM_000071.2(CBS):c.919G>A ; NM_000071.2(CBS):c.959T>C ; NM_000071.2(CBS):c.341C>T ; NM_000071.2(CBS):c.374G>A ; NM_000071.2(CBS):c.146C>T ; NM_000071.2(CBS):c.415G>A ; c.526G>T ; NM_000071.2(CBS):c.1058C>T ; NM_000071.2(CBS):c.969G>A ; NM_000071.2(CBS):c.797G>A ; NM_000071.2(CBS):c.1330G>A ; NM_000071.2(CBS):c.1136G>A ; NM_000071.2(CBS):c.1150A>G ; NM_000071.2(CBS):c.1006C>T ; NM_000071.2(CBS):c.325T>C ; NM_000071.2(CBS):c.572C>T ; NM_000071.2(CBS):c.992C>A ; NM_000071.2(CBS):c.919G>A ; NM_000071.2(CBS):c.959T>C ; NM_000071.2(CBS):c.341C>T

CDH23	Autosomal recessive non-syndromic sensorineural deafness type DFNB	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	c.3141C>A ; NM_022124.5(CDH23):c.6050-9G>A ; NM_022124.5(CDH23):c.5663T>C ; c.3579+2T>C ; c.9319+3_9319+6del ; c.288+1G>A ; c.3516_3519del ; c.1858+2T>G ; NC_000010.11:g.71740837C>T ; NM_022124.5(CDH23):c.193delC ; NM_022124.5(CDH23):c.5237G>A ; c.6393del ; NM_022124.5(CDH23):c.146-2A>G ; c.3141C>A ; NM_022124.5(CDH23):c.6050-9G>A ; NM_022124.5(CDH23):c.5663T>C ; c.3579+2T>C ; c.9319+3_9319+6del ; c.288+1G>A ; c.3516_3519del ; c.1858+2T>G ; NC_000010.11:g.71740837C>T ; NM_022124.5(CDH23):c.193delC ; NM_022124.5(CDH23):c.5237G>A ; c.6393del ; NM_022124.5(CDH23):c.146-2A>G
CDH23	Cushing disease	Cushing disease (CD) is the most common cause of endogenous Cushing syndrome (CS; see this term) and is due to pituitary chronic over-secretion of ACTH by a pituitary corticotroph adenoma.	The female-to-male ratio of CD is 4-5:1, except in prepubertal patients, in which a strong male predominance is observed. The peak incidence is at 25-40 years of age. The disease manifests with signs of CS (truncal and facial obesity and signs of hypercatabolism) as well as skin hyperpigmentation and/or neurological complications in some cases of corticotroph macro-adenoma.	c.3141C>A ; NM_022124.5(CDH23):c.6050-9G>A ; NM_022124.5(CDH23):c.5663T>C ; c.3579+2T>C ; c.9319+3_9319+6del ; c.288+1G>A ; c.3516_3519del ; c.1858+2T>G ; NC_000010.11:g.71740837C>T ; NM_022124.5(CDH23):c.193delC ; NM_022124.5(CDH23):c.5237G>A ; c.6393del ; NM_022124.5(CDH23):c.146-2A>G

CDH23	Familial isolated pituitary adenoma	A rare, hereditary endocrine tumor characterized by a benign pituitary adenoma that is either secreting (e.g. prolactin, growth hormone, thyroid stimulating hormone) or non-secreting. Symptoms may occur due to either the hormonal hypersecretion and/or the mass effect of the lesion on local structures in the brain.	In FIPA, pituitary adenomas can be of any secretory type (e.g. prolactinoma, acromegaly, Cushing's disease, TSH-secreting) or can be non-secreting. FIPA kindreds usually have 2-4 members affected with pituitary adenomas, while larger numbers of affected patients per family can occur infrequently. In FIPA, pituitary adenomas generally begin at a younger age and are larger than corresponding sporadic non-FIPA cases. Pituitary adenomas in FIPA can cause symptoms due to hormonal hypersecretion and/or due to the mass effect of the pituitary adenoma on local structures in the brain (e.g. visual disturbance). In FIPA families withÂ AIPÂ mutations pituitary adenoma growth characteristics are often aggressive and hormonal hypersecretion may be marked.	c.3141C>A ; NM_022124.5(CDH23):c.6050-9G>A ; NM_022124.5(CDH23):c.5663T>C ; c.3579+2T>C ; c.9319+3_9319+6del ; c.288+1G>A ; c.3516_3519del ; c.1858+2T>G ; NC_000010.11:g.71740837C>T ; NM_022124.5(CDH23):c.193delC ; NM_022124.5(CDH23):c.5237G>A ; c.6393del ; NM_022124.5(CDH23):c.146-2A>G ; c.3141C>A ; NM_022124.5(CDH23):c.6050-9G>A ; NM_022124.5(CDH23):c.5663T>C ; c.3579+2T>C ; c.9319+3_9319+6del ; c.288+1G>A ; c.3516_3519del ; c.1858+2T>G ; NC_000010.11:g.71740837C>T ; NM_022124.5(CDH23):c.193delC ; NM_022124.5(CDH23):c.5237G>A ; c.6393del ; NM_022124.5(CDH23):c.146-2A>G
CDH23	Prolactinoma	A rare, usually benign, neoplasm of the anterior pituitary gland that results in hyperprolactinemia. The most common clinical manifestations are amenorrhea and infertility in women; and impotence, decreased libido and infertility in men.	Disease onset is usually in the second to fourth decades of life with galactorrhea, amenorrhea and infertility presenting in women and impotence, decreased libido and infertility in men. In male patients prolactinoma may exhibit more aggressive clinical course. Prolactinoma can also cause mass effects (visual field defects, headaches) or psychiatric manifestations (anxiety, depression).	c.3141C>A ; NM_022124.5(CDH23):c.6050-9G>A ; NM_022124.5(CDH23):c.5663T>C ; c.3579+2T>C ; c.9319+3_9319+6del ; c.288+1G>A ; c.3516_3519del ; c.1858+2T>G ; NC_000010.11:g.71740837C>T ; NM_022124.5(CDH23):c.193delC ; NM_022124.5(CDH23):c.5237G>A ; c.6393del ; NM_022124.5(CDH23):c.146-2A>G ; c.3141C>A ; NM_022124.5(CDH23):c.6050-9G>A ; NM_022124.5(CDH23):c.5663T>C ; c.3579+2T>C ; c.9319+3_9319+6del ; c.288+1G>A ; c.3516_3519del ; c.1858+2T>G ; NC_000010.11:g.71740837C>T ; NM_022124.5(CDH23):c.193delC ; NM_022124.5(CDH23):c.5237G>A ; c.6393del ; NM_022124.5(CDH23):c.146-2A>G

CDH23	TSH-secreting pituitary adenoma	Both familial and sporadic pituitary adenomas have been found to be caused by germline mutation in the CDH23 gene. Familial pituitary adenoma types include growth hormone (GH)-secreting and nonfunctional tumors. Sporadic pituitary adenoma types include GH-secreting, nonfunctional, prolactin (PRL)-secreting, adrenocorticotropin (ACTH)-secreting, thyroid-stimulating hormone (TSH)-secreting, and plurihormonal (GH and TSH) tumors.	A rare, functioning, pituitary adenoma characterized by the presence of a pituitary mass associated with high levels of circulating, free, thyroid hormones in conjunction with normal to high levels of TSH and unresponsiveness of TSH levels to TRH stimulation and T3 suppression tests, typically manifesting with signs and symtoms of mild to moderate hyperthyroidism (e.g. goiter (most frequently observed), palpitation, excessive sweating, arrhythmia, weight loss, tremor) and/or tumor mass effect (such as headache, visual field defects, hypopituitarism). Occasionally, cosecretion of prolactin and/or growth hormone may cause galactorrhea and/or acromegaly.	c.3141C>A ; NM_022124.5(CDH23):c.6050-9G>A ; NM_022124.5(CDH23):c.5663T>C ; c.3579+2T>C ; c.9319+3_9319+6del ; c.288+1G>A ; c.3516_3519del ; c.1858+2T>G ; NC_000010.11:g.71740837C>T ; NM_022124.5(CDH23):c.193delC ; NM_022124.5(CDH23):c.5237G>A ; c.6393del ; NM_022124.5(CDH23):c.146-2A>G ; c.3141C>A ; NM_022124.5(CDH23):c.6050-9G>A ; NM_022124.5(CDH23):c.5663T>C ; c.3579+2T>C ; c.9319+3_9319+6del ; c.288+1G>A ; c.3516_3519del ; c.1858+2T>G ; NC_000010.11:g.71740837C>T ; NM_022124.5(CDH23):c.193delC ; NM_022124.5(CDH23):c.5237G>A ; c.6393del ; NM_022124.5(CDH23):c.146-2A>G

CDH23	Usher syndrome type 1	Usher syndrome type I is an autosomal recessive condition characterized by profound congenital hearing impairment with unintelligible speech, early retinitis pigmentosa (usually evident within the first decade), and constant vestibular dysfunction. Type I is distinguished from type II on the basis of severity of hearing loss and the extent of vestibular involvement. Type I patients are profoundly deaf, whereas type II patients are 'hard of hearing.' Vestibular function is defective in type I patients, whereas type II patients have normal vestibular function. Patients with type III (USH3) have progressive hearing loss.	A rare ciliopathy characterized by profound congenital deafness, retinitis pigmentosa and vestibular dysfunction. Retinitis pigmentosa results in visual loss and generally manifests as night blindness, progressively constricted visual fields, and impaired visual acuity. Vestibular dysfunction a defining feature of this form, manifests as delayed motor development with affected infants taking longer to sit independently and to walk. Later on, vestibular dysfunction results in difficulty with activities requiring balance.	c.3141C>A ; NM_022124.5(CDH23):c.6050-9G>A ; NM_022124.5(CDH23):c.5663T>C ; c.3579+2T>C ; c.9319+3_9319+6del ; c.288+1G>A ; c.3516_3519del ; c.1858+2T>G ; NC_000010.11:g.71740837C>T ; NM_022124.5(CDH23):c.193delC ; NM_022124.5(CDH23):c.5237G>A ; c.6393del ; NM_022124.5(CDH23):c.146-2A>G ; c.3141C>A ; NM_022124.5(CDH23):c.6050-9G>A ; NM_022124.5(CDH23):c.5663T>C ; c.3579+2T>C ; c.9319+3_9319+6del ; c.288+1G>A ; c.3516_3519del ; c.1858+2T>G ; NC_000010.11:g.71740837C>T ; NM_022124.5(CDH23):c.193delC ; NM_022124.5(CDH23):c.5237G>A ; c.6393del ; NM_022124.5(CDH23):c.146-2A>G
CEP290	Bardet-Biedl syndrome	Bardet-Biedl syndrome (BBS) is a ciliopathy with multisystem involvement.	This disorder is characterized by a combination of clinical signs: obesity, pigmentary retinopathy, post-axial polydactyly, polycystic kidneys, hypogenitalism, and learning disabilities, many of which appear several years after disease onset. Clinical expression is variable but most patients manifest the majority of clinical signs during the disease course. Pigmentary retinopathy is the only constant clinical sign after childhood. BBS may also be associated with several other manifestations including diabetes, hypertension, congenital cardiopathy and Hirschsprung disease (see this term).	NM_025114.3(CEP290):c.6798G>A ; NM_025114.3(CEP290):c.4393C>T ; NM_025114.3(CEP290):c.1665_1666delAA ; NM_025114.3(CEP290):c.4723A>T ; c.6624del ; NM_025114.3(CEP290):c.4705-1G>T ; NM_025114.3(CEP290):c.384_387delTAGA ; c.6448_6455del ; c.1681C>T ; NM_025114.3(CEP290):c.164_167delCTCA ; NM_025114.3(CEP290):c.613C>T ; c.4916C>A ; NM_025114.3(CEP290):c.21G>T ; NM_025114.3(CEP290):c.4962_4963delAA ; NM_025114.3(CEP290):c.5668G>T ; c.7324G>T ; NM_025114.3(CEP290):c.5611_5614delCAAA ; NM_025114.3(CEP290):c.3185delT ; c.1501G>T ; NM_025114.3(CEP290):c.2249T>G ; NM_025114.3(CEP290):c.6798G>A ; NM_025114.3(CEP290):c.4393C>T ; NM_025114.3(CEP290):c.1665_1666delAA ; NM_025114.3(CEP290):c.4723A>T ; c.6624del ; NM_025114.3(CEP290):c.4705-1G>T ; NM_025114.3(CEP290):c.384_387delTAGA ; c.6448_6455del ; c.1681C>T ; NM_025114.3(CEP290):c.164_167delCTCA ; NM_025114.3(CEP290):c.613C>T ; c.4916C>A ; NM_025114.3(CEP290):c.21G>T ; NM_025114.3(CEP290):c.4962_4963delAA ; NM_025114.3(CEP290):c.5668G>T ; c.7324G>T ; NM_025114.3(CEP290):c.5611_5614delCAAA ; NM_025114.3(CEP290):c.3185delT ; c.1501G>T ; NM_025114.3(CEP290):c.2249T>G

CEP290	Joubert syndrome with oculorenal defect	A rare subtype of Joubert syndrome (JS) and related disorders (JSRD) characterized by the neurological features of JS associated with both renal and ocular disease.	Patients present retinal involvement (manifesting with either Leber congenital amaurosis (LCA, see this term), or progressive retinal dystrophy) and nephronophthisis (NPH, usually juvenile). Retinal involvement is present at birth (LCA) or may manifest later in life. Juvenile NPH usually becomes clinically symptomatic towards the late first decade or the early second decade of life.	NM_025114.3(CEP290):c.6798G>A ; NM_025114.3(CEP290):c.4393C>T ; NM_025114.3(CEP290):c.1665_1666delAA ; NM_025114.3(CEP290):c.4723A>T ; c.6624del ; NM_025114.3(CEP290):c.4705-1G>T ; NM_025114.3(CEP290):c.384_387delTAGA ; c.6448_6455del ; c.1681C>T ; NM_025114.3(CEP290):c.164_167delCTCA ; NM_025114.3(CEP290):c.613C>T ; c.4916C>A ; NM_025114.3(CEP290):c.21G>T ; NM_025114.3(CEP290):c.4962_4963delAA ; NM_025114.3(CEP290):c.5668G>T ; c.7324G>T ; NM_025114.3(CEP290):c.5611_5614delCAAA ; NM_025114.3(CEP290):c.3185delT ; c.1501G>T ; NM_025114.3(CEP290):c.2249T>G ; NM_025114.3(CEP290):c.6798G>A ; NM_025114.3(CEP290):c.4393C>T ; NM_025114.3(CEP290):c.1665_1666delAA ; NM_025114.3(CEP290):c.4723A>T ; c.6624del ; NM_025114.3(CEP290):c.4705-1G>T ; NM_025114.3(CEP290):c.384_387delTAGA ; c.6448_6455del ; c.1681C>T ; NM_025114.3(CEP290):c.164_167delCTCA ; NM_025114.3(CEP290):c.613C>T ; c.4916C>A ; NM_025114.3(CEP290):c.21G>T ; NM_025114.3(CEP290):c.4962_4963delAA ; NM_025114.3(CEP290):c.5668G>T ; c.7324G>T ; NM_025114.3(CEP290):c.5611_5614delCAAA ; NM_025114.3(CEP290):c.3185delT ; c.1501G>T ; NM_025114.3(CEP290):c.2249T>G
CEP290	Leber congenital amaurosis	Leber congenital amaurosis (LCA) is a retinal dystrophy defined by blindness and responses to electrophysiological stimulation (Ganzfeld electroretinogram (ERG)) below threshold, associated with severe visual impairment within the first year of life.	LCA is characterized by severely reduced visual acuity (less or equal 20/400) or blindness within in the first year of life. Sluggish pupillary responses, roving eye movement, photophobia, high hyperopia, nystagmus, convergent strabismus, or keratoconus may occur depending on the genetic cause. The Franceschetti's oculo-digital sign, comprising eye poking, pressing, and rubbing is pathognomonic. LCA may be associated with mutations in genes linked to syndromes presenting with neurodevelopmental delay, intellectual disability, oculomotor apraxia-type behavior (difficulty moving the eye) and renal dysfunction.	NM_025114.3(CEP290):c.6798G>A ; NM_025114.3(CEP290):c.4393C>T ; NM_025114.3(CEP290):c.1665_1666delAA ; NM_025114.3(CEP290):c.4723A>T ; c.6624del ; NM_025114.3(CEP290):c.4705-1G>T ; NM_025114.3(CEP290):c.384_387delTAGA ; c.6448_6455del ; c.1681C>T ; NM_025114.3(CEP290):c.164_167delCTCA ; NM_025114.3(CEP290):c.613C>T ; c.4916C>A ; NM_025114.3(CEP290):c.21G>T ; NM_025114.3(CEP290):c.4962_4963delAA ; NM_025114.3(CEP290):c.5668G>T ; c.7324G>T ; NM_025114.3(CEP290):c.5611_5614delCAAA ; NM_025114.3(CEP290):c.3185delT ; c.1501G>T ; NM_025114.3(CEP290):c.2249T>G ; NM_025114.3(CEP290):c.6798G>A ; NM_025114.3(CEP290):c.4393C>T ; NM_025114.3(CEP290):c.1665_1666delAA ; NM_025114.3(CEP290):c.4723A>T ; c.6624del ; NM_025114.3(CEP290):c.4705-1G>T ; NM_025114.3(CEP290):c.384_387delTAGA ; c.6448_6455del ; c.1681C>T ; NM_025114.3(CEP290):c.164_167delCTCA ; NM_025114.3(CEP290):c.613C>T ; c.4916C>A ; NM_025114.3(CEP290):c.21G>T ; NM_025114.3(CEP290):c.4962_4963delAA ; NM_025114.3(CEP290):c.5668G>T ; c.7324G>T ; NM_025114.3(CEP290):c.5611_5614delCAAA ; NM_025114.3(CEP290):c.3185delT ; c.1501G>T ; NM_025114.3(CEP290):c.2249T>G

CEP290	Meckel syndrome	A rare, lethal, genetic, multiple congenital anomaly disorder characterized by the triad of brain malformation (mainly occipital encephalocele), large polycystic kidneys, and polydactyly, as well as associated abnormalities that may include cleft lip/palate, cardiac and genital anomalies, central nervous system (CNS) malformations, liver fibrosis, and bone dysplasia.	Fetuses affected by Meckel syndrome (MKS) survive only a few days to a few weeks at the most, or dieÃ in utero. The main CNS features include occipital encephalocele, hydrocephalus, anencephaly, holoprosencephaly, as well as Dandy-Walker. Large polycystic kidneys with cystic dysplasia are a constant feature of Meckel syndrome. Hepatic dysgenesis and liver fibrosis are frequent. Polydactyly may affect all four extremities and is typically postaxial (80%) or very rarely preaxial. Affected individuals have pulmonary hypoplasia secondary to oligohydramnios. Cleft lip and palate, microphthalmia and micrognathia may be observed. Cardiac malformations may include atrial septal defect, aorta coarctation, patent arterial duct, and valvular pulmonary stenosis. Incomplete development of internal and external genitalia, and cryptorchidism in males are common.	NM_025114.3(CEP290):c.6798G>A ; NM_025114.3(CEP290):c.4393C>T ; NM_025114.3(CEP290):c.1665_1666delAA ; NM_025114.3(CEP290):c.4723A>T ; c.6624del ; NM_025114.3(CEP290):c.4705-1G>T ; NM_025114.3(CEP290):c.384_387delTAGA ; c.6448_6455del ; c.1681C>T ; NM_025114.3(CEP290):c.164_167delCTCA ; NM_025114.3(CEP290):c.613C>T ; c.4916C>A ; NM_025114.3(CEP290):c.21G>T ; NM_025114.3(CEP290):c.4962_4963delAA ; NM_025114.3(CEP290):c.5668G>T ; c.7324G>T ; NM_025114.3(CEP290):c.5611_5614delCAAA ; NM_025114.3(CEP290):c.3185delT ; c.1501G>T ; NM_025114.3(CEP290):c.2249T>G ; NM_025114.3(CEP290):c.6798G>A ; NM_025114.3(CEP290):c.4393C>T ; NM_025114.3(CEP290):c.1665_1666delAA ; NM_025114.3(CEP290):c.4723A>T ; c.6624del ; NM_025114.3(CEP290):c.4705-1G>T ; NM_025114.3(CEP290):c.384_387delTAGA ; c.6448_6455del ; c.1681C>T ; NM_025114.3(CEP290):c.164_167delCTCA ; NM_025114.3(CEP290):c.613C>T ; c.4916C>A ; NM_025114.3(CEP290):c.21G>T ; NM_025114.3(CEP290):c.4962_4963delAA ; NM_025114.3(CEP290):c.5668G>T ; c.7324G>T ; NM_025114.3(CEP290):c.5611_5614delCAAA ; NM_025114.3(CEP290):c.3185delT ; c.1501G>T ; NM_025114.3(CEP290):c.2249T>G
CEP290	Senior-Loken syndrome	A rare autosomal recessive oculo-renal ciliopathy characterized by the association of nephronophthisis (NPHP), a chronic kidney disease, with retinal dystrophy.	The disease typically presents in the first two decades of life as a combination of nephronophthisis (NPH) with retinal degeneration. Depending on the genetic background either the visual disorder or chronic kidney disease determine the clinical picture. NPH typically presents with symptoms such as polyuria, polydipsia, secondary enuresis and anemia. Chronic kidney disease usually slowly progresses to end-stage kidney disease (ESKD). Ocular features include congenital or early-onset severe visual loss due to retinal dystrophy (Leber congenital amaurosis) or a milder phenotype determined by a slowly progressing tube-like restriction of visual fields and night blindness (tapeto-retinal degeneration). Funduscopy reveals various degrees of atrophic and pigmentary retinal alterations. In rare occasions, other additional clinical signs may be observed like liver fibrosis, obesity and neurologic disorders.	NM_025114.3(CEP290):c.6798G>A ; NM_025114.3(CEP290):c.4393C>T ; NM_025114.3(CEP290):c.1665_1666delAA ; NM_025114.3(CEP290):c.4723A>T ; c.6624del ; NM_025114.3(CEP290):c.4705-1G>T ; NM_025114.3(CEP290):c.384_387delTAGA ; c.6448_6455del ; c.1681C>T ; NM_025114.3(CEP290):c.164_167delCTCA ; NM_025114.3(CEP290):c.613C>T ; c.4916C>A ; NM_025114.3(CEP290):c.21G>T ; NM_025114.3(CEP290):c.4962_4963delAA ; NM_025114.3(CEP290):c.5668G>T ; c.7324G>T ; NM_025114.3(CEP290):c.5611_5614delCAAA ; NM_025114.3(CEP290):c.3185delT ; c.1501G>T ; NM_025114.3(CEP290):c.2249T>G

CERKL				c.312del ; NM_201548.4(CERKL):c.1012C>T ; c.1631_1647dup ; NM_201548.4(CERKL):c.769C>T ; NM_201548.4(CERKL):c.780del ; c.312del ; NM_201548.4(CERKL):c.1012C>T ; c.1631_1647dup ; NM_201548.4(CERKL):c.769C>T ; NM_201548.4(CERKL):c.780del
CFTR	Cystic fibrosis	A rare, genetic pulmonary disorder characterized by sweat, thick mucus secretions causing multisystem disease, chronic infections of the lungs, bulky diarrhea and short stature.	CF is chronic and usually progressive. Symptoms often start at birth and involve the lungs and gastrointestinal tract. A common presentation might include thick secretions and chronic infections in the lung, bulky diarrhea and short stature. Abnormal airway secretions, inflammation and infections lead to bronchiectasis and early death. CF-related diabetes (CFRD) occurs at high frequency, rising to nearly 50% of patients surviving to age 50. Male sterility is common. Individuals with mild phenotypes may have mild or absent respiratory symptoms in childhood, but some may have infertility or may develop bronchiectasis or pancreatitis later in life. These individuals are typically diagnosed by newborn screening, but may be diagnosed later in life.	NM_000492.3(CFTR):c.571T>G (p.Phe191Val) ; NM_000492.3(CFTR):c.592G>A (p.Ala198Thr) ; NM_000492.3(CFTR):c.1046C>T (p.Ala349Val) ; NM_000492.3(CFTR):c.1399C>T (p.Leu467Phe) ; NM_000492.3(CFTR):c.1684G>C (p.Val562Leu) ; NM_000492.3(CFTR):c.2249C>T (p.Pro750Leu) ; NM_000492.3(CFTR):c.2855T>C (p.Met952Thr) ; NM_000492.3(CFTR):c.2939T>A (p.Ile980Lys) ; NM_000492.3(CFTR):c.4056G>T (p.Gln1352His) ; NM_000492.3(CFTR):c.328G>T (p.Asp110Tyr) ; NM_000492.3(CFTR):c.445G>T (p.Gly149Ter) ; NM_000492.3(CFTR):c.1438G>T (p.Gly480Cys) ; NM_000492.3(CFTR):c.3067_3072delATAGTG (p.Ile1023_Val1024del) ; NM_000492.3(CFTR):c.3536_3539delCCAA (p.Thr1179Asnfs) ; NM_000492.3(CFTR):c.445G>A (p.Gly149Arg) ; NM_000492.4:c.115C>T ; NM_000492.4:c.178G>T ; NM_000492.4:c.200C>T ; NM_000492.4:c.223C>T ; NM_000492.4:c.254G>A ; NM_000492.4:c.262_263delTT ; NM_000492.4:c.273+1G>A ; NM_000492.4:c.274-1G>A ; NM_000492.4:c.274G>A ; NM_000492.4:c.274G>T ; NM_000492.4:c.292C>T ; NM_000492.4:c.328G>C ; NM_000492.4:c.349C>T ; NM_000492.4:c.366T>A ; NM_000492.4:c.442delA ; NM_000492.4:c.489+1G>T ; NM_000492.4:c.531delT ; NM_000048.4:c.532G>A ; NM_000492.4:c.577G>T ; NM_000492.4:c.579+1G>T ; NM_000492.4:c.579+3A>G ; NM_000492.4:c.579+5G>A ; NM_000492.4:c.595C>T ; NM_000492.4:c.613C>T ; NM_000492.4:c.617T>G ; NM_000492.4:c.658C>T ; c.708del ; NM_000492.4:c.720_741delAGGGAGAATGATGATGAAGTAC ; NM_000492.4:c.803delA ; NC_000007.14:g.117540159_117540161TCT[2] ; NM_000492.4:c.988G>T ; NM_000492.4:c.1000C>T ; NM_000492.4:c.1007T>A ; NM_000492.4:c.1013C>T ; NM_000492.4:c.1021_1022dupTC ; NM_000492.4:c.1021T>C ; NM_000492.4:c.1040G>A ; NM_000492.4:c.1040G>C ; NM_000492.4:c.1055G>A ; NM_000492.4:c.1081delT ; NM_000492.3(CFTR):c.1297_1303delTTCTCAC (p.Ser434Leufs) ; NM_000492.4:c.1327_1330dupGATA ; NM_000492.4:c.1340delA ; NM_000492.4:c.1364C>A ; NM_000492.4:c.1393-1G>A ; NM_000492.4:c.1397C>A ; NM_000492.4:c.1397C>G ; NM_000492.4:c.1400T>C ; NM_000492.4:c.1466C>A ; NM_000492.4:c.1475C>T ; NM_000492.4:c.1477C>T ; NM_000492.4:c.1519_1521delATC ; NM_000492.4:c.1521_1523delCTT ; NM_000492.4:c.1545_1546delTA ; NM_000492.4:c.1585-1G>A ; NM_000492.4:c.1624G>T ; NM_000492.4:c.1692delA ; NM_000492.3(CFTR):c.1706A>G (p.Tyr569Cys) ; NM_000492.4:c.1721C>A ; NM_000492.4:c.1766+1G>A ; NM_000492.3:c.1970delG ; NM_000492.4:c.2012delT ; NM_000492.4:c.2052dupA ; NM_000492.4:c.2052delA ; NM_000492.4:c.2125C>T ; NM_000492.4:c.2128A>T ; NM_000492.4:c.2175dupA ; NM_000492.4:c.2195T>G ; NM_000492.4:c.2215delG ; NM_000492.4:c.2537G>A ; NM_000492.3(CFTR):c.2538G>A (p.Trp846Ter) ; NM_000492.4:c.2551C>T ; NM_000492.4:c.2583delT ; NM_000492.4:c.2657+5G>A ; NM_000492.4:c.2668C>T ; NM_000492.4:c.2737_2738insG ; NM_000492.4:c.2739T>A ; NM_000492.4:c.2780T>C ; NM_000492.4:c.2834C>T ; NM_000492.3:c.2869_2870insG ; NM_000492.4:c.2875delG ; NM_000492.4:c.2908G>C ; NM_000492.4:c.2989-1G>A ; NM_000492.4:c.3140-26A>G ; NM_000492.4:c.3194T>C ; NM_000492.4:c.3196C>T ; NM_000492.4:c.3197G>A ; NM_000492.4:c.3230T>C ; NM_000492.4:c.3266G>A ; NM_000492.4:c.3276C>A ; NM_000492.4:c.3276C>G ; NM_000492.4:c.3302T>A ; NM_000492.4:c.3310G>T ; NM_000492.4:c.3528delC ; NM_000492.4:c.3587C>G ; NM_000492.4:c.3611G>A ; NM_000492.4:c.3612G>A ; NM_000492.4:c.3659delC ; NM_000492.4:c.3731G>A ; NM_000492.4:c.3744delA ; NM_000492.4:c.3752G>A ; NM_000492.4:c.3761T>G ; NM_000492.4:c.3764C>A ; NM_000492.4:c.3773dupT ; NM_000492.4:c.3846G>A ; NM_000492.4:c.3909C>G ; NM_000492.4:c.3937C>T ; NM_000492.4:c.4251delA ; NM_000492.3(CFTR):c.4426C>T (p.Gln1476Ter) ; NM_000492.4:c.2175dupA ; NM_000492.4:c.2175dupA ; NM_000492.4:c.4077_4080delTGTTinsAA
CFTR	Aquagenic palmoplantar keratoderma	A rare skin disease characterized by transient wrinkling of the skin, edema, formation of whitish papules, pruritus, burning sensation, or pain, on the palms and/or soles in response to contact with water. Duration of exposure and water temperature affect the rate of development and intensity of the lesions. The condition is more common in females than in males and frequently occurs in patients with cystic fibrosis.		NM_000492.3(CFTR):c.571T>G (p.Phe191Val) ; NM_000492.3(CFTR):c.592G>A (p.Ala198Thr) ; NM_000492.3(CFTR):c.1046C>T (p.Ala349Val) ; NM_000492.3(CFTR):c.1399C>T (p.Leu467Phe) ; NM_000492.3(CFTR):c.1684G>C (p.Val562Leu) ; NM_000492.3(CFTR):c.2249C>T (p.Pro750Leu) ; NM_000492.3(CFTR):c.2855T>C (p.Met952Thr) ; NM_000492.3(CFTR):c.2939T>A (p.Ile980Lys) ; NM_000492.3(CFTR):c.4056G>T (p.Gln1352His) ; NM_000492.3(CFTR):c.328G>T (p.Asp110Tyr) ; NM_000492.3(CFTR):c.445G>T (p.Gly149Ter) ; NM_000492.3(CFTR):c.1438G>T (p.Gly480Cys) ; NM_000492.3(CFTR):c.3067_3072delATAGTG (p.Ile1023_Val1024del) ; NM_000492.3(CFTR):c.3536_3539delCCAA (p.Thr1179Asnfs) ; NM_000492.3(CFTR):c.445G>A (p.Gly149Arg) ; NM_000492.4:c.115C>T ; NM_000492.4:c.178G>T ; NM_000492.4:c.200C>T ; NM_000492.4:c.223C>T ; NM_000492.4:c.254G>A ; NM_000492.4:c.262_263delTT ; NM_000492.4:c.273+1G>A ; NM_000492.4:c.274-1G>A ; NM_000492.4:c.274G>A ; NM_000492.4:c.274G>T ; NM_000492.4:c.292C>T ; NM_000492.4:c.328G>C ; NM_000492.4:c.349C>T ; NM_000492.4:c.366T>A ; NM_000492.4:c.442delA ; NM_000492.4:c.489+1G>T ; NM_000492.4:c.531delT ; NM_000048.4:c.532G>A ; NM_000492.4:c.577G>T ; NM_000492.4:c.579+1G>T ; NM_000492.4:c.579+3A>G ; NM_000492.4:c.579+5G>A ; NM_000492.4:c.595C>T ; NM_000492.4:c.613C>T ; NM_000492.4:c.617T>G ; NM_000492.4:c.658C>T ; c.708del ; NM_000492.4:c.720_741delAGGGAGAATGATGATGAAGTAC ; NM_000492.4:c.803delA ; NC_000007.14:g.117540159_117540161TCT[2] ; NM_000492.4:c.988G>T ; NM_000492.4:c.1000C>T ; NM_000492.4:c.1007T>A ; NM_000492.4:c.1013C>T ; NM_000492.4:c.1021_1022dupTC ; NM_000492.4:c.1021T>C ; NM_000492.4:c.1040G>A ; NM_000492.4:c.1040G>C ; NM_000492.4:c.1055G>A ; NM_000492.4:c.1081delT ; NM_000492.3(CFTR):c.1297_1303delTTCTCAC (p.Ser434Leufs) ; NM_000492.4:c.1327_1330dupGATA ; NM_000492.4:c.1340delA ; NM_000492.4:c.1364C>A ; NM_000492.4:c.1393-1G>A ; NM_000492.4:c.1397C>A ; NM_000492.4:c.1397C>G ; NM_000492.4:c.1400T>C ; NM_000492.4:c.1466C>A ; NM_000492.4:c.1475C>T ; NM_000492.4:c.1477C>T ; NM_000492.4:c.1519_1521delATC ; NM_000492.4:c.1521_1523delCTT ; NM_000492.4:c.1545_1546delTA ; NM_000492.4:c.1585-1G>A ; NM_000492.4:c.1624G>T ; NM_000492.4:c.1692delA ; NM_000492.3(CFTR):c.1706A>G (p.Tyr569Cys) ; NM_000492.4:c.1721C>A ; NM_000492.4:c.1766+1G>A ; NM_000492.3:c.1970delG ; NM_000492.4:c.2012delT ; NM_000492.4:c.2052dupA ; NM_000492.4:c.2052delA ; NM_000492.4:c.2125C>T ; NM_000492.4:c.2128A>T ; NM_000492.4:c.2175dupA ; NM_000492.4:c.2195T>G ; NM_000492.4:c.2215delG ; NM_000492.4:c.2537G>A ; NM_000492.3(CFTR):c.2538G>A (p.Trp846Ter) ; NM_000492.4:c.2551C>T ; NM_000492.4:c.2583delT ; NM_000492.4:c.2657+5G>A ; NM_000492.4:c.2668C>T ; NM_000492.4:c.2737_2738insG ; NM_000492.4:c.2739T>A ; NM_000492.4:c.2780T>C ; NM_000492.4:c.2834C>T ; NM_000492.3:c.2869_2870insG ; NM_000492.4:c.2875delG ; NM_000492.4:c.2908G>C ; NM_000492.4:c.2989-1G>A ; NM_000492.4:c.3140-26A>G ; NM_000492.4:c.3194T>C ; NM_000492.4:c.3196C>T ; NM_000492.4:c.3197G>A ; NM_000492.4:c.3230T>C ; NM_000492.4:c.3266G>A ; NM_000492.4:c.3276C>A ; NM_000492.4:c.3276C>G ; NM_000492.4:c.3302T>A ; NM_000492.4:c.3310G>T ; NM_000492.4:c.3528delC ; NM_000492.4:c.3587C>G ; NM_000492.4:c.3611G>A ; NM_000492.4:c.3612G>A ; NM_000492.4:c.3659delC ; NM_000492.4:c.3731G>A ; NM_000492.4:c.3744delA ; NM_000492.4:c.3752G>A ; NM_000492.4:c.3761T>G ; NM_000492.4:c.3764C>A ; NM_000492.4:c.3773dupT ; NM_000492.4:c.3846G>A ; NM_000492.4:c.3909C>G ; NM_000492.4:c.3937C>T ; NM_000492.4:c.4251delA ; NM_000492.3(CFTR):c.4426C>T (p.Gln1476Ter) ; NM_000492.4:c.2175dupA ; NM_000492.4:c.2175dupA ; NM_000492.4:c.4077_4080delTGTTinsAA

CFTR	Congenital bilateral absence of vas deferens	Congenital bilateral absence of the vas deferens (CBAVD) is a condition leading to male infertility.	Infertile patients with CBAVD produce small volumes of acidic sperm (<1 ml with a pH<7.0).	NM_000492.3(CFTR):c.571T>G (p.Phe191Val) ; NM_000492.3(CFTR):c.592G>A (p.Ala198Thr) ; NM_000492.3(CFTR):c.1046C>T (p.Ala349Val) ; NM_000492.3(CFTR):c.1399C>T (p.Leu467Phe) ; NM_000492.3(CFTR):c.1684G>C (p.Val562Leu) ; NM_000492.3(CFTR):c.2249C>T (p.Pro750Leu) ; NM_000492.3(CFTR):c.2855T>C (p.Met952Thr) ; NM_000492.3(CFTR):c.2939T>A (p.Ile980Lys) ; NM_000492.3(CFTR):c.4056G>T (p.Gln1352His) ; NM_000492.3(CFTR):c.328G>T (p.Asp110Tyr) ; NM_000492.3(CFTR):c.445G>T (p.Gly149Ter) ; NM_000492.3(CFTR):c.1438G>T (p.Gly480Cys) ; NM_000492.3(CFTR):c.3067_3072delATAGTG (p.Ile1023_Val1024del) ; NM_000492.3(CFTR):c.3536_3539delCCAA (p.Thr1179Asnfs) ; NM_000492.3(CFTR):c.445G>A (p.Gly149Arg) ; NM_000492.4:c.115C>T ; NM_000492.4:c.178G>T ; NM_000492.4:c.200C>T ; NM_000492.4:c.223C>T ; NM_000492.4:c.254G>A ; NM_000492.4:c.262_263delTT ; NM_000492.4:c.273+1G>A ; NM_000492.4:c.274-1G>A ; NM_000492.4:c.274G>A ; NM_000492.4:c.274G>T ; NM_000492.4:c.292C>T ; NM_000492.4:c.328G>C ; NM_000492.4:c.349C>T ; NM_000492.4:c.366T>A ; NM_000492.4:c.442delA ; NM_000492.4:c.489+1G>T ; NM_000492.4:c.531delT ; NM_000048.4:c.532G>A ; NM_000492.4:c.577G>T ; NM_000492.4:c.579+1G>T ; NM_000492.4:c.579+3A>G ; NM_000492.4:c.579+5G>A ; NM_000492.4:c.595C>T ; NM_000492.4:c.613C>T ; NM_000492.4:c.617T>G ; NM_000492.4:c.658C>T ; c.708del ; NM_000492.4:c.720_741delAGGGAGAATGATGATGAAGTAC ; NM_000492.4:c.803delA ; NC_000007.14:g.117540159_117540161TCT[2] ; NM_000492.4:c.988G>T ; NM_000492.4:c.1000C>T ; NM_000492.4:c.1007T>A ; NM_000492.4:c.1013C>T ; NM_000492.4:c.1021_1022dupTC ; NM_000492.4:c.1021T>C ; NM_000492.4:c.1040G>A ; NM_000492.4:c.1040G>C ; NM_000492.4:c.1055G>A ; NM_000492.4:c.1081delT ; NM_000492.3(CFTR):c.1297_1303delTTCTCAC (p.Ser434Leufs) ; NM_000492.4:c.1327_1330dupGATA ; NM_000492.4:c.1340delA ; NM_000492.4:c.1364C>A ; NM_000492.4:c.1393-1G>A ; NM_000492.4:c.1397C>A ; NM_000492.4:c.1397C>G ; NM_000492.4:c.1400T>C ; NM_000492.4:c.1466C>A ; NM_000492.4:c.1475C>T ; NM_000492.4:c.1477C>T ; NM_000492.4:c.1519_1521delATC ; NM_000492.4:c.1521_1523delCTT ; NM_000492.4:c.1545_1546delTA ; NM_000492.4:c.1585-1G>A ; NM_000492.4:c.1624G>T ; NM_000492.4:c.1692delA ; NM_000492.3(CFTR):c.1706A>G (p.Tyr569Cys) ; NM_000492.4:c.1721C>A ; NM_000492.4:c.1766+1G>A ; NM_000492.3:c.1970delG ; NM_000492.4:c.2012delT ; NM_000492.4:c.2052dupA ; NM_000492.4:c.2052delA ; NM_000492.4:c.2125C>T ; NM_000492.4:c.2128A>T ; NM_000492.4:c.2175dupA ; NM_000492.4:c.2195T>G ; NM_000492.4:c.2215delG ; NM_000492.4:c.2537G>A ; NM_000492.3(CFTR):c.2538G>A (p.Trp846Ter) ; NM_000492.4:c.2551C>T ; NM_000492.4:c.2583delT ; NM_000492.4:c.2657+5G>A ; NM_000492.4:c.2668C>T ; NM_000492.4:c.2737_2738insG ; NM_000492.4:c.2739T>A ; NM_000492.4:c.2780T>C ; NM_000492.4:c.2834C>T ; NM_000492.3:c.2869_2870insG ; NM_000492.4:c.2875delG ; NM_000492.4:c.2908G>C ; NM_000492.4:c.2989-1G>A ; NM_000492.4:c.3140-26A>G ; NM_000492.4:c.3194T>C ; NM_000492.4:c.3196C>T ; NM_000492.4:c.3197G>A ; NM_000492.4:c.3230T>C ; NM_000492.4:c.3266G>A ; NM_000492.4:c.3276C>A ; NM_000492.4:c.3276C>G ; NM_000492.4:c.3302T>A ; NM_000492.4:c.3310G>T ; NM_000492.4:c.3528delC ; NM_000492.4:c.3587C>G ; NM_000492.4:c.3611G>A ; NM_000492.4:c.3612G>A ; NM_000492.4:c.3659delC ; NM_000492.4:c.3731G>A ; NM_000492.4:c.3744delA ; NM_000492.4:c.3752G>A ; NM_000492.4:c.3761T>G ; NM_000492.4:c.3764C>A ; NM_000492.4:c.3773dupT ; NM_000492.4:c.3846G>A ; NM_000492.4:c.3909C>G ; NM_000492.4:c.3937C>T ; NM_000492.4:c.4251delA ; NM_000492.3(CFTR):c.4426C>T (p.Gln1476Ter) ; NM_000492.4:c.2175dupA ; NM_000492.4:c.2175dupA ; NM_000492.4:c.4077_4080delTGTTinsAA
CFTR	Hereditary chronic pancreatitis	A rare gastroenterologic disease characterized by recurrent acute pancreatitis and/or chronic pancreatitis in at least 2 first-degree relatives, or 3 or more second-degree relatives in 2 or more generations, for which no predisposing factors are identified. This rare inherited form of pancreatitis leads to irreversible damage to both exocrine and endocrine components of the pancreas.	Onset of HCP is typically early in life, during childhood and adolescence. The clinical presentation is highly variable and includes chronic or intermittent mild to severe abdominal pain associated with exocrine pancreatic insufficiency, leading to maldigestion and/or pancreatic endocrine insufficiency (glucose intolerance progressing to diabetes mellitus type 3c) in some cases. The disease is slowly progressive. The risk of developing pancreatic carcinoma after the age of 50 is elevated in patients with HCP. However, the exact risk increase is difficult to assess.	NM_000492.3(CFTR):c.571T>G (p.Phe191Val) ; NM_000492.3(CFTR):c.592G>A (p.Ala198Thr) ; NM_000492.3(CFTR):c.1046C>T (p.Ala349Val) ; NM_000492.3(CFTR):c.1399C>T (p.Leu467Phe) ; NM_000492.3(CFTR):c.1684G>C (p.Val562Leu) ; NM_000492.3(CFTR):c.2249C>T (p.Pro750Leu) ; NM_000492.3(CFTR):c.2855T>C (p.Met952Thr) ; NM_000492.3(CFTR):c.2939T>A (p.Ile980Lys) ; NM_000492.3(CFTR):c.4056G>T (p.Gln1352His) ; NM_000492.3(CFTR):c.328G>T (p.Asp110Tyr) ; NM_000492.3(CFTR):c.445G>T (p.Gly149Ter) ; NM_000492.3(CFTR):c.1438G>T (p.Gly480Cys) ; NM_000492.3(CFTR):c.3067_3072delATAGTG (p.Ile1023_Val1024del) ; NM_000492.3(CFTR):c.3536_3539delCCAA (p.Thr1179Asnfs) ; NM_000492.3(CFTR):c.445G>A (p.Gly149Arg) ; NM_000492.4:c.115C>T ; NM_000492.4:c.178G>T ; NM_000492.4:c.200C>T ; NM_000492.4:c.223C>T ; NM_000492.4:c.254G>A ; NM_000492.4:c.262_263delTT ; NM_000492.4:c.273+1G>A ; NM_000492.4:c.274-1G>A ; NM_000492.4:c.274G>A ; NM_000492.4:c.274G>T ; NM_000492.4:c.292C>T ; NM_000492.4:c.328G>C ; NM_000492.4:c.349C>T ; NM_000492.4:c.366T>A ; NM_000492.4:c.442delA ; NM_000492.4:c.489+1G>T ; NM_000492.4:c.531delT ; NM_000048.4:c.532G>A ; NM_000492.4:c.577G>T ; NM_000492.4:c.579+1G>T ; NM_000492.4:c.579+3A>G ; NM_000492.4:c.579+5G>A ; NM_000492.4:c.595C>T ; NM_000492.4:c.613C>T ; NM_000492.4:c.617T>G ; NM_000492.4:c.658C>T ; c.708del ; NM_000492.4:c.720_741delAGGGAGAATGATGATGAAGTAC ; NM_000492.4:c.803delA ; NC_000007.14:g.117540159_117540161TCT[2] ; NM_000492.4:c.988G>T ; NM_000492.4:c.1000C>T ; NM_000492.4:c.1007T>A ; NM_000492.4:c.1013C>T ; NM_000492.4:c.1021_1022dupTC ; NM_000492.4:c.1021T>C ; NM_000492.4:c.1040G>A ; NM_000492.4:c.1040G>C ; NM_000492.4:c.1055G>A ; NM_000492.4:c.1081delT ; NM_000492.3(CFTR):c.1297_1303delTTCTCAC (p.Ser434Leufs) ; NM_000492.4:c.1327_1330dupGATA ; NM_000492.4:c.1340delA ; NM_000492.4:c.1364C>A ; NM_000492.4:c.1393-1G>A ; NM_000492.4:c.1397C>A ; NM_000492.4:c.1397C>G ; NM_000492.4:c.1400T>C ; NM_000492.4:c.1466C>A ; NM_000492.4:c.1475C>T ; NM_000492.4:c.1477C>T ; NM_000492.4:c.1519_1521delATC ; NM_000492.4:c.1521_1523delCTT ; NM_000492.4:c.1545_1546delTA ; NM_000492.4:c.1585-1G>A ; NM_000492.4:c.1624G>T ; NM_000492.4:c.1692delA ; NM_000492.3(CFTR):c.1706A>G (p.Tyr569Cys) ; NM_000492.4:c.1721C>A ; NM_000492.4:c.1766+1G>A ; NM_000492.3:c.1970delG ; NM_000492.4:c.2012delT ; NM_000492.4:c.2052dupA ; NM_000492.4:c.2052delA ; NM_000492.4:c.2125C>T ; NM_000492.4:c.2128A>T ; NM_000492.4:c.2175dupA ; NM_000492.4:c.2195T>G ; NM_000492.4:c.2215delG ; NM_000492.4:c.2537G>A ; NM_000492.3(CFTR):c.2538G>A (p.Trp846Ter) ; NM_000492.4:c.2551C>T ; NM_000492.4:c.2583delT ; NM_000492.4:c.2657+5G>A ; NM_000492.4:c.2668C>T ; NM_000492.4:c.2737_2738insG ; NM_000492.4:c.2739T>A ; NM_000492.4:c.2780T>C ; NM_000492.4:c.2834C>T ; NM_000492.3:c.2869_2870insG ; NM_000492.4:c.2875delG ; NM_000492.4:c.2908G>C ; NM_000492.4:c.2989-1G>A ; NM_000492.4:c.3140-26A>G ; NM_000492.4:c.3194T>C ; NM_000492.4:c.3196C>T ; NM_000492.4:c.3197G>A ; NM_000492.4:c.3230T>C ; NM_000492.4:c.3266G>A ; NM_000492.4:c.3276C>A ; NM_000492.4:c.3276C>G ; NM_000492.4:c.3302T>A ; NM_000492.4:c.3310G>T ; NM_000492.4:c.3528delC ; NM_000492.4:c.3587C>G ; NM_000492.4:c.3611G>A ; NM_000492.4:c.3612G>A ; NM_000492.4:c.3659delC ; NM_000492.4:c.3731G>A ; NM_000492.4:c.3744delA ; NM_000492.4:c.3752G>A ; NM_000492.4:c.3761T>G ; NM_000492.4:c.3764C>A ; NM_000492.4:c.3773dupT ; NM_000492.4:c.3846G>A ; NM_000492.4:c.3909C>G ; NM_000492.4:c.3937C>T ; NM_000492.4:c.4251delA ; NM_000492.3(CFTR):c.4426C>T (p.Gln1476Ter) ; NM_000492.4:c.2175dupA ; NM_000492.4:c.2175dupA ; NM_000492.4:c.4077_4080delTGTTinsAA

CFTR	Idiopathic bronchiectasis	Idiopathic bronchiectasis(IB) is a progressive lung disease characterized by chronic dilation of the bronchi and destruction of the bronchial walls in the absence of any underlying cause (such as post infectious disease, aspiration, immunodeficiency, congenital abnormalities and ciliary anomalies).		NM_000492.3(CFTR):c.571T>G (p.Phe191Val) ; NM_000492.3(CFTR):c.592G>A (p.Ala198Thr) ; NM_000492.3(CFTR):c.1046C>T (p.Ala349Val) ; NM_000492.3(CFTR):c.1399C>T (p.Leu467Phe) ; NM_000492.3(CFTR):c.1684G>C (p.Val562Leu) ; NM_000492.3(CFTR):c.2249C>T (p.Pro750Leu) ; NM_000492.3(CFTR):c.2855T>C (p.Met952Thr) ; NM_000492.3(CFTR):c.2939T>A (p.Ile980Lys) ; NM_000492.3(CFTR):c.4056G>T (p.Gln1352His) ; NM_000492.3(CFTR):c.328G>T (p.Asp110Tyr) ; NM_000492.3(CFTR):c.445G>T (p.Gly149Ter) ; NM_000492.3(CFTR):c.1438G>T (p.Gly480Cys) ; NM_000492.3(CFTR):c.3067_3072delATAGTG (p.Ile1023_Val1024del) ; NM_000492.3(CFTR):c.3536_3539delCCAA (p.Thr1179Asnfs) ; NM_000492.3(CFTR):c.445G>A (p.Gly149Arg) ; NM_000492.4:c.115C>T ; NM_000492.4:c.178G>T ; NM_000492.4:c.200C>T ; NM_000492.4:c.223C>T ; NM_000492.4:c.254G>A ; NM_000492.4:c.262_263delTT ; NM_000492.4:c.273+1G>A ; NM_000492.4:c.274-1G>A ; NM_000492.4:c.274G>A ; NM_000492.4:c.274G>T ; NM_000492.4:c.292C>T ; NM_000492.4:c.328G>C ; NM_000492.4:c.349C>T ; NM_000492.4:c.366T>A ; NM_000492.4:c.442delA ; NM_000492.4:c.489+1G>T ; NM_000492.4:c.531delT ; NM_000048.4:c.532G>A ; NM_000492.4:c.577G>T ; NM_000492.4:c.579+1G>T ; NM_000492.4:c.579+3A>G ; NM_000492.4:c.579+5G>A ; NM_000492.4:c.595C>T ; NM_000492.4:c.613C>T ; NM_000492.4:c.617T>G ; NM_000492.4:c.658C>T ; c.708del ; NM_000492.4:c.720_741delAGGGAGAATGATGATGAAGTAC ; NM_000492.4:c.803delA ; NC_000007.14:g.117540159_117540161TCT[2] ; NM_000492.4:c.988G>T ; NM_000492.4:c.1000C>T ; NM_000492.4:c.1007T>A ; NM_000492.4:c.1013C>T ; NM_000492.4:c.1021_1022dupTC ; NM_000492.4:c.1021T>C ; NM_000492.4:c.1040G>A ; NM_000492.4:c.1040G>C ; NM_000492.4:c.1055G>A ; NM_000492.4:c.1081delT ; NM_000492.3(CFTR):c.1297_1303delTTCTCAC (p.Ser434Leufs) ; NM_000492.4:c.1327_1330dupGATA ; NM_000492.4:c.1340delA ; NM_000492.4:c.1364C>A ; NM_000492.4:c.1393-1G>A ; NM_000492.4:c.1397C>A ; NM_000492.4:c.1397C>G ; NM_000492.4:c.1400T>C ; NM_000492.4:c.1466C>A ; NM_000492.4:c.1475C>T ; NM_000492.4:c.1477C>T ; NM_000492.4:c.1519_1521delATC ; NM_000492.4:c.1521_1523delCTT ; NM_000492.4:c.1545_1546delTA ; NM_000492.4:c.1585-1G>A ; NM_000492.4:c.1624G>T ; NM_000492.4:c.1692delA ; NM_000492.3(CFTR):c.1706A>G (p.Tyr569Cys) ; NM_000492.4:c.1721C>A ; NM_000492.4:c.1766+1G>A ; NM_000492.3:c.1970delG ; NM_000492.4:c.2012delT ; NM_000492.4:c.2052dupA ; NM_000492.4:c.2052delA ; NM_000492.4:c.2125C>T ; NM_000492.4:c.2128A>T ; NM_000492.4:c.2175dupA ; NM_000492.4:c.2195T>G ; NM_000492.4:c.2215delG ; NM_000492.4:c.2537G>A ; NM_000492.3(CFTR):c.2538G>A (p.Trp846Ter) ; NM_000492.4:c.2551C>T ; NM_000492.4:c.2583delT ; NM_000492.4:c.2657+5G>A ; NM_000492.4:c.2668C>T ; NM_000492.4:c.2737_2738insG ; NM_000492.4:c.2739T>A ; NM_000492.4:c.2780T>C ; NM_000492.4:c.2834C>T ; NM_000492.3:c.2869_2870insG ; NM_000492.4:c.2875delG ; NM_000492.4:c.2908G>C ; NM_000492.4:c.2989-1G>A ; NM_000492.4:c.3140-26A>G ; NM_000492.4:c.3194T>C ; NM_000492.4:c.3196C>T ; NM_000492.4:c.3197G>A ; NM_000492.4:c.3230T>C ; NM_000492.4:c.3266G>A ; NM_000492.4:c.3276C>A ; NM_000492.4:c.3276C>G ; NM_000492.4:c.3302T>A ; NM_000492.4:c.3310G>T ; NM_000492.4:c.3528delC ; NM_000492.4:c.3587C>G ; NM_000492.4:c.3611G>A ; NM_000492.4:c.3612G>A ; NM_000492.4:c.3659delC ; NM_000492.4:c.3731G>A ; NM_000492.4:c.3744delA ; NM_000492.4:c.3752G>A ; NM_000492.4:c.3761T>G ; NM_000492.4:c.3764C>A ; NM_000492.4:c.3773dupT ; NM_000492.4:c.3846G>A ; NM_000492.4:c.3909C>G ; NM_000492.4:c.3937C>T ; NM_000492.4:c.4251delA ; NM_000492.3(CFTR):c.4426C>T (p.Gln1476Ter) ; NM_000492.4:c.2175dupA ; NM_000492.4:c.2175dupA ; NM_000492.4:c.4077_4080delTGTTinsAA
CFTR	Male infertility with azoospermia or oligozoospermia due to single gene mutation	Male infertility with azoospermia or oligospermia due to single gene mutation is a rare, genetic male infertility due to sperm disorder characterized by the absence of a measurable amount of spermatozoa in the ejaculate (azoospermia), or a number of sperm in the ejaculate inferior to 15 million/mL (oligozoospermia), resulting from a mutation in a single gene known to cause azoo- or oligo-spermia. Sperm morphology may be normal.	Congenital bilateral aplasia of the vas deferens (CBAVD), which leads to male infertility, may occur in isolation or as a manifestation of cystic fibrosis.Â It has beenÂ found that males with cystic fibrosis are infertile because of failure of normal development of the vas deferens.Â OthersÂ concluded that the changes in the transport ducts of the male genital system are responsible for infertility and are not a developmental anomaly but a degenerative change due to obstruction similar to that which occurs in the pancreas and salivary glands in cystic fibrosis.Â	NM_000492.3(CFTR):c.571T>G (p.Phe191Val) ; NM_000492.3(CFTR):c.592G>A (p.Ala198Thr) ; NM_000492.3(CFTR):c.1046C>T (p.Ala349Val) ; NM_000492.3(CFTR):c.1399C>T (p.Leu467Phe) ; NM_000492.3(CFTR):c.1684G>C (p.Val562Leu) ; NM_000492.3(CFTR):c.2249C>T (p.Pro750Leu) ; NM_000492.3(CFTR):c.2855T>C (p.Met952Thr) ; NM_000492.3(CFTR):c.2939T>A (p.Ile980Lys) ; NM_000492.3(CFTR):c.4056G>T (p.Gln1352His) ; NM_000492.3(CFTR):c.328G>T (p.Asp110Tyr) ; NM_000492.3(CFTR):c.445G>T (p.Gly149Ter) ; NM_000492.3(CFTR):c.1438G>T (p.Gly480Cys) ; NM_000492.3(CFTR):c.3067_3072delATAGTG (p.Ile1023_Val1024del) ; NM_000492.3(CFTR):c.3536_3539delCCAA (p.Thr1179Asnfs) ; NM_000492.3(CFTR):c.445G>A (p.Gly149Arg) ; NM_000492.4:c.115C>T ; NM_000492.4:c.178G>T ; NM_000492.4:c.200C>T ; NM_000492.4:c.223C>T ; NM_000492.4:c.254G>A ; NM_000492.4:c.262_263delTT ; NM_000492.4:c.273+1G>A ; NM_000492.4:c.274-1G>A ; NM_000492.4:c.274G>A ; NM_000492.4:c.274G>T ; NM_000492.4:c.292C>T ; NM_000492.4:c.328G>C ; NM_000492.4:c.349C>T ; NM_000492.4:c.366T>A ; NM_000492.4:c.442delA ; NM_000492.4:c.489+1G>T ; NM_000492.4:c.531delT ; NM_000048.4:c.532G>A ; NM_000492.4:c.577G>T ; NM_000492.4:c.579+1G>T ; NM_000492.4:c.579+3A>G ; NM_000492.4:c.579+5G>A ; NM_000492.4:c.595C>T ; NM_000492.4:c.613C>T ; NM_000492.4:c.617T>G ; NM_000492.4:c.658C>T ; c.708del ; NM_000492.4:c.720_741delAGGGAGAATGATGATGAAGTAC ; NM_000492.4:c.803delA ; NC_000007.14:g.117540159_117540161TCT[2] ; NM_000492.4:c.988G>T ; NM_000492.4:c.1000C>T ; NM_000492.4:c.1007T>A ; NM_000492.4:c.1013C>T ; NM_000492.4:c.1021_1022dupTC ; NM_000492.4:c.1021T>C ; NM_000492.4:c.1040G>A ; NM_000492.4:c.1040G>C ; NM_000492.4:c.1055G>A ; NM_000492.4:c.1081delT ; NM_000492.3(CFTR):c.1297_1303delTTCTCAC (p.Ser434Leufs) ; NM_000492.4:c.1327_1330dupGATA ; NM_000492.4:c.1340delA ; NM_000492.4:c.1364C>A ; NM_000492.4:c.1393-1G>A ; NM_000492.4:c.1397C>A ; NM_000492.4:c.1397C>G ; NM_000492.4:c.1400T>C ; NM_000492.4:c.1466C>A ; NM_000492.4:c.1475C>T ; NM_000492.4:c.1477C>T ; NM_000492.4:c.1519_1521delATC ; NM_000492.4:c.1521_1523delCTT ; NM_000492.4:c.1545_1546delTA ; NM_000492.4:c.1585-1G>A ; NM_000492.4:c.1624G>T ; NM_000492.4:c.1692delA ; NM_000492.3(CFTR):c.1706A>G (p.Tyr569Cys) ; NM_000492.4:c.1721C>A ; NM_000492.4:c.1766+1G>A ; NM_000492.3:c.1970delG ; NM_000492.4:c.2012delT ; NM_000492.4:c.2052dupA ; NM_000492.4:c.2052delA ; NM_000492.4:c.2125C>T ; NM_000492.4:c.2128A>T ; NM_000492.4:c.2175dupA ; NM_000492.4:c.2195T>G ; NM_000492.4:c.2215delG ; NM_000492.4:c.2537G>A ; NM_000492.3(CFTR):c.2538G>A (p.Trp846Ter) ; NM_000492.4:c.2551C>T ; NM_000492.4:c.2583delT ; NM_000492.4:c.2657+5G>A ; NM_000492.4:c.2668C>T ; NM_000492.4:c.2737_2738insG ; NM_000492.4:c.2739T>A ; NM_000492.4:c.2780T>C ; NM_000492.4:c.2834C>T ; NM_000492.3:c.2869_2870insG ; NM_000492.4:c.2875delG ; NM_000492.4:c.2908G>C ; NM_000492.4:c.2989-1G>A ; NM_000492.4:c.3140-26A>G ; NM_000492.4:c.3194T>C ; NM_000492.4:c.3196C>T ; NM_000492.4:c.3197G>A ; NM_000492.4:c.3230T>C ; NM_000492.4:c.3266G>A ; NM_000492.4:c.3276C>A ; NM_000492.4:c.3276C>G ; NM_000492.4:c.3302T>A ; NM_000492.4:c.3310G>T ; NM_000492.4:c.3528delC ; NM_000492.4:c.3587C>G ; NM_000492.4:c.3611G>A ; NM_000492.4:c.3612G>A ; NM_000492.4:c.3659delC ; NM_000492.4:c.3731G>A ; NM_000492.4:c.3744delA ; NM_000492.4:c.3752G>A ; NM_000492.4:c.3761T>G ; NM_000492.4:c.3764C>A ; NM_000492.4:c.3773dupT ; NM_000492.4:c.3846G>A ; NM_000492.4:c.3909C>G ; NM_000492.4:c.3937C>T ; NM_000492.4:c.4251delA ; NM_000492.3(CFTR):c.4426C>T (p.Gln1476Ter) ; NM_000492.4:c.2175dupA ; NM_000492.4:c.2175dupA ; NM_000492.4:c.4077_4080delTGTTinsAA

CLN3	CLN3 disease	Juvenile neuronal ceroid lipofuscinoses (JNCLs) are a genetically heterogeneous group of neuronal ceroid lipofuscinoses (NCLs; see this term) typically characterized by onset at early school age with vision loss due to retinopathy, seizures and the decline of mental and motor capacities.	The classic form of JNCLs (cJNCLs, also referred to as Batten disease and Spielmeyer-Vogt disease) typically manifests with deteriorating vision in an otherwise healthy child at about six years of age. Blindness occurs within a few years. Several years after the onset of visual problems, cognitive abilities decline and epilepsy starts. Dementia and motor disturbances worsen progressively. Psychiatric problems (such as aggressive behavior and sleep problems) have also been reported. Rare cases of JNCL have also been described in which eye involvement is not a striking feature. Epilepsy and dementia without visual loss in these patients may be indicative of a form of JNCL known as the Northern epilepsy variant (progressive epilepsy-intellectual deficit, Finnish type; see this term).	NM_001042432.1(CLN3):c.1272delG ; NM_001042432.1(CLN3):c.622dupT ; NM_001042432.1(CLN3):c.597C>A ; NM_000086.2(CLN3):c.883G>A ; NM_001042432.1(CLN3):c.1272delG ; NM_001042432.1(CLN3):c.622dupT ; NM_001042432.1(CLN3):c.597C>A ; NM_000086.2(CLN3):c.883G>A
CLN5	CLN5 disease	Late infantile neuronal ceroid lipofuscinoses (LINCLs) are a genetically heterogeneous group of neuronal ceroid lipofuscinoses (NCLs; see this term) typically characterized by onset during infancy or early childhood with decline of mental and motor capacities, epilepsy, and vision loss through retinal degeneration.	The initial clinical symptoms are motor or/and cognitive decline or epilepsy but the mean age of onset and speed of progression may vary depending on the underlying genetic defect. Patients with classic LINCL generally present with a standstill of mental development or the onset of severe epilepsy around the third year of life. The disorder progresses to complete loss of almost all motor and mental capacities before school age. As visual loss is not a prominent finding in the early stages of the disease course, it is frequently not recognized. Several variant forms have also been described in the literature (vLINCL) in which the mean ages of onset generally vary from 2-7 years and which commonly manifest with severe epilepsy followed by cognitive and motor decline and vision loss.	NM_006493.2(CLN5):c.919delA ; NM_006493.2(CLN5):c.924_925delAT ; NM_006493.2(CLN5):c.595C>T ; NM_006493.2(CLN5):c.335G>C ; NM_006493.2(CLN5):c.613C>T ; NM_006493.2(CLN5):c.669dupC ; NM_006493.2(CLN5):c.565C>T ; NM_006493.2(CLN5):c.620G>C ; NM_006493.2(CLN5):c.955_970del16 ; NM_006493.2(CLN5):c.524T>G ; NM_006493.2(CLN5):c.575A>G ; NM_006493.2(CLN5):c.377G>A ; NM_006493.2(CLN5):c.1026C>A ; NM_006493.2(CLN5):c.835G>A ; c.526dup ; NM_006493.2(CLN5):c.433C>T ; NM_006493.2(CLN5):c.593T>C ; NM_006493.2(CLN5):c.919delA ; NM_006493.2(CLN5):c.924_925delAT ; NM_006493.2(CLN5):c.595C>T ; NM_006493.2(CLN5):c.335G>C ; NM_006493.2(CLN5):c.613C>T ; NM_006493.2(CLN5):c.669dupC ; NM_006493.2(CLN5):c.565C>T ; NM_006493.2(CLN5):c.620G>C ; NM_006493.2(CLN5):c.955_970del16 ; NM_006493.2(CLN5):c.524T>G ; NM_006493.2(CLN5):c.575A>G ; NM_006493.2(CLN5):c.377G>A ; NM_006493.2(CLN5):c.1026C>A ; NM_006493.2(CLN5):c.835G>A ; c.526dup ; NM_006493.2(CLN5):c.433C>T ; NM_006493.2(CLN5):c.593T>C

CLN6	CLN4A disease	A genetically heterogeneous group of neuronal ceroid lipofuscinoses (NCLs) with onset during the third decade of life, characterized by dementia, seizures and loss of motor capacities, and sometimes associated with visual loss caused by retinal degeneration.	The clinical picture is characterized by onset with progressive myoclonic epilepsy or behavioral disturbances, dementia and extrapyramidal motor symptoms that appear at the age of 20-30 years. Vision loss is an uncommon feature and depends on the underlying genetic cause.	NM_017882.2(CLN6):c.214G>T ; NM_017882.2(CLN6):c.200T>C ; NM_017882.2(CLN6):c.663C>G ; NM_017882.2(CLN6):c.214G>T ; NM_017882.2(CLN6):c.200T>C ; NM_017882.2(CLN6):c.663C>G
CLN6	CLN6 disease	Late infantile neuronal ceroid lipofuscinoses (LINCLs) are a genetically heterogeneous group of neuronal ceroid lipofuscinoses (NCLs; see this term) typically characterized by onset during infancy or early childhood with decline of mental and motor capacities, epilepsy, and vision loss through retinal degeneration.	The initial clinical symptoms are motor or/and cognitive decline or epilepsy but the mean age of onset and speed of progression may vary depending on the underlying genetic defect. Patients with classic LINCL generally present with a standstill of mental development or the onset of severe epilepsy around the third year of life. The disorder progresses to complete loss of almost all motor and mental capacities before school age. As visual loss is not a prominent finding in the early stages of the disease course, it is frequently not recognized. Several variant forms have also been described in the literature (vLINCL) in which the mean ages of onset generally vary from 2-7 years and which commonly manifest with severe epilepsy followed by cognitive and motor decline and vision loss.	NM_017882.2(CLN6):c.214G>T ; NM_017882.2(CLN6):c.200T>C ; NM_017882.2(CLN6):c.663C>G ; NM_017882.2(CLN6):c.214G>T ; NM_017882.2(CLN6):c.200T>C ; NM_017882.2(CLN6):c.663C>G

CLN8	CLN8 disease	Neuronal ceroid lipofuscinoses (NCLs) are a group of inherited progressive degenerative brain diseases characterized clinically by a decline of mental and other capacities, epilepsy, and vision loss through retinal degeneration, and histopathologically by intracellular accumulation of an autofluorescent material, ceroid lipofuscin, in the neuronal cells in the brain and in the retina.	The clinical presentation varies widely between forms but the clinical hallmark is a combination of dementia, visual loss, and epilepsy. Manifestations may begin between the neonatal period and young adult age depending on the form, leading to the original classification of NCLs by age at onset into congenital, infantile, late infantile, juvenile and adult NCL subgroups (see these terms). A Northern epilepsy variant (progressive epilepsy-intellectual deficit, Finnish type; see this term), in which the visual problems may be absent or be mild and go unrecognized, has also been described.	NM_018941.3(CLN8):c.610C>T ; NM_018941.3(CLN8):c.789G>C ; NM_018941.3(CLN8):c.88delG ; NM_018941.3(CLN8):c.88G>C ; NM_018941.3(CLN8):c.610C>T ; NM_018941.3(CLN8):c.789G>C ; NM_018941.3(CLN8):c.88delG ; NM_018941.3(CLN8):c.88G>C
CLN8	Progressive epilepsy-intellectual disability syndrome, Finnish type	Progressive epilepsy-intellectual deficit, Finnish type (also known as Northern epilepsy) is a subtype of neuronal ceroid lipofuscinosis (NCL; see this term) characterized by seizures, progressive decline of intellectual capacities and variable loss of vision.	The disorder is characterized by generalized tonic-clonic seizures with onset at 5 to 10 years of age and subsequent slowly progressive mental deterioration. The seizures increase in frequency until puberty after which the epileptic activity starts to decline. The intellectual deficit is severe, develops 2-5 years after the onset of seizures and progresses continuously through adulthood. Visual problems are not a prominent feature of this disorder; if present they may be mild and go unrecognized.	NM_018941.3(CLN8):c.610C>T ; NM_018941.3(CLN8):c.789G>C ; NM_018941.3(CLN8):c.88delG ; NM_018941.3(CLN8):c.88G>C ; NM_018941.3(CLN8):c.610C>T ; NM_018941.3(CLN8):c.789G>C ; NM_018941.3(CLN8):c.88delG ; NM_018941.3(CLN8):c.88G>C

CLRN1	Retinitis pigmentosa	Retinitis pigmentosa (RP) is an inherited retinal dystrophy leading to progressive loss of the photoreceptors and retinal pigment epithelium and resulting in blindness usually after several decades.	Retinitis pigmentosa is slowly progressive but relentless. There is however broad variability in age of onset, rate of progression and secondary clinical manifestations. Affected individuals generally first develop night blindness (nyctalopia) due to loss of rod function, often in adolescence or earlier. They then develop peripheral visual field impairment, and over time loss of central vision, usually at late stages, often around midlife. Central visual acuity loss may occur at any age as a result of cystoid macular edema or photoreceptor loss. Posterior subcapsular cataracts are common and severity is age dependent. Reduced color vision may also be found. Fundus examination reveals bone spicule pigment deposits, attenuated retinal vessels, retinal atrophy and waxy optic nerve pallor. Severity is partly correlated with the pattern of inheritance with X-linked cases having the most severe course, autosomal recessive and single occurrence cases having intermediate severity, and autosomal dominant the most favorable course.	NM_001195794.1:c.144T>G ; c.633dup ; NM_001195794.1(CLRN1):c.92C>T ; NM_001195794.1(CLRN1):c.189C>A ; NM_001195794.1:c.144T>G ; c.633dup ; NM_001195794.1(CLRN1):c.92C>T ; NM_001195794.1(CLRN1):c.189C>A

CLRN1	Usher syndrome type 3	Usher syndrome type I is an autosomal recessive condition characterized by profound congenital hearing impairment with unintelligible speech, early retinitis pigmentosa (usually evident within the first decade), and constant vestibular dysfunction. Type I is distinguished from type II on the basis of severity of hearing loss and the extent of vestibular involvement. Type I patients are profoundly deaf, whereas type II patients are 'hard of hearing.' Vestibular function is defective in type I patients, whereas type II patients have normal vestibular function. Patients with type III (USH3) have progressive hearing loss.	A rare ciliopathy characterized by progressive hearing and visual loss in the first decades of life and, in some cases, vestibular dysfunction. Patients have normal hearing at birth. Onset of hearing loss is usually in late childhood or adolescence after development of speech. Profound deafness is mostly reported by middle age. Retinitis pigmentosa related visual loss also develops in late childhood or adolescence. Developmental motor milestones are generally normal but vestibular dysfunction may occur in adulthood.	NM_001195794.1:c.144T>G ; c.633dup ; NM_001195794.1(CLRN1):c.92C>T ; NM_001195794.1(CLRN1):c.189C>A ; NM_001195794.1:c.144T>G ; c.633dup ; NM_001195794.1(CLRN1):c.92C>T ; NM_001195794.1(CLRN1):c.189C>A
CNGB3	Achromatopsia		ACHM is characterized by reduced visual acuity, pendular nystagmus, increased sensitivity to light (photophobia), a small central scotoma, and reduced or complete loss of color discrimination. Most individuals have complete ACHM, with total lack of function in all three types of cones. Rarely, individuals have incomplete ACHM, with similar, but generally less severe symptoms.	NM_019098.4(CNGB3):c.819_826delCAGACTCC ; c.2048_2049del ; c.893_897del ; c.887_896del ; NM_019098.4(CNGB3):c.1063C>T ; c.2011G>T ; NM_019098.4(CNGB3):c.446_447insT ; NM_019098.4:c.1148delC ; c.886_890del ; NM_019098.4(CNGB3):c.819_826delCAGACTCC ; c.2048_2049del ; c.893_897del ; c.887_896del ; NM_019098.4(CNGB3):c.1063C>T ; c.2011G>T ; NM_019098.4(CNGB3):c.446_447insT ; NM_019098.4:c.1148delC ; c.886_890del

CNGB3	Progressive cone dystrophy	A rare retinal dystrophy characterized by photophobia, progressive loss of visual acuity, nystagmus, visual field abnormalities, abnormal color vision, and psychophysical and electrophysiological evidence of abnormal cone function. Progressive cone dystrophy usually presents in childhood or early adult life, and patients tend to develop rod photoreceptor dysfunction in later life.		NM_019098.4(CNGB3):c.819_826delCAGACTCC ; c.2048_2049del ; c.893_897del ; c.887_896del ; NM_019098.4(CNGB3):c.1063C>T ; c.2011G>T ; NM_019098.4(CNGB3):c.446_447insT ; NM_019098.4:c.1148delC ; c.886_890del ; NM_019098.4(CNGB3):c.819_826delCAGACTCC ; c.2048_2049del ; c.893_897del ; c.887_896del ; NM_019098.4(CNGB3):c.1063C>T ; c.2011G>T ; NM_019098.4(CNGB3):c.446_447insT ; NM_019098.4:c.1148delC ; c.886_890del
CNGB3	Stargardt disease	A rare ophthalmic disorder that is usually characterized by a progressive loss of central vision associated with irregular macular and perimacular yellow-white fundus flecks, and a so-called "beaten bronze" atrophic central macular lesion.	The disease typically presents within the first two decades of life, even though symptoms can also appear during adulthood and as late as the seventh decade. Although disease progression and severity varies widely, Stargardt disease (STGD1) is usually characterized by a progressive loss of central vision causing blurry vision and, occasionally, an increasing difficulty to adapt in the dark. Peripheral vision is usually normal. Most affected individuals also have impaired color vision. Photophobia may be present.	NM_019098.4(CNGB3):c.819_826delCAGACTCC ; c.2048_2049del ; c.893_897del ; c.887_896del ; NM_019098.4(CNGB3):c.1063C>T ; c.2011G>T ; NM_019098.4(CNGB3):c.446_447insT ; NM_019098.4:c.1148delC ; c.886_890del ; NM_019098.4(CNGB3):c.819_826delCAGACTCC ; c.2048_2049del ; c.893_897del ; c.887_896del ; NM_019098.4(CNGB3):c.1063C>T ; c.2011G>T ; NM_019098.4(CNGB3):c.446_447insT ; NM_019098.4:c.1148delC ; c.886_890del

COL4A3	Autosomal dominant Alport syndrome	A rare renal disease characterized by glomerular nephropathy with hematuria progressing to end-stage renal disease (ESRD), frequently associated with sensorineural deafness, and occasionally with ocular anomalies.	The clinical subtypes of AS include X-linked (XL), autosomal recessive (AR) and autosomal dominant (AD) AS and count for about 80%, 15% and 5% of all AS cases, respectively. AS can present anywhere from childhood to elderly age, although it generally manifests earlier (during childhood or adolescence) in XL and AR forms. Males are severely affected in XLAS and present with microhematuria very early in life, followed by micro-albuminuria, macroproteinuria and progression to ESRD before the age of 40 years old. XLAS is highly variable in females, ranging from an asymptomatic disease to lifelong microscopic hematuria (with preserved renal function), or renal failure at a young age. Sensorineural hearing loss is common. Occasional ocular anomalies (e.g. anterior lenticonus, retinal flecks, corneal lesions) may develop in late childhood or early adulthood, males being more commonly affected than females. Rarely, leiomyomatosis (esophagus, tracheobronchial tree or female genitalia) can be associated, forming the X-linked diffuse leiomyomatosis-AS (XL-DLAS). ARAS is similar to XLAS in males, but presents without any gender differentiation in the disease course and the family history. ADAS varies from an asymptomatic disease (mostly presenting as a familial benign hematuria) to AD forms of proteinuria and focal segmental glomerulosclerosis (in cases without hematuria or not as a first line presentation). The progression to ESRD is usually slower than in XLAS, and extra-renal manifestations are less common.	NM_000091.4(COL4A3):c.2083G>A ; NM_000091.4(COL4A3):c.898G>A ; NM_000091.4(COL4A3):c.4441C>T ; c.2111del ; NM_000091.4(COL4A3):c.345delG ; NM_000091.4(COL4A3):c.4420_4424del5 ; NM_000091.4(COL4A3):c.4571C>G ; NM_000091.4(COL4A3):c.2083G>A ; NM_000091.4(COL4A3):c.898G>A ; NM_000091.4(COL4A3):c.4441C>T ; c.2111del ; NM_000091.4(COL4A3):c.345delG ; NM_000091.4(COL4A3):c.4420_4424del5 ; NM_000091.4(COL4A3):c.4571C>G

COL4A3	Autosomal recessive Alport syndrome	A rare renal disease characterized by glomerular nephropathy with hematuria progressing to end-stage renal disease (ESRD), frequently associated with sensorineural deafness, and occasionally with ocular anomalies.	The clinical subtypes of AS include X-linked (XL), autosomal recessive (AR) and autosomal dominant (AD) AS and count for about 80%, 15% and 5% of all AS cases, respectively. AS can present anywhere from childhood to elderly age, although it generally manifests earlier (during childhood or adolescence) in XL and AR forms. Males are severely affected in XLAS and present with microhematuria very early in life, followed by micro-albuminuria, macroproteinuria and progression to ESRD before the age of 40 years old. XLAS is highly variable in females, ranging from an asymptomatic disease to lifelong microscopic hematuria (with preserved renal function), or renal failure at a young age. Sensorineural hearing loss is common. Occasional ocular anomalies (e.g. anterior lenticonus, retinal flecks, corneal lesions) may develop in late childhood or early adulthood, males being more commonly affected than females. Rarely, leiomyomatosis (esophagus, tracheobronchial tree or female genitalia) can be associated, forming the X-linked diffuse leiomyomatosis-AS (XL-DLAS). ARAS is similar to XLAS in males, but presents without any gender differentiation in the disease course and the family history. ADAS varies from an asymptomatic disease (mostly presenting as a familial benign hematuria) to AD forms of proteinuria and focal segmental glomerulosclerosis (in cases without hematuria or not as a first line presentation). The progression to ESRD is usually slower than in XLAS, and extra-renal manifestations are less common.	NM_000091.4(COL4A3):c.2083G>A ; NM_000091.4(COL4A3):c.898G>A ; NM_000091.4(COL4A3):c.4441C>T ; c.2111del ; NM_000091.4(COL4A3):c.345delG ; NM_000091.4(COL4A3):c.4420_4424del5 ; NM_000091.4(COL4A3):c.4571C>G ; NM_000091.4(COL4A3):c.2083G>A ; NM_000091.4(COL4A3):c.898G>A ; NM_000091.4(COL4A3):c.4441C>T ; c.2111del ; NM_000091.4(COL4A3):c.345delG ; NM_000091.4(COL4A3):c.4420_4424del5 ; NM_000091.4(COL4A3):c.4571C>G

COL4A3	Genetic steroid-resistant nephrotic syndrome	A rare, hereditary nephrotic syndrome characterized by proteinuria, hypoalbuminemia, edema, and hyperlipidemia, with an absence of response to an initial trial of corticosteroids (i.e. steroid-resistant nephrotic syndrome; SRNS) and a generally complicated course.	Disease onset may occur anywhere between birth and adulthood but predominantly presents in younger populations. The nephrotic syndrome is defined by severe proteinuria (Urinary Protein/Creatinine ration > 200 mg/mmol) with low serum albumin (<30 g/l) and possible edema. Biopsy shows minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS) or, more rarely, diffuse mesangial sclerosis (DMS), and podocyte foot process effacement by electron microscopy. It is multi-drug resistant and usually progresses to end-stage kidney failure; however, patients have a very low risk of recurrence after kidney transplantation.	NM_000091.4(COL4A3):c.2083G>A ; NM_000091.4(COL4A3):c.898G>A ; NM_000091.4(COL4A3):c.4441C>T ; c.2111del ; NM_000091.4(COL4A3):c.345delG ; NM_000091.4(COL4A3):c.4420_4424del5 ; NM_000091.4(COL4A3):c.4571C>G ; NM_000091.4(COL4A3):c.2083G>A ; NM_000091.4(COL4A3):c.898G>A ; NM_000091.4(COL4A3):c.4441C>T ; c.2111del ; NM_000091.4(COL4A3):c.345delG ; NM_000091.4(COL4A3):c.4420_4424del5 ; NM_000091.4(COL4A3):c.4571C>G
COL4A3	NON RARE IN EUROPE: Benign familial hematuria	Benign familial hematuria is an autosomal dominant condition manifest as nonprogressive isolated microscopic hematuria that does not result in renal failure. It is characterized pathologically by thinning of the glomerular basement membrane (GBM), and can be considered the mildest end of the spectrum of renal diseases due to type IV collagen defects of the basement membrane. The most severe end of the spectrum is represented by Alport syndrome, which results in end-stage renal failure and may be associated with hearing loss and ocular anomalies.	0	NM_000091.4(COL4A3):c.2083G>A ; NM_000091.4(COL4A3):c.898G>A ; NM_000091.4(COL4A3):c.4441C>T ; c.2111del ; NM_000091.4(COL4A3):c.345delG ; NM_000091.4(COL4A3):c.4420_4424del5 ; NM_000091.4(COL4A3):c.4571C>G ; NM_000091.4(COL4A3):c.2083G>A ; NM_000091.4(COL4A3):c.898G>A ; NM_000091.4(COL4A3):c.4441C>T ; c.2111del ; NM_000091.4(COL4A3):c.345delG ; NM_000091.4(COL4A3):c.4420_4424del5 ; NM_000091.4(COL4A3):c.4571C>G

COL4A4	Autosomal dominant Alport syndrome	A rare renal disease characterized by glomerular nephropathy with hematuria progressing to end-stage renal disease (ESRD), frequently associated with sensorineural deafness, and occasionally with ocular anomalies.	The clinical subtypes of AS include X-linked (XL), autosomal recessive (AR) and autosomal dominant (AD) AS and count for about 80%, 15% and 5% of all AS cases, respectively. AS can present anywhere from childhood to elderly age, although it generally manifests earlier (during childhood or adolescence) in XL and AR forms. Males are severely affected in XLAS and present with microhematuria very early in life, followed by micro-albuminuria, macroproteinuria and progression to ESRD before the age of 40 years old. XLAS is highly variable in females, ranging from an asymptomatic disease to lifelong microscopic hematuria (with preserved renal function), or renal failure at a young age. Sensorineural hearing loss is common. Occasional ocular anomalies (e.g. anterior lenticonus, retinal flecks, corneal lesions) may develop in late childhood or early adulthood, males being more commonly affected than females. Rarely, leiomyomatosis (esophagus, tracheobronchial tree or female genitalia) can be associated, forming the X-linked diffuse leiomyomatosis-AS (XL-DLAS). ARAS is similar to XLAS in males, but presents without any gender differentiation in the disease course and the family history. ADAS varies from an asymptomatic disease (mostly presenting as a familial benign hematuria) to AD forms of proteinuria and focal segmental glomerulosclerosis (in cases without hematuria or not as a first line presentation). The progression to ESRD is usually slower than in XLAS, and extra-renal manifestations are less common.	NM_000092.4(COL4A4):c.3713C>A ; c.2312del ; NM_000092.4(COL4A4):c.3601G>A ; NM_000092.4(COL4A4):c.71+1G>A ; NM_000092.4(COL4A4):c.4129C>T ; NM_000092.4(COL4A4):c.4923C>A ; NM_000092.4(COL4A4):c.3713C>A ; c.2312del ; NM_000092.4(COL4A4):c.3601G>A ; NM_000092.4(COL4A4):c.71+1G>A ; NM_000092.4(COL4A4):c.4129C>T ; NM_000092.4(COL4A4):c.4923C>A

COL4A4	Autosomal recessive Alport syndrome	A rare renal disease characterized by glomerular nephropathy with hematuria progressing to end-stage renal disease (ESRD), frequently associated with sensorineural deafness, and occasionally with ocular anomalies.	The clinical subtypes of AS include X-linked (XL), autosomal recessive (AR) and autosomal dominant (AD) AS and count for about 80%, 15% and 5% of all AS cases, respectively. AS can present anywhere from childhood to elderly age, although it generally manifests earlier (during childhood or adolescence) in XL and AR forms. Males are severely affected in XLAS and present with microhematuria very early in life, followed by micro-albuminuria, macroproteinuria and progression to ESRD before the age of 40 years old. XLAS is highly variable in females, ranging from an asymptomatic disease to lifelong microscopic hematuria (with preserved renal function), or renal failure at a young age. Sensorineural hearing loss is common. Occasional ocular anomalies (e.g. anterior lenticonus, retinal flecks, corneal lesions) may develop in late childhood or early adulthood, males being more commonly affected than females. Rarely, leiomyomatosis (esophagus, tracheobronchial tree or female genitalia) can be associated, forming the X-linked diffuse leiomyomatosis-AS (XL-DLAS). ARAS is similar to XLAS in males, but presents without any gender differentiation in the disease course and the family history. ADAS varies from an asymptomatic disease (mostly presenting as a familial benign hematuria) to AD forms of proteinuria and focal segmental glomerulosclerosis (in cases without hematuria or not as a first line presentation). The progression to ESRD is usually slower than in XLAS, and extra-renal manifestations are less common.	NM_000092.4(COL4A4):c.3713C>A ; c.2312del ; NM_000092.4(COL4A4):c.3601G>A ; NM_000092.4(COL4A4):c.71+1G>A ; NM_000092.4(COL4A4):c.4129C>T ; NM_000092.4(COL4A4):c.4923C>A ; NM_000092.4(COL4A4):c.3713C>A ; c.2312del ; NM_000092.4(COL4A4):c.3601G>A ; NM_000092.4(COL4A4):c.71+1G>A ; NM_000092.4(COL4A4):c.4129C>T ; NM_000092.4(COL4A4):c.4923C>A

COL4A4	NON RARE IN EUROPE: Benign familial hematuria	Benign familial hematuria is an autosomal dominant condition manifest as nonprogressive isolated microscopic hematuria that does not result in renal failure. It is characterized pathologically by thinning of the glomerular basement membrane (GBM), and can be considered the mildest end of the spectrum of renal diseases due to type IV collagen defects of the basement membrane. The most severe end of the spectrum is represented by Alport syndrome, which results in end-stage renal failure and may be associated with hearing loss and ocular anomalies.	0	NM_000092.4(COL4A4):c.3713C>A ; c.2312del ; NM_000092.4(COL4A4):c.3601G>A ; NM_000092.4(COL4A4):c.71+1G>A ; NM_000092.4(COL4A4):c.4129C>T ; NM_000092.4(COL4A4):c.4923C>A ; NM_000092.4(COL4A4):c.3713C>A ; c.2312del ; NM_000092.4(COL4A4):c.3601G>A ; NM_000092.4(COL4A4):c.71+1G>A ; NM_000092.4(COL4A4):c.4129C>T ; NM_000092.4(COL4A4):c.4923C>A

COL7A1	Autosomal dominant generalized dystrophic epidermolysis bullosa	Generalized dominant dystrophic epidermolysis bullosa (DDEB-gen) is a subtype of dystrophic epidermolysis bullosa (DEB, see this term), formerly known as DDEB, Pasini and Cockayne-Touraine types, characterized by generalized blistering, milia formation, atrophic scarring, and dystrophic nails.	The clinical picture of intermediate dominant dystrophic epidermolysis bullosa (DDEB-intermediate) is generally milder than that of the autosomal recessive generalized DEB forms. DDEB-intermediate manifests usually at birth with the development of blisters, primarily affecting the limbs. Blisters heal by developing numerous milia and atrophic scars with an onion-like appearance, particularly visible on the elbows, knees, and hands. Nail dystrophy, always present, can lead to loss of nail plates. Usually, fingers and toes are not affected by major cicatricial retractions. Blisters can develop in the mucosa, mainly in the oral cavity and, less commonly, in the esophagus, where they can cause strictures, often in sharp contrast with the scarce cutaneous involvement. Dental caries are relatively frequent. Corneal and genitourinary tract involvement, anemia, and growth delay are rare.	NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A ; NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A

COL7A1	Autosomal recessive generalized dystrophic epidermolysis bullosa, intermediate form	Recessive dystrophic epidermolysis bullosa (RDEB)-generalized other, also known as RDEB non-Hallopeau-Siemens type, is a subtype of DEB (see this term) characterized by generalized cutaneous and mucosal blistering that is not associated with severe deformities.	Under the term intermediate RDEB are grouped a spectrum of phenotypes, showing highly variable severity of the cutaneous and mucosal involvement. The disease manifests at birth or during the neonatal period with generalized blistering. Aplasia cutis congenita (congenital absence of the skin) can also be observed at birth. Healing of blisters results in the development of milia, atrophic scarring (less severe than in severe RDEB), dystrophic nails, and, occasionally, albopapuloid lesions (ivory-white colored, scar-like papules) and scalp abnormalities. In some patients, the scarring phenomena can lead to a certain degree of pseudosyndactyly and loss of nail plates. Extracutaneous involvement is similar but less severe than in severe RDEB with no hand/foot deformities associated with this disease. Oral cavity lesions and excessive dental caries are common. Patients have a lower risk of esophageal strictures and corneal injury than severe RDEB. Growth delay and anemia are rare. Genitourinary tract involvement is rare. The risk of developing squamous cell carcinomas (SCC) is also increased but less common than in severe RDEB and occurs later in adulthood.	NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A ; NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A

COL7A1	Autosomal recessive generalized dystrophic epidermolysis bullosa, severe form	Severe generalized recessive dystrophic epidermolysis bullosa (RDEB-sev gen) is the most severe subtype of dystrophic epidermolysis bullosa (DEB, see this term), formerly known as the Hallopeau-Siemens type, and is characterized by generalized cutaneous and mucosal blistering and scarring associated with severe deformities and major extracutaneous involvement.	Blisters develop spontaneously or after the mildest trauma at birth or during the neonatal period and affect all of the body (with predilection for skin over bony prominences) with extensive involvement of the oral and gastrointestinal mucosa. Congenital skin ulceration with extensive denudation of a body area may be present. Lesions heal with retracting scars and milia. Epidermolysis bullosa (EB) nevi may occur. Excessive scarring can lead to adhesion of fingers and toes resulting to pseudosyndactyly, and to joint contractures that further cause disabling hand and foot deformities ("mitten deformities"). Scarring alopecia of the scalp and permanent loss of nail plates are also observed. Eye involvement is frequent and includes blepharitis, loss of eyelashes, ectropion, symblepharon, and corneal blisters that can lead to loss of vision. Chewing and swallowing difficulties are due to ankyloglossia, obliteration of the oral vestibules and progressive microstomia. Dental caries are numerous. Esophageal stricture is frequent and results in severe dysphagia. Anal and perianal erosions cause major pain during defecation and foster constipation. Extensive gastrointestinal involvement in combination with a hypercatabolic state due to permanent wounding, infection and inflammation, induce a state of chronic malnutrition which contributes to growth retardation, delayed puberty, osteopenia and osteoporosis. Urethral strictures may occur. Refractory anemia, iron deficiency and hypoalbuminemia are also observed. Nearly all patients develop at least one aggressive squamous cell carcinoma (SCC), typically during the third-fourth decade of life.	NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A ; NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A

COL7A1	Dystrophic epidermolysis bullosa inversa	Recessive dystrophic epidermolysis bullosa inversa (RDEB-I) is rare subtype of dystrophic epidermolysis bullosa (DEB, see this term) characterized by blisters and erosions which are primarily confined to intertriginous skin sites, the base of the neck, the uppermost back, and the lumbosacral area.	The disease manifests at birth or shortly thereafter with generalized blistering and superficial erosions of intermediate severity that heal with atrophic scarring and milia formation. From adolescence to early adulthood, blistering tends to localize to folds, particularly axillae, groin, perianal area and natal cleft. Women may present with marked vulvovaginal and inframammary skin blistering. Other predilection sites include the base of the neck, the uppermost back, and the lumbosacral area. Nail dystrophy is typical but of variable severity. Mucosal lesions with blistering and scarring in the mouth are characteristic and can lead to microglossia (loss of lingual papillae and fusion of the tongue to the mouth floor) and ankyloglossia (obliteration of the oral vestibules and progressive restriction of oral aperture). Esophageal involvement is often severe and is associated with a risk of esophageal stricture that can impair intake of nutrients. Lesions of the lowermost portion of the genitourinary tract are also common and may lead to the development of vaginal strictures that may impair normal sexual function. Other less common extracutaneous features include external auditory canal stenosis or complete occlusion with varying degrees of hearing loss; corneal erosions, and anemia. Growth delay is rare. Patients may develop squamous cell carcinomas, with a cumulative risk reaching 23% by age 50 which is much lower than in either of the two generalized forms of RDEB (severe RDEB and intermediate RDEB).	NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A ; NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A

COL7A1	Dystrophic epidermolysis bullosa pruriginosa	Dystrophic epidermolysis bullosa pruriginosa is a rare subtype of dystrophic epidermolysis bullosa (DEB, see this term) characterized by generalized or localized skin lesions associated with severe, if not intractable, pruritus.	While skin fragility and blistering lesions usually manifest in infancy, which heal with atrophic scarring and milia formation, the onset of intense pruritus is frequently delayed until the adolescence or even adulthood. At the onset of pruritus, the clinical picture generally worsens with the development of papules, nodules, lichenoid and hypertrophic lesions in a linear distribution, preferentially on the extensor surfaces of the limbs. Nail dystrophy is usually present.	NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A ; NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A
COL7A1	Localized dystrophic epidermolysis bullosa, acral form	A very rare dystrophic epidermolysis bullosa (DEB) characterized by blistering confined primarily to the hands and feet.		NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A ; NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A
COL7A1	Localized dystrophic epidermolysis bullosa, nails only	Dystrophic epidermolysis bullosa, nails only is a rare subtype of dystrophic epidermolysis bullosa (DEB, see this term) that shows no blistering and that is characterized by dystrophic or absent nails.		NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A ; NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A
COL7A1	Localized dystrophic epidermolysis bullosa, pretibial form	Pretibial dystrophic epidermolysis bullosa is characterized by recurrent blistering and scarring, mainly in the pretibial area. The lesions often show lichenoid features.	Pretibial dystrophic epidermolysis bullosa is a rare subtype of dystrophic epidermolysis bullosa (DEB, see this term) characterized by the development of blisters, erosions, and lichenoid lesions predominantly in the pretibial region.	NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A

COL7A1	Self-improving dystrophic epidermolysis bullosa	Transient bullous dermolysis of the newborn is a rare subtype of dystrophic epidermolysis bullosa (DEB, see this term) characterized by generalized blistering at birth that usually regresses within the first 6 to 24 months of life.	The disease usually manifests at birth, or soon after. Skin blisters generally affect the whole body. Blisters can also affect the oral cavity. Healing of blisters is associated with mild, mostly atrophic, scarring and milia formation. Disease activity usually ceases within the first 6 to 24 months of life, although there are a few cases with continued blistering past age 3 years. Nail dystrophy and some degree of skin fragility can persist in adulthood. Ultrastructurally, the presence in basal keratinocytes of peculiar cytoplasmic inclusions, known as stellate bodies, filled with unsecreted procollagen VII, is typical of the disease.	NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A ; NC_000003.12:g.48572412C>T ; NM_000094.3(COL7A1):c.6527dupC ; c.6670G>T ; c.5821-1G>A ; c.7930-1G>C ; NC_000003.12:g.48588759dup ; NM_000094.3(COL7A1):c.6859G>A ; NM_000094.3(COL7A1):c.7411C>T ; NM_000094.3(COL7A1):c.7957G>A ; NM_000094.3(COL7A1):c.6187C>T ; NM_000094.3(COL7A1):c.8479C>T ; c.5443G>C ; NM_000094.3(COL7A1):c.5532+1G>A ; NM_000094.3(COL7A1):c.8393T>A ; c.7345-1G>A ; NM_000094.3(COL7A1):c.933C>A ; c.336C>G ; c.7912G>T ; c.8524_8527+10del ; c.6573+1G>T ; c.5287C>T ; c.5052+1G>A ; NM_000094.3(COL7A1):c.8440C>T ; NM_000094.3(COL7A1):c.4039G>C ; NC_000003.12:g.48584484C>A ; NM_000094.3(COL7A1):c.4888C>T ; NM_000094.3(COL7A1):c.6752G>A ; NM_000094.3(COL7A1):c.4373C>T ; NM_000094.3(COL7A1):c.706C>T ; NM_000094.3(COL7A1):c.425A>G ; NM_000094.3(COL7A1):c.5096C>T ; NM_000094.3(COL7A1):c.4783G>C ; NM_000094.3(COL7A1):c.8245G>A ; NM_000094.3(COL7A1):c.6205C>T ; NM_000094.3(COL7A1):c.887delG ; NC_000003.12:g.48585689C>A
CPS1	Carbamoyl-phosphate synthetase 1 deficiency	A rare, severe disorder of urea cycle metabolism typically characterized by either a neonatal-onset of severe hyperammonemia that occurs few days after birth and manifests with lethargy, vomiting, hypothermia, seizures, coma and death or a presentation outside the newborn period at any age with (sometimes) milder symptoms of hyperammonemia.	In the neonatal-onset form of carbamoyl-phosphate synthetase 1 deficiency (CPS1D), patients are usually healthy at birth but after few days they begin to manifest with lethargy and unwillingness to feed. Severe hyperammonemia continues and manifests with vomiting, hypothermia, hypotonia, seizures, coma, and can lead to death. Outside the newborn period, patients can present at any time in life. Risk factors for manifestation include catabolic stressors such as fasting and intercurrent illness. Manifestations include hyperammonemia with irritability, lethargy, headache, seizures, confusion, avoidance of high-protein meals, axial hypotonia and cognitive disability.	NM_001875.4(CPS1):c.1631C>T ; c.3556del ; NM_001875.4(CPS1):c.1912C>T ; NM_001875.4(CPS1):c.1631C>T ; c.3556del ; NM_001875.4(CPS1):c.1912C>T

CPT1A	Carnitine palmitoyl transferase 1A deficiency	Carnitine palmitoyltransferase 1A (CPT-1A) deficiency is an inborn error of metabolism that affects mitochondrial oxidation of long chain fatty acids (LCFA) in the liver and kidneys, and is characterized by recurrent attacks of fasting-induced hypoketotic hypoglycemia and risk of liver failure.	CPT-1A deficiency manifests between birth and 18 months of age with recurrent attacks of hypoketotic hypoglycemia of varying severity, triggered by fasting or intercurrent illness, that can lead to severe neurological sequelae. CPT-1A-deficient patients can also present with hepatic encephalopathy with loss of consciousness, seizures, coma, or even sudden death. There may be a risk of progression to liver failure. Patients with severe CPT-1A deficiency may also have renal tubular acidosis.	NM_001876.4:c.1361A>G ; NM_001876.3(CPT1A):c.1393G>T ; NM_001031847.2(CPT1A):c.281+1G>A ; NM_001876.3(CPT1A):c.298C>T ; c.335_336del ; NM_001876.3(CPT1A):c.1436C>T ; NM_001876.3(CPT1A):c.1241C>T ; NM_001876.3(CPT1A):c.1079A>G ; NC_000011.10:g.68781907G>A ; NM_001876.3(CPT1A):c.222C>A ; NM_001876.4:c.1361A>G ; NM_001876.3(CPT1A):c.1393G>T ; NM_001031847.2(CPT1A):c.281+1G>A ; NM_001876.3(CPT1A):c.298C>T ; c.335_336del ; NM_001876.3(CPT1A):c.1436C>T ; NM_001876.3(CPT1A):c.1241C>T ; NM_001876.3(CPT1A):c.1079A>G ; NC_000011.10:g.68781907G>A ; NM_001876.3(CPT1A):c.222C>A
CPT2	Acute necrotizing encephalopathy of childhood	Acute encephalopathy is a severe neurologic complication of an infection that usually occurs in children. It is characterized by a high-grade fever accompanied within 12 to 48 hours by febrile convulsions, often leading to coma, multiple-organ failure, brain edema, and high morbidity and mortality. The infections are usually viral, particularly influenza, although other viruses and even mycoplasma have been found to cause the disorder	A rare neurologic disease characterized by a rapid onset of seizures, an altered state of consciousness, neurologic decline, and variable degrees of hepatic dysfunction following a respiratory or gastrointesitnal infection (e.g. mycoplasma, influenza virus) in a previously healthy child. Brain MRI of patients reveals bilateral, multiple, symmetrical lesions predominantly observed in thalami and brainstem, but also in periventricular white matter and cerebellum in some cases.	NM_000098.2(CPT2):c.359A>G ; NM_000098.3:c.338C>T ; NM_000098.2(CPT2):c.725_726delAC ; NM_000098.2(CPT2):c.1784delC ; c.1237C>T ; NM_000098.2(CPT2):c.1883A>C ; c.1437C>G ; NM_000098.3:c.1239_1240delGA ; NM_000098.2(CPT2):c.1369A>T ; NM_000098.2(CPT2):c.149C>A ; NM_000098.2(CPT2):c.638A>G ; NM_000098.2(CPT2):c.1891C>T ; NM_000098.2(CPT2):c.520G>A ; NM_000098.2(CPT2):c.452G>A ; NM_000098.2(CPT2):c.1148T>A ; NM_000098.2(CPT2):c.370C>T ; c.464dup ; NM_000098.2(CPT2):c.886C>T ; NM_000098.2(CPT2):c.680C>T ; NM_000098.2(CPT2):c.359A>G ; NM_000098.3:c.338C>T ; NM_000098.2(CPT2):c.725_726delAC ; NM_000098.2(CPT2):c.1784delC ; c.1237C>T ; NM_000098.2(CPT2):c.1883A>C ; c.1437C>G ; NM_000098.3:c.1239_1240delGA ; NM_000098.2(CPT2):c.1369A>T ; NM_000098.2(CPT2):c.149C>A ; NM_000098.2(CPT2):c.638A>G ; NM_000098.2(CPT2):c.1891C>T ; NM_000098.2(CPT2):c.520G>A ; NM_000098.2(CPT2):c.452G>A ; NM_000098.2(CPT2):c.1148T>A ; NM_000098.2(CPT2):c.370C>T ; c.464dup ; NM_000098.2(CPT2):c.886C>T ; NM_000098.2(CPT2):c.680C>T

CPT2	Carnitine palmitoyl transferase II deficiency, myopathic form	The myopathic form of carnitine palmitoyltransferase II (CPT II) deficiency, an inherited metabolic disorder that affects mitochondrial oxidation of long chain fatty acids (LCFA), is the most common and the least severe form of CPT II deficiency (see this term).	The age of onset varies between 1 and 61 years of age with 70% of cases first presenting in childhood. The disease is more common in men, probably reflecting an ascertainment bias related to exposure to prolonged exercise. The clinical manifestations are characterized by recurrent attacks of rhabdomyolysis, muscle pain, and weakness triggered usually by prolonged physical exercise and sometimes exacerbated by extremes in temperature; episodes may also be provoked or exacerbated by prolonged fasting, such as may occur with intercurrent viral illness. Episodes of rhabdomyolysis may be associated with extreme elevation of serum creatine phosphokinase (CPK) and myoglobinuria (75% of cases) and can lead to renal failure (in 8-25% of cases, but rarely requiring dialysis). Patients are asymptomatic between episodes of rhabdomyolysis.	NM_000098.2(CPT2):c.359A>G ; NM_000098.3:c.338C>T ; NM_000098.2(CPT2):c.725_726delAC ; NM_000098.2(CPT2):c.1784delC ; c.1237C>T ; NM_000098.2(CPT2):c.1883A>C ; c.1437C>G ; NM_000098.3:c.1239_1240delGA ; NM_000098.2(CPT2):c.1369A>T ; NM_000098.2(CPT2):c.149C>A ; NM_000098.2(CPT2):c.638A>G ; NM_000098.2(CPT2):c.1891C>T ; NM_000098.2(CPT2):c.520G>A ; NM_000098.2(CPT2):c.452G>A ; NM_000098.2(CPT2):c.1148T>A ; NM_000098.2(CPT2):c.370C>T ; c.464dup ; NM_000098.2(CPT2):c.886C>T ; NM_000098.2(CPT2):c.680C>T ; NM_000098.2(CPT2):c.359A>G ; NM_000098.3:c.338C>T ; NM_000098.2(CPT2):c.725_726delAC ; NM_000098.2(CPT2):c.1784delC ; c.1237C>T ; NM_000098.2(CPT2):c.1883A>C ; c.1437C>G ; NM_000098.3:c.1239_1240delGA ; NM_000098.2(CPT2):c.1369A>T ; NM_000098.2(CPT2):c.149C>A ; NM_000098.2(CPT2):c.638A>G ; NM_000098.2(CPT2):c.1891C>T ; NM_000098.2(CPT2):c.520G>A ; NM_000098.2(CPT2):c.452G>A ; NM_000098.2(CPT2):c.1148T>A ; NM_000098.2(CPT2):c.370C>T ; c.464dup ; NM_000098.2(CPT2):c.886C>T ; NM_000098.2(CPT2):c.680C>T
CPT2	Carnitine palmitoyl transferase II deficiency, neonatal form	The neonatal form of carnitine palmitoyltransferase II (CPT II) deficiency (see this term), an inherited disorder that affects mitochondrial oxidation of long chain fatty acids (LCFA), is the lethal form of the disease which presents with multisystem failure.	Affected infants experience hypoketotic hypoglycemia, liver and respiratory failure and can present with cardiomyopathy, muscle hypotonia, liver calcification, cystic dysplastic kidneys and malformations of the brain due to a neuronal migration defect. Seizures and coma can occur as well as cardiac arrhythmias that generally lead to cardiac arrest in the perinatal/ early infantile period. Death occurs within days to months.	NM_000098.2(CPT2):c.359A>G ; NM_000098.3:c.338C>T ; NM_000098.2(CPT2):c.725_726delAC ; NM_000098.2(CPT2):c.1784delC ; c.1237C>T ; NM_000098.2(CPT2):c.1883A>C ; c.1437C>G ; NM_000098.3:c.1239_1240delGA ; NM_000098.2(CPT2):c.1369A>T ; NM_000098.2(CPT2):c.149C>A ; NM_000098.2(CPT2):c.638A>G ; NM_000098.2(CPT2):c.1891C>T ; NM_000098.2(CPT2):c.520G>A ; NM_000098.2(CPT2):c.452G>A ; NM_000098.2(CPT2):c.1148T>A ; NM_000098.2(CPT2):c.370C>T ; c.464dup ; NM_000098.2(CPT2):c.886C>T ; NM_000098.2(CPT2):c.680C>T
CPT2	Carnitine palmitoyl transferase II deficiency, severe infantile form	The severe infantile form of carnitine palmitoyltransferase II (CPT II) deficiency (see this term), an inherited disorder that affects mitochondrial oxidation of long chain fatty acids (LCFA), is the early-onset form of the disease.	Presentation can be in the newborn period but most cases have an age of onset between 6 and 24 months. The disease is characterized by a severe fasting intolerance leading to metabolic derangements of hypoketotic hypoglycemia, resulting in coma and seizures, and hepatic encephalopathy leading to liver failure. There is associated skeletal muscle myopathy and cardiomyopathy which can lead to fatal paroxysmal cardiac arrhythmias.	NM_000098.2(CPT2):c.359A>G ; NM_000098.3:c.338C>T ; NM_000098.2(CPT2):c.725_726delAC ; NM_000098.2(CPT2):c.1784delC ; c.1237C>T ; NM_000098.2(CPT2):c.1883A>C ; c.1437C>G ; NM_000098.3:c.1239_1240delGA ; NM_000098.2(CPT2):c.1369A>T ; NM_000098.2(CPT2):c.149C>A ; NM_000098.2(CPT2):c.638A>G ; NM_000098.2(CPT2):c.1891C>T ; NM_000098.2(CPT2):c.520G>A ; NM_000098.2(CPT2):c.452G>A ; NM_000098.2(CPT2):c.1148T>A ; NM_000098.2(CPT2):c.370C>T ; c.464dup ; NM_000098.2(CPT2):c.886C>T ; NM_000098.2(CPT2):c.680C>T

CRB1	Leber congenital amaurosis	Leber congenital amaurosis (LCA) is a retinal dystrophy defined by blindness and responses to electrophysiological stimulation (Ganzfeld electroretinogram (ERG)) below threshold, associated with severe visual impairment within the first year of life.	LCA is characterized by severely reduced visual acuity (less or equal 20/400) or blindness within in the first year of life. Sluggish pupillary responses, roving eye movement, photophobia, high hyperopia, nystagmus, convergent strabismus, or keratoconus may occur depending on the genetic cause. The Franceschetti's oculo-digital sign, comprising eye poking, pressing, and rubbing is pathognomonic. LCA may be associated with mutations in genes linked to syndromes presenting with neurodevelopmental delay, intellectual disability, oculomotor apraxia-type behavior (difficulty moving the eye) and renal dysfunction.	NM_201253.2(CRB1):c.3383delT ; c.3083T>A ; NM_201253.2(CRB1):c.613_619delATAGGAA ; NM_201253.2(CRB1):c.2290C>T ; NM_201253.2(CRB1):c.2401A>T ; NM_201253.2(CRB1):c.2983G>T ; NM_201253.2(CRB1):c.3122T>C ; NM_201253.2(CRB1):c.2688T>A ; NM_201253.2(CRB1):c.2843G>A ; c.2080G>T ; NM_201253.2(CRB1):c.3997G>T ; c.2719_2723dup ; NM_201253.2(CRB1):c.3299T>G ; NM_201253.2(CRB1):c.3383delT ; c.3083T>A ; NM_201253.2(CRB1):c.613_619delATAGGAA ; NM_201253.2(CRB1):c.2290C>T ; NM_201253.2(CRB1):c.2401A>T ; NM_201253.2(CRB1):c.2983G>T ; NM_201253.2(CRB1):c.3122T>C ; NM_201253.2(CRB1):c.2688T>A ; NM_201253.2(CRB1):c.2843G>A ; c.2080G>T ; NM_201253.2(CRB1):c.3997G>T ; c.2719_2723dup ; NM_201253.2(CRB1):c.3299T>G
CRB1	Nanophthalmos	A rare ophthalmic disease and a severe form of microphthalmia (small eye phenotype) characterized by a small eye with a short axial length, severe hyperopia, an elevated lens/eye ratio, and a high incidence of angle-closure glaucoma.	The disease occurs neonatally or during infancy. Typical clinical signs include an axial length inferior to 20 mm, a lens/eye ratio 4 to 8 times greater than normal, thickened and abnormally dense sclera, a thickened lens and choroids, and severe hyperopia (+7.00 D to +13.00 D). Despite its small size, the functionality and organization of the eye are preserved. Nanophthalmos is generally bilateral. Strabismus is present in most patients. The association of nanophthalmos and pigmentary retinopathy or Best disease has been reported. The condition can be simple (occurring in isolation), complex (associated with other malformations such as colobomas, anterior segment dysgenesis, and lens and posterior segment abnormalities) or syndromic (as part of a rare syndrome).	NM_201253.2(CRB1):c.3383delT ; c.3083T>A ; NM_201253.2(CRB1):c.613_619delATAGGAA ; NM_201253.2(CRB1):c.2290C>T ; NM_201253.2(CRB1):c.2401A>T ; NM_201253.2(CRB1):c.2983G>T ; NM_201253.2(CRB1):c.3122T>C ; NM_201253.2(CRB1):c.2688T>A ; NM_201253.2(CRB1):c.2843G>A ; c.2080G>T ; NM_201253.2(CRB1):c.3997G>T ; c.2719_2723dup ; NM_201253.2(CRB1):c.3299T>G ; NM_201253.2(CRB1):c.3383delT ; c.3083T>A ; NM_201253.2(CRB1):c.613_619delATAGGAA ; NM_201253.2(CRB1):c.2290C>T ; NM_201253.2(CRB1):c.2401A>T ; NM_201253.2(CRB1):c.2983G>T ; NM_201253.2(CRB1):c.3122T>C ; NM_201253.2(CRB1):c.2688T>A ; NM_201253.2(CRB1):c.2843G>A ; c.2080G>T ; NM_201253.2(CRB1):c.3997G>T ; c.2719_2723dup ; NM_201253.2(CRB1):c.3299T>G

CRB1	Pigmented paravenous retinochoroidal atrophy	Pigmented paravenous chorioretinal atrophy is a stationary disease of the ocular fundus in which bone corpuscle pigmentation is seen in a paravenous distribution. Patients are usually asymptomatic; diagnosis is based on the characteristic fundus appearance. Most cases have been reported in males.	Pigmented paravenous retinochoroidal atrophy (PPRCA) is a rare, commonly bilateral and symmetric retinal disease characterized by non-progressive or slowly progressive chorioretinal atrophy, peripapillary pigmentary changes and accumulation of "bone-corpuscle" pigmentation along the retinal veins and which is usually asymptomatic or can present with mild blurred vision.	NM_201253.2(CRB1):c.3383delT ; c.3083T>A ; NM_201253.2(CRB1):c.613_619delATAGGAA ; NM_201253.2(CRB1):c.2290C>T ; NM_201253.2(CRB1):c.2401A>T ; NM_201253.2(CRB1):c.2983G>T ; NM_201253.2(CRB1):c.3122T>C ; NM_201253.2(CRB1):c.2688T>A ; NM_201253.2(CRB1):c.2843G>A ; c.2080G>T ; NM_201253.2(CRB1):c.3997G>T ; c.2719_2723dup ; NM_201253.2(CRB1):c.3299T>G ; NM_201253.2(CRB1):c.3383delT ; c.3083T>A ; NM_201253.2(CRB1):c.613_619delATAGGAA ; NM_201253.2(CRB1):c.2290C>T ; NM_201253.2(CRB1):c.2401A>T ; NM_201253.2(CRB1):c.2983G>T ; NM_201253.2(CRB1):c.3122T>C ; NM_201253.2(CRB1):c.2688T>A ; NM_201253.2(CRB1):c.2843G>A ; c.2080G>T ; NM_201253.2(CRB1):c.3997G>T ; c.2719_2723dup ; NM_201253.2(CRB1):c.3299T>G
CRB1	Retinitis pigmentosa	Retinitis pigmentosa (RP) is an inherited retinal dystrophy leading to progressive loss of the photoreceptors and retinal pigment epithelium and resulting in blindness usually after several decades.	Retinitis pigmentosa is slowly progressive but relentless. There is however broad variability in age of onset, rate of progression and secondary clinical manifestations. Affected individuals generally first develop night blindness (nyctalopia) due to loss of rod function, often in adolescence or earlier. They then develop peripheral visual field impairment, and over time loss of central vision, usually at late stages, often around midlife. Central visual acuity loss may occur at any age as a result of cystoid macular edema or photoreceptor loss. Posterior subcapsular cataracts are common and severity is age dependent. Reduced color vision may also be found. Fundus examination reveals bone spicule pigment deposits, attenuated retinal vessels, retinal atrophy and waxy optic nerve pallor. Severity is partly correlated with the pattern of inheritance with X-linked cases having the most severe course, autosomal recessive and single occurrence cases having intermediate severity, and autosomal dominant the most favorable course.	NM_201253.2(CRB1):c.3383delT ; c.3083T>A ; NM_201253.2(CRB1):c.613_619delATAGGAA ; NM_201253.2(CRB1):c.2290C>T ; NM_201253.2(CRB1):c.2401A>T ; NM_201253.2(CRB1):c.2983G>T ; NM_201253.2(CRB1):c.3122T>C ; NM_201253.2(CRB1):c.2688T>A ; NM_201253.2(CRB1):c.2843G>A ; c.2080G>T ; NM_201253.2(CRB1):c.3997G>T ; c.2719_2723dup ; NM_201253.2(CRB1):c.3299T>G ; NM_201253.2(CRB1):c.3383delT ; c.3083T>A ; NM_201253.2(CRB1):c.613_619delATAGGAA ; NM_201253.2(CRB1):c.2290C>T ; NM_201253.2(CRB1):c.2401A>T ; NM_201253.2(CRB1):c.2983G>T ; NM_201253.2(CRB1):c.3122T>C ; NM_201253.2(CRB1):c.2688T>A ; NM_201253.2(CRB1):c.2843G>A ; c.2080G>T ; NM_201253.2(CRB1):c.3997G>T ; c.2719_2723dup ; NM_201253.2(CRB1):c.3299T>G

CTNS	Infantile nephropathic cystinosis	A subtype of cystinosis characterized by an accumulation of cystine in the organs and tissues, particularly in the kidneys and eyes, and that clinically manifests from infancy with renal Fanconi syndrome, photophobia, hypothyroidism, impaired growth and rickets, in addition to various other systemic effects. Progressive extra-renal manifestations include hypothyroidism, hypogonadism and male infertility, insulin-dependent diabetes, hepatosplenomegaly with portal hypertension, muscle involvement with distal muscle weakness and atrophy, pharyngeal and oral dysfunction, swallowing difficulties, cerebral involvement with hypotonia, speech and walking difficulties, and cerebellar syndrome.	Cystinosis has been classified as a lysosomal storage disorder on the basis of cytologic and other evidence pointing to the intralysosomal localization of stored cystine. Cystinosis differs from the other lysosomal diseases inasmuch as acid hydrolysis, the principal enzyme function of lysosomes, is not known to play a role in the metabolic disposition of cystine. The fact that plasma levels are well below saturation indicates that the defect is a cellular one. Within the cell, cystine is compartmentalized with acid phosphatase and is membrane-bound as demonstrated by electron microscopy. Ferritin accumulates in the same organelle which appears to be the lysosome.	NM_001031681.2(CTNS):c.283G>T ; NM_001031681.2(CTNS):c.506G>A ; NM_004937.2(CTNS):c.416C>T ; NM_004937.2(CTNS):c.646dupA ; c.357_360del ; NM_004937.2(CTNS):c.589G>A ; NM_004937.2(CTNS):c.414G>A ; c.397_398del ; NM_004937.3:c.1015G>A ; NM_004937.2(CTNS):c.853-3C>G ; NM_001031681.2(CTNS):c.329G>T ; NM_001031681.2(CTNS):c.283G>T ; NM_001031681.2(CTNS):c.506G>A ; NM_004937.2(CTNS):c.416C>T ; NM_004937.2(CTNS):c.646dupA ; c.357_360del ; NM_004937.2(CTNS):c.589G>A ; NM_004937.2(CTNS):c.414G>A ; c.397_398del ; NM_004937.3:c.1015G>A ; NM_004937.2(CTNS):c.853-3C>G ; NM_001031681.2(CTNS):c.329G>T

CTNS	Juvenile nephropathic cystinosis	A subtype of cystinosis characterized by an accumulation of cystine in different organs and tissues, particularly in the kidneys and eyes, and that clinically manifests between childhood and adolescence with a slowly progressive proximal tubulopathy and/or proteinuria, and photophobia. Extra-renal manifestations (e.g. hypothyroidism, insulin-dependent diabetes, hepatosplenomegaly, muscular and cerebral involvement) are less severe than in the infantile form of the disease.	Adolescent nephropathic cystinosis manifests itself first at age 10 to 12 years with proteinuria due to glomerular damage rather than with the manifestations of tubular damage that occur first in infantile cystinosis. There is no excess amino aciduria and stature is normal. Photophobia, late development of pigmentary retinopathy, and chronic headaches are features. White cells show high cystine content in heterozygotes for this form of cystinosis, just as they do in infantile cystinosis. Clinically the disorder shows a slowly progressive glomerular insufficiency rather than the prominent Fanconi syndrome, electrolyte and water disturbances, growth arrest, and rickets typical of infantile cystinosis. The patient was the only affected person in the family and the parents were not related (as one would expect if juvenile cystinosis is the genetic compound of infantile cystinosis and adult cystinosis).	NM_001031681.2(CTNS):c.283G>T ; NM_001031681.2(CTNS):c.506G>A ; NM_004937.2(CTNS):c.416C>T ; NM_004937.2(CTNS):c.646dupA ; c.357_360del ; NM_004937.2(CTNS):c.589G>A ; NM_004937.2(CTNS):c.414G>A ; c.397_398del ; NM_004937.3:c.1015G>A ; NM_004937.2(CTNS):c.853-3C>G ; NM_001031681.2(CTNS):c.329G>T ; NM_001031681.2(CTNS):c.283G>T ; NM_001031681.2(CTNS):c.506G>A ; NM_004937.2(CTNS):c.416C>T ; NM_004937.2(CTNS):c.646dupA ; c.357_360del ; NM_004937.2(CTNS):c.589G>A ; NM_004937.2(CTNS):c.414G>A ; c.397_398del ; NM_004937.3:c.1015G>A ; NM_004937.2(CTNS):c.853-3C>G ; NM_001031681.2(CTNS):c.329G>T
CTNS	Ocular cystinosis	Ocular cystinosis is the benign, adult form of cystinosis, a metabolic disease characterized by an accumulation of cystine crystals in the cornea and conjunctiva responsible for tearing and photophobia and associated with no other additional manifestations.	Ocular nonnephropathic cystinosis, a variant of the classic nephropathic type of cystinosis (219800), is an autosomal recessive lysosomal storage disorder characterized by photophobia due to corneal cystine crystals but absence of renal disease.	NM_001031681.2(CTNS):c.283G>T ; NM_001031681.2(CTNS):c.506G>A ; NM_004937.2(CTNS):c.416C>T ; NM_004937.2(CTNS):c.646dupA ; c.357_360del ; NM_004937.2(CTNS):c.589G>A ; NM_004937.2(CTNS):c.414G>A ; c.397_398del ; NM_004937.3:c.1015G>A ; NM_004937.2(CTNS):c.853-3C>G ; NM_001031681.2(CTNS):c.329G>T ; NM_001031681.2(CTNS):c.283G>T ; NM_001031681.2(CTNS):c.506G>A ; NM_004937.2(CTNS):c.416C>T ; NM_004937.2(CTNS):c.646dupA ; c.357_360del ; NM_004937.2(CTNS):c.589G>A ; NM_004937.2(CTNS):c.414G>A ; c.397_398del ; NM_004937.3:c.1015G>A ; NM_004937.2(CTNS):c.853-3C>G ; NM_001031681.2(CTNS):c.329G>T

CTSD	CLN10 disease	Neuronal ceroid lipofuscinoses (NCLs) are a group of inherited progressive degenerative brain diseases characterized clinically by a decline of mental and other capacities, epilepsy, and vision loss through retinal degeneration, and histopathologically by intracellular accumulation of an autofluorescent material, ceroid lipofuscin, in the neuronal cells in the brain and in the retina.	The clinical presentation varies widely between forms but the clinical hallmark is a combination of dementia, visual loss, and epilepsy. Manifestations may begin between the neonatal period and young adult age depending on the form, leading to the original classification of NCLs by age at onset into congenital, infantile, late infantile, juvenile and adult NCL subgroups (see these terms). A Northern epilepsy variant (progressive epilepsy-intellectual deficit, Finnish type; see this term), in which the visual problems may be absent or be mild and go unrecognized, has also been described.	NM_001909.4(CTSD):c.1149G>C ; NM_001909.4(CTSD):c.685T>A ; NM_001909.4(CTSD):c.1149G>C ; NM_001909.4(CTSD):c.685T>A
CTSK	Pycnodysostosis	Pycnodysostosis is a genetic lysosomal disease characterized by osteosclerosis of the skeleton, short stature and brittle bones.	The disease is discovered at variable ages, ranging from 9 months to 50 years. The condition is most often diagnosed in childhood, but sometimes the condition is not detected until adulthood, usually as a result of a fracture or a routine examination. The most frequent clinical or radiological manifestations of the disease are osteosclerosis, short stature or dwarfism, acroosteolysis of the distal phalanges, fragile bones associated with spontaneous fractures and dysplasia of the clavicles. Patients present with characteristic cranial malformations: a voluminous skull with wormian bones present and persistence of the anterior fontanelle, and a small mandible. Dental abnormalities such as decayed, poorly located or abnormally shaped (pointed or conical) teeth and delayed tooth eruption may be observed. Nails are sometimes irregular and cracked. Very rarely, the disease is associated with anemia, hepatosplenomegaly, hematologic alterations, respiratory distress and sleep apnea. The short stature is variable but moderate (1.35m to 1.50m).	NM_000396.3(CTSK):c.926T>C ; NM_000396.3(CTSK):c.436G>C ; NM_000396.3(CTSK):c.236G>A ; NM_000396.3(CTSK):c.154A>T ; NM_000396.3(CTSK):c.721C>T ; NM_000396.3(CTSK):c.926T>C ; NM_000396.3(CTSK):c.436G>C ; NM_000396.3(CTSK):c.236G>A ; NM_000396.3(CTSK):c.154A>T ; NM_000396.3(CTSK):c.721C>T

CYP21A2	Classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency, salt wasting form	The salt wasting form of classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency (classical 21 OHD CAH; see this term) is characterized by virilization of the external genitalia in females, hypocortisolism, precocious pseudopuberty and renal salt loss due to aldosterone deficiency.	Patients suffer from glucocorticoid deficiency, aldosterone deficiency with salt wasting, failure to thrive, and potentially fatal hypovolemia and shock. Virilization of external genitalia in females is seen from birth. During the firstweeks of life this salt wasting form can manifest in a salt-losing crisis (failure to thrive, vomiting, hyponatremia, hyperkaliema, acidosis, hypovolemia) which requires life saving treatment immediately. Precocious pseudopuberty, manifesting with various symptoms including accelerated growth velocity and bone maturation, is also present in both sexes.	NM_000500.7(CYP21A2):c.719T>A (p.Met240Lys) ; NM_000500.7(CYP21A2):c.713T>A (p.Val238Glu) ; NM_000500.7(CYP21A2):c.710T>A (p.Ile237Asn) ; NM_000500.7(CYP21A2):c.518T>A (p.Ile173Asn) ; NM_000500.7(CYP21A2):c.1069C>T ; NM_000500.7(CYP21A2):c.293-13C>G ; NM_000500.7(CYP21A2):c.332_339delGAGACTAC (p.Gly111Valfs) ; NM_000500.9(CYP21A2):c.923dup (p.Leu308Phefs) ; NM_000500.7(CYP21A2):c.92C>T (p.Pro31Leu) ; NM_000500.7(CYP21A2):c.844G>T (p.Val282Leu) ; NM_000500.7(CYP21A2):c.1360C>T (p.Pro454Ser) ; NM_000500.7(CYP21A2):c.955C>T (p.Gln319Ter)
CYP21A2	Classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency, simple virilizing form	The simple virilizing form of classical congenital adrenal hyperplasia due to 21-hydroxylase deficiency (classical 21 OHD CAH; see this term) is characterized by genital ambiguity and virilization of the external genitalia in females, hypocortisolism and precocious pseudopuberty without salt-wasting.	Girls present at birth with ambiguous genitalia and variable levels of virilization. They have a normal uterus but abnormal vaginal development. The external genitalia in boys are normal. Precocious pseudopuberty, manifesting with various symptoms including accelerated growth velocity and bone maturation, is also present in both sexes. Unlike the salt wasting form of classical 21 OHD CAH, the simple virilizing form has no symptoms of dehydration, but has a glucocorticoid deficiency requiring life-long substitution therapy and carrying a life-long risk of adrenal crisis.	NM_000500.7(CYP21A2):c.719T>A (p.Met240Lys) ; NM_000500.7(CYP21A2):c.713T>A (p.Val238Glu) ; NM_000500.7(CYP21A2):c.710T>A (p.Ile237Asn) ; NM_000500.7(CYP21A2):c.518T>A (p.Ile173Asn) ; NM_000500.7(CYP21A2):c.1069C>T ; NM_000500.7(CYP21A2):c.293-13C>G ; NM_000500.7(CYP21A2):c.332_339delGAGACTAC (p.Gly111Valfs) ; NM_000500.9(CYP21A2):c.923dup (p.Leu308Phefs) ; NM_000500.7(CYP21A2):c.92C>T (p.Pro31Leu) ; NM_000500.7(CYP21A2):c.844G>T (p.Val282Leu) ; NM_000500.7(CYP21A2):c.1360C>T (p.Pro454Ser) ; NM_000500.7(CYP21A2):c.955C>T (p.Gln319Ter)

CYP21A2	NON RARE IN EUROPE: Non-classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency	In female newborns, the external genitalia are masculinized; gonads and internal genitalia are normal. Postnatally, untreated males as well as females may manifest rapid growth, penile or clitoral enlargement, precocious adrenarche, and ultimately early epiphyseal closure and short stature. A mild form of late-onset adrenal hyperplasia due to 21-hydroxylase deficiency can occur in adults and has hirsutism as the only manifestation in the most attenuated form.	Congenital adrenal hyperplasia (CAH) results from a deficiency in one or another of the enzymes of cortisol biosynthesis. In about 95% of cases, 21-hydroxylation is impaired in the zona fasciculata of the adrenal cortex so that 17-hydroxyprogesterone (17-OHP) is not converted to 11-deoxycortisol. Because of defective cortisol synthesis, ACTH levels increase, resulting in overproduction and accumulation of cortisol precursors, particularly 17-OHP, proximal to the block. This causes excessive production of androgens, resulting in virilization.	NM_000500.7(CYP21A2):c.719T>A (p.Met240Lys) ; NM_000500.7(CYP21A2):c.713T>A (p.Val238Glu) ; NM_000500.7(CYP21A2):c.710T>A (p.Ile237Asn) ; NM_000500.7(CYP21A2):c.518T>A (p.Ile173Asn) ; NM_000500.7(CYP21A2):c.1069C>T ; NM_000500.7(CYP21A2):c.293-13C>G ; NM_000500.7(CYP21A2):c.332_339delGAGACTAC (p.Gly111Valfs) ; NM_000500.9(CYP21A2):c.923dup (p.Leu308Phefs) ; NM_000500.7(CYP21A2):c.92C>T (p.Pro31Leu) ; NM_000500.7(CYP21A2):c.844G>T (p.Val282Leu) ; NM_000500.7(CYP21A2):c.1360C>T (p.Pro454Ser) ; NM_000500.7(CYP21A2):c.955C>T (p.Gln319Ter)
DBT	Classic maple syrup urine disease	Classic maple syrup urine disease (classic MSUD) is the most severe and probably common form of MSUD (see this term) characterized by a maple syrup odor in the cerumen at birth, poor feeding, lethargy and focal dystonia, followed by progressive encephalopathy and central respiratory failure if untreated.	Onset of classic MSUD occurs in the neonatal period (usually 12 hours after birth) with the presence of a maple syrup odor in the cerumen and later in urine, poor feeding and drowsiness. Progressive encephalopathy with lethargy, intermittent apnea, stereotyped movements (described as "fencing" and bicycling") and opisthotonus occur in the first few days of life. Without treatment, coma and central respiratory failure occur by days 7 to 10. Later, catabolic stress, infection or injury may cause acute, potentially fatal, leucine intoxication with vomiting, altered consciousness, ataxia and acute dystonia in toddlers and hallucinations, hyperactivity, focal dystonia, ataxia and choreoathetosis in children and adults.	c.1281+1G>A ; NM_001918.3(DBT):c.294C>G ; c.772+1G>A ; NM_001918.3(DBT):c.126T>G ; NM_001918.3(DBT):c.272_275delCAGT ; NM_001918.3(DBT):c.670G>T ; NM_001918.3(DBT):c.901C>T ; NM_001918.3(DBT):c.871C>T ; NM_001918.4:c.581C>G ; NM_001918.3(DBT):c.939G>C ; c.1281+1G>A ; NM_001918.3(DBT):c.294C>G ; c.772+1G>A ; NM_001918.3(DBT):c.126T>G ; NM_001918.3(DBT):c.272_275delCAGT ; NM_001918.3(DBT):c.670G>T ; NM_001918.3(DBT):c.901C>T ; NM_001918.3(DBT):c.871C>T ; NM_001918.4:c.581C>G ; NM_001918.3(DBT):c.939G>C

DBT	Intermediate maple syrup urine disease	Intermediate maple syrup urine disease (intermediate MSUD) is a milder form of MSUD (see this term) characterized by persistently raised branched-chain amino acids (BCAAs) and ketoacids, but fewer or no acute episodes of decompensation.	Symptom onset of intermediate MSUD varies between the early months and the early years of childhood. Infants may have feeding problems, poor growth, maple syrup odor in urine and developmental delay. Older children usually present with learning difficulties. Like classic MSUD (see this term), catabolic stress can result in acute decompensation with anorexia, vomiting, ataxia (in infants/toddlers), cognitive impairment, sleep disturbances, hallucinations, hyperactivity, mood swings, acute dystonia, choreoathetosis (in adults), stupor, coma and cerebral edema, if untreated.	c.1281+1G>A ; NM_001918.3(DBT):c.294C>G ; c.772+1G>A ; NM_001918.3(DBT):c.126T>G ; NM_001918.3(DBT):c.272_275delCAGT ; NM_001918.3(DBT):c.670G>T ; NM_001918.3(DBT):c.901C>T ; NM_001918.3(DBT):c.871C>T ; NM_001918.4:c.581C>G ; NM_001918.3(DBT):c.939G>C ; c.1281+1G>A ; NM_001918.3(DBT):c.294C>G ; c.772+1G>A ; NM_001918.3(DBT):c.126T>G ; NM_001918.3(DBT):c.272_275delCAGT ; NM_001918.3(DBT):c.670G>T ; NM_001918.3(DBT):c.901C>T ; NM_001918.3(DBT):c.871C>T ; NM_001918.4:c.581C>G ; NM_001918.3(DBT):c.939G>C
DBT	Intermittent maple syrup urine disease	Intermittent maple syrup urine disease (intermittent MSUD) is a mild form of MSUD (see this term) where patients (when well) are asymptomatic with normal levels of branched-chain amino acids (BCAAs) but with catabolic stress are at risk of acute decompensation with ketoacidosis, which can lead to cerebral edema and coma if untreated.	Unlike classic MSUD (see this term), patients with intermittent MSUD show normal growth and intellectual development during infancy and childhood. They may develop symptoms (mainly in childhood) with any catabolic stress (i.e. fasting, dehydration, fever, infections or pregnancy (in adults)). These precipitating factors can lead to a potentially fatal episode of acute decompensation with anorexia, nausea, vomiting, lethargy, ataxia (in infants/toddlers), cognitive impairment, sleep disturbances, hallucinations, hyperactivity, mood swings, acute dystonia, and choreoathetosis (in adults), that can progress to stupor, coma and cerebral edema. Intelligence and development are not usually affected by these episodes.	c.1281+1G>A ; NM_001918.3(DBT):c.294C>G ; c.772+1G>A ; NM_001918.3(DBT):c.126T>G ; NM_001918.3(DBT):c.272_275delCAGT ; NM_001918.3(DBT):c.670G>T ; NM_001918.3(DBT):c.901C>T ; NM_001918.3(DBT):c.871C>T ; NM_001918.4:c.581C>G ; NM_001918.3(DBT):c.939G>C ; c.1281+1G>A ; NM_001918.3(DBT):c.294C>G ; c.772+1G>A ; NM_001918.3(DBT):c.126T>G ; NM_001918.3(DBT):c.272_275delCAGT ; NM_001918.3(DBT):c.670G>T ; NM_001918.3(DBT):c.901C>T ; NM_001918.3(DBT):c.871C>T ; NM_001918.4:c.581C>G ; NM_001918.3(DBT):c.939G>C

DBT	Thiamine-responsive maple syrup urine disease	Thiamine-responsive maple syrup urine disease (thiamine-responsive MSUD) is a less severe variant of MSUD (see this term) that manifests with a phenotype similar to intermediate MSUD (see this term) but that responds positively to treatment with thiamine.	Thiamine-responsive MSUD is poorly characterized. It appears to usually present after infancy with a phenotype very similar to that seen in intermediate MSUD (see this term). Manifestations include feeding problems, poor growth, maple syrup odor in urine and developmental delay. Older children usually present with learning difficulties. Like classic MSUD (see this term), physiological stress can result in acute decompensation with anorexia, nausea, vomiting (at all ages), ataxia (in infants/toddlers), cognitive impairment, sleep disturbances, hallucinations, hyperactivity, mood swings, acute / focal dystonia and choreoathetosis (in adults) that can progress to stupor, coma and cerebral edema, if untreated. Thiamine (doses of 10-1000 mg per day) has improved the leucine tolerance in the few reported cases of this MSUD subtype, but some dietary branched-chain amino-acid (BCAA) restriction remains necessary.	c.1281+1G>A ; NM_001918.3(DBT):c.294C>G ; c.772+1G>A ; NM_001918.3(DBT):c.126T>G ; NM_001918.3(DBT):c.272_275delCAGT ; NM_001918.3(DBT):c.670G>T ; NM_001918.3(DBT):c.901C>T ; NM_001918.3(DBT):c.871C>T ; NM_001918.4:c.581C>G ; NM_001918.3(DBT):c.939G>C ; c.1281+1G>A ; NM_001918.3(DBT):c.294C>G ; c.772+1G>A ; NM_001918.3(DBT):c.126T>G ; NM_001918.3(DBT):c.272_275delCAGT ; NM_001918.3(DBT):c.670G>T ; NM_001918.3(DBT):c.901C>T ; NM_001918.3(DBT):c.871C>T ; NM_001918.4:c.581C>G ; NM_001918.3(DBT):c.939G>C
DCLRE1C	Omenn syndrome	Omenn syndrome (OS) is an inflammatory condition characterized by erythroderma, desquamation, alopecia, chronic diarrhea, failure to thrive, lymphadenopathy, and hepatosplenomegaly, associated with severe combined immunodeficiency (SCID; see this term).	OS presents during the first year of life with features of SCID including chronic diarrhea, pneumonitis and failure to thrive. In addition, patients present with inflammatory symptoms including lymphadenopathy, hepatosplenomegaly and generalized erythroderma, which may often cause alopecia and loss of eyebrows and eyelashes; protein loss may lead to generalized edema and metabolic disturbances. The signs and symptoms of OS can evolve over time and may not appear simultaneously. Some patients present with some but not all of these symptoms and may be described as having atypical Omenn syndrome. OS may also be associated with syndromic disorders including cartilage-hair hypoplasia (CHH), adenosine deaminase (ADA) deficiency, monosomy 22q11, coloboma of the eye, CHARGE syndrome and ligase 4 deficiency (see these terms).	c.1294G>T ; NM_022487.3(DCLRE1C):c.435del ; c.1214dup ; NM_001033855.2(DCLRE1C):c.597C>A ; NM_001033855.2(DCLRE1C):c.2T>C ; c.1294G>T ; NM_022487.3(DCLRE1C):c.435del ; c.1214dup ; NM_001033855.2(DCLRE1C):c.597C>A ; NM_001033855.2(DCLRE1C):c.2T>C

DCLRE1C	Severe combined immunodeficiency due to DCLRE1C deficiency	Severe combined immunodeficiency (SCID) due to DCLRE1C deficiency is a type of SCID (see this term) characterized by severe and recurrent infections, diarrhea, failure to thrive, and cell sensitivity to ionizing radiation.	Patients present with the classical features of SCID such as failure to thrive, severe infections (pneumonia, gastrointestinal infections, sepsis), recurrent or persistent thrush, and chronic diarrhea. Materno-fetal transfusion-associated graft versus host disease is also associated with the disease. Immunological findings include absence of T and B lymphocytes with normal natural killer (NK) cell count.	c.1294G>T ; NM_022487.3(DCLRE1C):c.435del ; c.1214dup ; NM_001033855.2(DCLRE1C):c.597C>A ; NM_001033855.2(DCLRE1C):c.2T>C ; c.1294G>T ; NM_022487.3(DCLRE1C):c.435del ; c.1214dup ; NM_001033855.2(DCLRE1C):c.597C>A ; NM_001033855.2(DCLRE1C):c.2T>C
DDB2	Xeroderma pigmentosum	Xeroderma pigmentosum (XP) is a rare genodermatosis characterized by extreme sensitivity to ultraviolet (UV)-induced changes in the skin and eyes, and multiple skin cancers. It is subdivided into 8 complementation groups, according to the affected gene: classical XP (XPA to XPG) and XP variant (XPV) (see these terms).	The severity of the clinical manifestations and the age of onset are extremely variable and are in part dependent on exposure to sunlight and the complementation group. Approximately 50% of affected individuals have acute sun sensitivity from the first few months of life, presenting with severe sunburn and/or persistent erythema which takes weeks to resolve. Others do not show any sunburn reaction and gradually develop marked freckling at sun exposed sites. Individuals have dry skin and hypo- or hyperpigmented lesions. There is a greater than 10,000-fold increased risk of non-melanoma skin cancers, and a 2,000 fold increased risk of melanoma under the age of 20 when compared to the general population. Patients with classical XP develop skin cancer generally before the age of 20, while patients with XP variant start to develop skin cancer at about 20-30 years of age. Ocular abnormalities include keratitis resulting in corneal opacification and vascularization. Photophobia is common. Ocular squamous cell carcinoma and melanoma are common. Neurologic abnormalities of varying severity have been reported in about 30% of cases. These include acquired microcephaly, diminished or absent deep tendon stretch reflexes, progressive sensorineural hearing loss, spasticity, ataxia, seizures and progressive cognitive impairment. De Sanctis-Cacchione syndrome is a term that was originally attributed to XP cases with severe neurological abnormalities but it is no longer in general use.	NM_000107.2(DDB2):c.730A>G ; NM_000107.2(DDB2):c.919G>T ; NM_000107.2(DDB2):c.937C>T ; NM_000107.2(DDB2):c.818G>A ; NM_000107.2(DDB2):c.730A>G ; NM_000107.2(DDB2):c.919G>T ; NM_000107.2(DDB2):c.937C>T ; NM_000107.2(DDB2):c.818G>A

DHCR7	Smith-Lemli-Opitz syndrome	Smith-Lemli-Opitz syndrome (SLOS) is characterized by multiple congenital anomalies, intellectual deficit, and behavioral problems.	The disease is present at birth, but may be detected in later childhood or adulthood in mild forms. Patients present with growth retardation and intellectual deficit. Behavioral problems include multiple autistic traits, hyperactivity, self-injurious behavior and sleep disturbances. The structural brain anomalies may include hypoplasia or absence of the corpus callosum, and holoprosencephaly. Microcephaly (80% of cases), bitemporal narrowing, ptosis, a broad nasal bridge, short nasal root, anteverted nares (90% of cases), a small chin, and micrognathia are common craniofacial features. Occasionally, cataract, strabismus, and nystagmus are observed. Other clinical features include cleft palate or bifid uvula (1/3 of patients), photosensitivity, rhizomelia and postaxial polydactyly of the hands or feet, syndactyly of the 2nd and 3rd toes (95% of cases), and short and proximally placed thumbs. Genital anomalies (small penis, hypospadias, ambiguous genitalia) are frequent in males (70% of cases). Cardiovascular anomalies (atrial and ventricular septal defects, patent ductus arteriosus, atrioventricular canal) can be present. Gastrointestinal anomalies including poor feeding, gastroesophageal reflux, pyloric stenosis, malrotation, and colonic aganglionosis are frequent.	NM_001360.2(DHCR7):c.1337G>A ; NM_001360.2(DHCR7):c.744G>T ; NM_001360.2(DHCR7):c.832-1G>C ; c.904T>C ; NM_001360.2(DHCR7):c.1342G>A ; NM_001360.2(DHCR7):c.730G>A ; NM_001360.2(DHCR7):c.453G>A ; NM_001360.2(DHCR7):c.725G>A ; NM_001360.2:c.964-1G>C ; NM_001360.2(DHCR7):c.1228G>A ; NM_001360.2(DHCR7):c.452G>A ; NM_001360.2(DHCR7):c.866C>T ; NM_001360.2(DHCR7):c.356A>T ; NM_001360.2(DHCR7):c.1055G>A ; NM_001360.2(DHCR7):c.724C>T ; NM_001360.2(DHCR7):c.976G>T ; NM_001360.2(DHCR7):c.292C>T ; NM_001360.2(DHCR7):c.1A>G ; NM_001360.2(DHCR7):c.1210C>T ; NM_001360.2(DHCR7):c.1054C>T ; NM_001360.2(DHCR7):c.151C>T ; NM_001360.2(DHCR7):c.278C>T ; NM_001360.2(DHCR7):c.839A>G ; NM_001360.2(DHCR7):c.1337G>A ; NM_001360.2(DHCR7):c.744G>T ; NM_001360.2(DHCR7):c.832-1G>C ; c.904T>C ; NM_001360.2(DHCR7):c.1342G>A ; NM_001360.2(DHCR7):c.730G>A ; NM_001360.2(DHCR7):c.453G>A ; NM_001360.2(DHCR7):c.725G>A ; NM_001360.2:c.964-1G>C ; NM_001360.2(DHCR7):c.1228G>A ; NM_001360.2(DHCR7):c.452G>A ; NM_001360.2(DHCR7):c.866C>T ; NM_001360.2(DHCR7):c.356A>T ; NM_001360.2(DHCR7):c.1055G>A ; NM_001360.2(DHCR7):c.724C>T ; NM_001360.2(DHCR7):c.976G>T ; NM_001360.2(DHCR7):c.292C>T ; NM_001360.2(DHCR7):c.1A>G ; NM_001360.2(DHCR7):c.1210C>T ; NM_001360.2(DHCR7):c.1054C>T ; NM_001360.2(DHCR7):c.151C>T ; NM_001360.2(DHCR7):c.278C>T ; NM_001360.2(DHCR7):c.839A>G

DHDDS	Non-specific early-onset epileptic encephalopathy	A rare infantile epilepsy syndrome characterized by early onset of seizures of variable type and severity, potentially associated with a spectrum of clinical signs and symptoms including delay or lack of psychomotor development, intellectual disability, poor or absent speech development, behavioral abnormalities, hypotonia, movement disorders, spasticity, microcephaly, and dysmorphic facial features, among others. Brain imaging findings are also variable and may include cerebral atrophy or white matter abnormalities.	0	c.995C>G ; NM_024887.3:c.124A>G ; c.330del ; c.995C>G ; NM_024887.3:c.124A>G ; c.330del

DHDDS	Retinitis pigmentosa	Retinitis pigmentosa (RP) is an inherited retinal dystrophy leading to progressive loss of the photoreceptors and retinal pigment epithelium and resulting in blindness usually after several decades.	Retinitis pigmentosa is slowly progressive but relentless. There is however broad variability in age of onset, rate of progression and secondary clinical manifestations. Affected individuals generally first develop night blindness (nyctalopia) due to loss of rod function, often in adolescence or earlier. They then develop peripheral visual field impairment, and over time loss of central vision, usually at late stages, often around midlife. Central visual acuity loss may occur at any age as a result of cystoid macular edema or photoreceptor loss. Posterior subcapsular cataracts are common and severity is age dependent. Reduced color vision may also be found. Fundus examination reveals bone spicule pigment deposits, attenuated retinal vessels, retinal atrophy and waxy optic nerve pallor. Severity is partly correlated with the pattern of inheritance with X-linked cases having the most severe course, autosomal recessive and single occurrence cases having intermediate severity, and autosomal dominant the most favorable course.	c.995C>G ; NM_024887.3:c.124A>G ; c.330del ; c.995C>G ; NM_024887.3:c.124A>G ; c.330del

DKC1	Dyskeratosis congenita	A rare ectodermal dysplasia syndrome that often presents with the classic triad of nail dysplasia, skin pigmentary changes, and oral leukoplakia associated with a high risk of bone marrow failure (BMF) and cancer.	DC has a wide phenotypic spectrum and age onset. It classically manifests during childhood with the triad of dysplastic nails, lacy reticular pigmentation and atrophy of the skin at the level of the neck and upper chest, and oral leukoplakia. Patients are at high risk of progressive BMF and may develop myelodysplastic syndrome or acute myelogenous leukemia at any age (the risk increasing with age). There is also an increased risk for solid tumors, typically squamous cell carcinoma of head and neck or anogenital cancer. Additional clinical findings have been reported and may include: developmental delay, short stature, microcephaly, blepharitis, epiphora, periodontal disease, taurodontism, decreased teeth/root ratio, esophageal stenosis, urethral stenosis, osteoporosis, avascular necrosis of femur and/or humerus, premature hair greying/alopecia, or abnormal eyelashes. Individuals with Patients with DC may also develop pulmonary fibrosis, pulmonary arteriovenous malformations, gastrointestinal telangiectasias, and liver disease. It is important to note that the clinical features of DC progress over time and that all features, including the mucocutaneous triad, may not be present.	NM_001363.4(DKC1):c.91C>A ; NM_001363.4(DKC1):c.204C>A ; NM_001363.4(DKC1):c.91C>G ; NM_001363.4(DKC1):c.196A>G ; NM_001363.4(DKC1):c.200C>T ; NM_001363.4(DKC1):c.194G>C ; NM_001363.4(DKC1):c.214_215delCTinsTA ; NM_001363.4(DKC1):c.91C>A ; NM_001363.4(DKC1):c.204C>A ; NM_001363.4(DKC1):c.91C>G ; NM_001363.4(DKC1):c.196A>G ; NM_001363.4(DKC1):c.200C>T ; NM_001363.4(DKC1):c.194G>C ; NM_001363.4(DKC1):c.214_215delCTinsTA
DKC1	Hoyeraal-Hreidarsson syndrome	An X-linked syndromic intellectual disability considered to be a severe variant of dyskeratosis congenita characterized by intrauterine growth retardation, microcephaly, cerebellar hypoplasia, progressive combined immune deficiency and aplastic anemia.	The disease generally presents in early childhood and primarily affects males. Growth retardation is usually of prenatal onset. Other clinical manifestations include microcephaly, mucocutaneous lesions (hyperpigmentation, nail dystrophy, premalignant leukoplakia affecting oral and gastrointestinal mucosa), early onset bone marrow failure, immunodeficiency and pancytopenia. Cancer predisposition is also reported.	NM_001363.4(DKC1):c.91C>A ; NM_001363.4(DKC1):c.204C>A ; NM_001363.4(DKC1):c.91C>G ; NM_001363.4(DKC1):c.196A>G ; NM_001363.4(DKC1):c.200C>T ; NM_001363.4(DKC1):c.194G>C ; NM_001363.4(DKC1):c.214_215delCTinsTA ; NM_001363.4(DKC1):c.91C>A ; NM_001363.4(DKC1):c.204C>A ; NM_001363.4(DKC1):c.91C>G ; NM_001363.4(DKC1):c.196A>G ; NM_001363.4(DKC1):c.200C>T ; NM_001363.4(DKC1):c.194G>C ; NM_001363.4(DKC1):c.214_215delCTinsTA

DLD	Pyruvate dehydrogenase E3 deficiency	Pyruvate dehydrogenase E3 deficiency is a very rare subtype of pyruvate dehydrogenase deficiency (PDHD, see this term) characterized by either early-onset lactic acidosis and delayed development, later-onset neurological dysfunction or liver disease.	The majority of patients have presented with neonatal lactic acidosis or with lactic acidosis, delayed development and hypotonia during infancy. A few patients have presented later in childhood with ataxia and dystonia with normal cognitive development. A separate group of patients, essentially all of Ashkenazi Jewish origin and many homozygous for a common G229C missense mutation, present with episodic vomiting, abdominal pain, encephalopathy and liver cell dysfunction. In some patients, there is evidence of branched chain alpha-ketoacid dehydrogenase deficiency, with elevated concentrations of the branched chain amino acids and their metabolites. However, clinical manifestations in most cases appear to be related to the pyruvate dehydrogenase deficiency.	NM_000108.4(DLD):c.1483A>G ; c.916_926del ; NM_000108.3:c.105_106insA ; NM_000108.4(DLD):c.1483A>G ; c.916_926del ; NM_000108.3:c.105_106insA

DMD	Becker muscular dystrophy	A rare, genetic muscular dystrophy characterized by progressive muscle wasting and weakness due to degeneration of skeletal, smooth and cardiac muscle.	Onset is usually in childhood, typically after 7 years of age, but can be later. Presenting features in children include toe walking gait and or exercise-related cramps with or without myoglobinuria. Some patients may present following anesthetic induced acute rhabdomyolysis. In older patients, cardiomyopathy may be the presenting feature. As the condition progresses, muscle weakness leads to functional difficulties (difficulty climbing stairs or rising from a chair). Rarely, cardiomyopathy may be the presenting feature. Clinical examination reveals muscle pseudohypertrophy of the calf muscles and there may be atrophy of more proximal muscles such as the quadriceps. There is symmetrical and proximal muscle weakness, with the lower limbs being more severely affected than the upper limbs. There may be joint contractures, especially of the tendo- Achilles. The facial, ophthalmic and bulbar muscles are not involved. The condition is slowly progressive and about 40% of affected patients will eventually become wheelchair-dependent. In wheelchair dependent patients, restrictive respiratory insufficiency occurs due to weakness of the intercostal muscles and diaphragm. Cardiac involvement leads to dilated cardiomyopathy, which can be disproportionate to skeletal muscle involvement.	c.3087G>A ; g.26102-57302794 ; NM_004006.2(DMD):c.8608C>T ; NM_004006.2(DMD):c.2804-1G>A ; NM_004006.2(DMD):c.8069T>G ; g.31645986-31773985 ; c.1664G>A ; NM_004006.2(DMD):c.4471_4472delAA ; NM_004006.2(DMD):c.5899C>T ; c.3076G>T ; NM_004006.2(DMD):c.9337C>T ; NM_004006.2(DMD):c.3432+3A>G ; NM_004006.2(DMD):c.4806A>T ; NM_004006.2(DMD):c.9361+1G>A ; c.171G>A ; NM_004006.2(DMD):c.2816T>A ; NM_004006.2(DMD):c.627delA ; NM_004006.2(DMD):c.10033C>T ; c.2380+2T>C ; NM_004006.2(DMD):c.2804-2A>T ; c.6936del ; NM_004006.2(DMD):c.2547delT ; c.2758C>T ; NM_004006.2(DMD):c.6000T>A ; c.220del ; g.32557406-32754551 ; c.1900_1903dup ; c.1734del ; NM_004006.2(DMD):c.1286C>A ; NM_004006.2(DMD):c.676_678delAAG ; NM_004006.2(DMD):c.3295C>T ; NM_004006.2(DMD):c.2125delC ; g.31540244-32059446 ; NM_004006.2(DMD):c.6986dupA ; NM_004006.2(DMD):c.8443C>T ; c.2803+1G>A ; c.2587del ; g.32341945-32596022 ; NM_004006.2(DMD):c.3432+1G>A ; c.2266_2267del ; c.2866C>T ; NM_004006.2(DMD):c.6238delC ; NM_004006.2(DMD):c.9650-2A>G ; g.31724913-31806626 ; NM_004006.2(DMD):c.9862G>T ; g.10679-36186635 ; NM_004006.2(DMD):c.8064_8065delTA ; NM_004006.2(DMD):c.1341_1342dupAG ; g.32203741-32353533 ; g.31744885-32562211 ; NM_004006.2(DMD):c.1012G>T ; c.3124A>T ; NM_004006.2(DMD):c.8652_8653delCT ; NM_004006.2(DMD):c.433C>T ; c.277C>T ; NM_004006.2:c.2169-3_2169-1delinsAA ; c.7764dup ; NM_004006.2(DMD):c.3276+1G>A ; g.32501716-32932295 ; g.31856886-32482971 ; NM_004006.2(DMD):c.10141C>T ; NM_004006.2(DMD):c.6906G>A ; NM_004006.2(DMD):c.1261C>T ; NM_004006.2(DMD):c.10086+1G>A ; NM_004006.2(DMD):c.10446_10447delCT ; NM_004006.2(DMD):c.2484T>G ; NM_004006.2(DMD):c.4375C>T ; g.251879-35885004 ; g.31745624-31876916 ; g.31121669-33339588 ; g.30093911-34060667 ; c.489G>A ; g.31180370-31206667 ; g.10679-52213731 ; c.4486del ; NM_004006.2(DMD):c.9164-1G>C ; NM_004006.2(DMD):c.9854_9863delTGAGACTGGA ; g.31632068-31954142 ; NM_004006.2(DMD):c.1371delG ; NM_004006.2(DMD):c.2281_2285delGAAAA ; c.5570_5571dup ; c.2929dup ; c.6964del ; NM_004006.2(DMD):c.6391_6392delCA ; c.1900A>T ; NM_004006.2(DMD):c.615T>A ; g.32631403-32907656 ; c.530+1del ; NM_004006.2(DMD):c.1048G>T ; NM_004006.2(DMD):c.2755A>T ; c.2479del ; NM_004006.2(DMD):c.3747delG ; NM_004006.2(DMD):c.2815_2816delTT ; c.4409_4412dup ; c.6943G>T ; c.977-1G>T ; NM_004006.2(DMD):c.6182delC ; NM_004006.2(DMD):c.4518+5G>A ; g.10701-49071220 ; g.251880-51643625 ; NM_004006.2(DMD):c.1529_1530delTC ; NM_004006.2(DMD):c.6373C>T ; g.32380341-32412502 ; NM_004006.2(DMD):c.2803+1G>T ; c.6340A>T ; NM_004006.2(DMD):c.5773G>T ; c.3697del ; g.32341945-32816915 ; c.6763-2A>G ; c.4735G>T ; c.5671A>T ; c.5807T>A ; g.31744863-31846787 ; g.31627435-31774446 ; g.31679229-31968838 ; NM_004006.2(DMD):c.1306dupG ; g.32697662-32699472 ; NM_004006.2(DMD):c.7682G>A ; c.4500del ; NM_004006.2(DMD):c.6392_6393insCA ; c.1159C>T ; NM_004006.2(DMD):c.137_138dupAT ; g.31444405-31806767 ; g.32452761-32645074 ; NM_004006.2(DMD):c.5530C>T ; NM_004006.2(DMD):c.6982A>T ; c.3022A>T ; c.2523del ; NM_004006.2(DMD):c.9568C>T ; g.31819658-31932544 ; NM_004006.2(DMD):c.583C>T ; c.8086del ; NM_004006.2(DMD):c.5363C>G ; g.31898812-32022323 ; NM_004006.2(DMD):c.4405C>T ; NM_004006.2(DMD):c.2332C>T ; NM_004006.2(DMD):c.4117C>T ; g.31679229-31932544 ; g.32662366-32758964 ; NM_004006.2(DMD):c.8656C>T ; NM_004006.2(DMD):c.2302C>T ; NM_004006.2(DMD):c.2380+1G>C ; c.6014_6017del ; c.204dup ; NM_004006.2(DMD):c.5353C>T ; NM_004006.2(DMD):c.6292C>T ; c.2137C>T ; NM_004006.2(DMD):c.2294_2297delCCAT ; c.5313dup ; c.199G>T ; g.32432957-32823439 ; g.32267823-32372572 ; NM_004006.2(DMD):c.3639dupA ; g.31147275-31173604 ; c.1193C>G ; c.6226G>T ; c.6834del ; g.13020141-143473520 ; NM_004006.2(DMD):c.10454delT ; g.31870708-32353592 ; NM_004006.2(DMD):c.8944C>T ; g.10701-53131191 ; NM_004006.2(DMD):c.7894C>T ; NM_004006.2(DMD):c.412_413delAA ; NM_004006.2(DMD):c.4843A>T ; NM_004006.2(DMD):c.1332-9A>G ; NM_004006.2(DMD):c.2650C>T ; NM_004006.2(DMD):c.8713C>T ; g.31874956-31932544 ; NM_004006.2(DMD):c.8374_8375delAA ; NM_004006.2(DMD):c.5554C>T ; NM_004006.2(DMD):c.7683G>A ; g.31518752-31636035 ; g.31609490-32699472 ; NM_004006.2(DMD):c.1070delC ; NM_004006.2(DMD):c.9361+1G>C ; g.31929292-31968838 ; g.32364355-32390415 ; NM_004006.2(DMD):c.133C>T ; g.32216645-32651039 ; NM_004006.2:c.3246_3247insTTTCTAAAAA ; NM_004006.2(DMD):c.1489C>T ; g.32275729-32353585 ; g.31695292-31840818 ; NM_004006.2(DMD):c.9564-1G>A ; NM_004006.2(DMD):c.3779_3785delCTTTGGAinsGG ; g.31773859-31932544 ; g.31627435-31932544 ; g.31836597-31932544 ; NM_004006.2(DMD):c.3121C>T ; NM_004006.2(DMD):c.5697delA ; NM_004006.2(DMD):c.7771G>T ; NM_004006.2(DMD):c.7922delA ; g.31640772-31665565 ; g.31431098-31525874 ; g.32411633-33020588 ; g.31121669-31134568 ; NM_004006.2(DMD):c.1886C>A ; g.31931923-31932544 ; g.31965009-31968838 ; g.33019769-33020588 ; NM_004006.2(DMD):c.5287C>T ; g.31189847-31945183 ; NM_004006.2(DMD):c.5640T>A ; g.31133877-31134568 ; g.32380341-32380904 ; c.3087G>A ; g.26102-57302794 ; NM_004006.2(DMD):c.8608C>T ; NM_004006.2(DMD):c.2804-1G>A ; NM_004006.2(DMD):c.8069T>G ; g.31645986-31773985 ; c.1664G>A ; NM_004006.2(DMD):c.4471_4472delAA ; NM_004006.2(DMD):c.5899C>T ; c.3076G>T ; NM_004006.2(DMD):c.9337C>T ; NM_004006.2(DMD):c.3432+3A>G ; NM_004006.2(DMD):c.4806A>T ; NM_004006.2(DMD):c.9361+1G>A ; c.171G>A ; NM_004006.2(DMD):c.2816T>A ; NM_004006.2(DMD):c.627delA ; NM_004006.2(DMD):c.10033C>T ; c.2380+2T>C ; NM_004006.2(DMD):c.2804-2A>T ; c.6936del ; NM_004006.2(DMD):c.2547delT ; c.2758C>T ; NM_004006.2(DMD):c.6000T>A ; c.220del ; g.32557406-32754551 ; c.1900_1903dup ; c.1734del ; NM_004006.2(DMD):c.1286C>A ; NM_004006.2(DMD):c.676_678delAAG ; NM_004006.2(DMD):c.3295C>T ; NM_004006.2(DMD):c.2125delC ; g.31540244-32059446 ; NM_004006.2(DMD):c.6986dupA ; NM_004006.2(DMD):c.8443C>T ; c.2803+1G>A ; c.2587del ; g.32341945-32596022 ; NM_004006.2(DMD):c.3432+1G>A ; c.2266_2267del ; c.2866C>T ; NM_004006.2(DMD):c.6238delC ; NM_004006.2(DMD):c.9650-2A>G ; g.31724913-31806626 ; NM_004006.2(DMD):c.9862G>T ; g.10679-36186635 ; NM_004006.2(DMD):c.8064_8065delTA ; NM_004006.2(DMD):c.1341_1342dupAG ; g.32203741-32353533 ; g.31744885-32562211 ; NM_004006.2(DMD):c.1012G>T ; c.3124A>T ; NM_004006.2(DMD):c.8652_8653delCT ; NM_004006.2(DMD):c.433C>T ; c.277C>T ; NM_004006.2:c.2169-3_2169-1delinsAA ; c.7764dup ; NM_004006.2(DMD):c.3276+1G>A ; g.32501716-32932295 ; g.31856886-32482971 ; NM_004006.2(DMD):c.10141C>T ; NM_004006.2(DMD):c.6906G>A ; NM_004006.2(DMD):c.1261C>T ; NM_004006.2(DMD):c.10086+1G>A ; NM_004006.2(DMD):c.10446_10447delCT ; NM_004006.2(DMD):c.2484T>G ; NM_004006.2(DMD):c.4375C>T ; g.251879-35885004 ; g.31745624-31876916 ; g.31121669-33339588 ; g.30093911-34060667 ; c.489G>A ; g.31180370-31206667 ; g.10679-52213731 ; c.4486del ; NM_004006.2(DMD):c.9164-1G>C ; NM_004006.2(DMD):c.9854_9863delTGAGACTGGA ; g.31632068-31954142 ; NM_004006.2(DMD):c.1371delG ; NM_004006.2(DMD):c.2281_2285delGAAAA ; c.5570_5571dup ; c.2929dup ; c.6964del ; NM_004006.2(DMD):c.6391_6392delCA ; c.1900A>T ; NM_004006.2(DMD):c.615T>A ; g.32631403-32907656 ; c.530+1del ; NM_004006.2(DMD):c.1048G>T ; NM_004006.2(DMD):c.2755A>T ; c.2479del ; NM_004006.2(DMD):c.3747delG ; NM_004006.2(DMD):c.2815_2816delTT ; c.4409_4412dup ; c.6943G>T ; c.977-1G>T ; NM_004006.2(DMD):c.6182delC ; NM_004006.2(DMD):c.4518+5G>A ; g.10701-49071220 ; g.251880-51643625 ; NM_004006.2(DMD):c.1529_1530delTC ; NM_004006.2(DMD):c.6373C>T ; g.32380341-32412502 ; NM_004006.2(DMD):c.2803+1G>T ; c.6340A>T ; NM_004006.2(DMD):c.5773G>T ; c.3697del ; g.32341945-32816915 ; c.6763-2A>G ; c.4735G>T ; c.5671A>T ; c.5807T>A ; g.31744863-31846787 ; g.31627435-31774446 ; g.31679229-31968838 ; NM_004006.2(DMD):c.1306dupG ; g.32697662-32699472 ; NM_004006.2(DMD):c.7682G>A ; c.4500del ; NM_004006.2(DMD):c.6392_6393insCA ; c.1159C>T ; NM_004006.2(DMD):c.137_138dupAT ; g.31444405-31806767 ; g.32452761-32645074 ; NM_004006.2(DMD):c.5530C>T ; NM_004006.2(DMD):c.6982A>T ; c.3022A>T ; c.2523del ; NM_004006.2(DMD):c.9568C>T ; g.31819658-31932544 ; NM_004006.2(DMD):c.583C>T ; c.8086del ; NM_004006.2(DMD):c.5363C>G ; g.31898812-32022323 ; NM_004006.2(DMD):c.4405C>T ; NM_004006.2(DMD):c.2332C>T ; NM_004006.2(DMD):c.4117C>T ; g.31679229-31932544 ; g.32662366-32758964 ; NM_004006.2(DMD):c.8656C>T ; NM_004006.2(DMD):c.2302C>T ; NM_004006.2(DMD):c.2380+1G>C ; c.6014_6017del ; c.204dup ; NM_004006.2(DMD):c.5353C>T ; NM_004006.2(DMD):c.6292C>T ; c.2137C>T ; NM_004006.2(DMD):c.2294_2297delCCAT ; c.5313dup ; c.199G>T ; g.32432957-32823439 ; g.32267823-32372572 ; NM_004006.2(DMD):c.3639dupA ; g.31147275-31173604 ; c.1193C>G ; c.6226G>T ; c.6834del ; g.13020141-143473520 ; NM_004006.2(DMD):c.10454delT ; g.31870708-32353592 ; NM_004006.2(DMD):c.8944C>T ; g.10701-53131191 ; NM_004006.2(DMD):c.7894C>T ; NM_004006.2(DMD):c.412_413delAA ; NM_004006.2(DMD):c.4843A>T ; NM_004006.2(DMD):c.1332-9A>G ; NM_004006.2(DMD):c.2650C>T ; NM_004006.2(DMD):c.8713C>T ; g.31874956-31932544 ; NM_004006.2(DMD):c.8374_8375delAA ; NM_004006.2(DMD):c.5554C>T ; NM_004006.2(DMD):c.7683G>A ; g.31518752-31636035 ; g.31609490-32699472 ; NM_004006.2(DMD):c.1070delC ; NM_004006.2(DMD):c.9361+1G>C ; g.31929292-31968838 ; g.32364355-32390415 ; NM_004006.2(DMD):c.133C>T ; g.32216645-32651039 ; NM_004006.2:c.3246_3247insTTTCTAAAAA ; NM_004006.2(DMD):c.1489C>T ; g.32275729-32353585 ; g.31695292-31840818 ; NM_004006.2(DMD):c.9564-1G>A ; NM_004006.2(DMD):c.3779_3785delCTTTGGAinsGG ; g.31773859-31932544 ; g.31627435-31932544 ; g.31836597-31932544 ; NM_004006.2(DMD):c.3121C>T ; NM_004006.2(DMD):c.5697delA ; NM_004006.2(DMD):c.7771G>T ; NM_004006.2(DMD):c.7922delA ; g.31640772-31665565 ; g.31431098-31525874 ; g.32411633-33020588 ; g.31121669-31134568 ; NM_004006.2(DMD):c.1886C>A ; g.31931923-31932544 ; g.31965009-31968838 ; g.33019769-33020588 ; NM_004006.2(DMD):c.5287C>T ; g.31189847-31945183 ; NM_004006.2(DMD):c.5640T>A ; g.31133877-31134568 ; g.32380341-32380904

DMD	Duchenne muscular dystrophy	A rare, genetic, muscular dystrophy characterized by rapidly progressive muscle weakness and wasting due to degeneration of skeletal, smooth and cardiac muscle.	Onset occurs in early childhood, and affected boys may show a delay in walking (after 18 months of age) accompanied with speech and/or global developmental delay. Autism and behavioral problems, such as ADHD (attention deficit hyperactivity disorder), anxiety, obsessive compulsive disorder, are relatively common. Untreated children with DMD rarely achieve the ability to run or jump. The condition progresses rapidly and the child develops a waddling gait and a positive Gowers' sign. Climbing stairs becomes difficult and the child falls frequently. Loss of independent ambulation occurs between the ages of 6 and 13 years, the average being 9.5 years in non-steroid treated patients. Once ambulation is lost, joint contractures and scoliosis develop rapidly. Untreated patients die during late teens to early twenties from respiratory failure and or cardiomyopathy	c.3087G>A ; g.26102-57302794 ; NM_004006.2(DMD):c.8608C>T ; NM_004006.2(DMD):c.2804-1G>A ; NM_004006.2(DMD):c.8069T>G ; g.31645986-31773985 ; c.1664G>A ; NM_004006.2(DMD):c.4471_4472delAA ; NM_004006.2(DMD):c.5899C>T ; c.3076G>T ; NM_004006.2(DMD):c.9337C>T ; NM_004006.2(DMD):c.3432+3A>G ; NM_004006.2(DMD):c.4806A>T ; NM_004006.2(DMD):c.9361+1G>A ; c.171G>A ; NM_004006.2(DMD):c.2816T>A ; NM_004006.2(DMD):c.627delA ; NM_004006.2(DMD):c.10033C>T ; c.2380+2T>C ; NM_004006.2(DMD):c.2804-2A>T ; c.6936del ; NM_004006.2(DMD):c.2547delT ; c.2758C>T ; NM_004006.2(DMD):c.6000T>A ; c.220del ; g.32557406-32754551 ; c.1900_1903dup ; c.1734del ; NM_004006.2(DMD):c.1286C>A ; NM_004006.2(DMD):c.676_678delAAG ; NM_004006.2(DMD):c.3295C>T ; NM_004006.2(DMD):c.2125delC ; g.31540244-32059446 ; NM_004006.2(DMD):c.6986dupA ; NM_004006.2(DMD):c.8443C>T ; c.2803+1G>A ; c.2587del ; g.32341945-32596022 ; NM_004006.2(DMD):c.3432+1G>A ; c.2266_2267del ; c.2866C>T ; NM_004006.2(DMD):c.6238delC ; NM_004006.2(DMD):c.9650-2A>G ; g.31724913-31806626 ; NM_004006.2(DMD):c.9862G>T ; g.10679-36186635 ; NM_004006.2(DMD):c.8064_8065delTA ; NM_004006.2(DMD):c.1341_1342dupAG ; g.32203741-32353533 ; g.31744885-32562211 ; NM_004006.2(DMD):c.1012G>T ; c.3124A>T ; NM_004006.2(DMD):c.8652_8653delCT ; NM_004006.2(DMD):c.433C>T ; c.277C>T ; NM_004006.2:c.2169-3_2169-1delinsAA ; c.7764dup ; NM_004006.2(DMD):c.3276+1G>A ; g.32501716-32932295 ; g.31856886-32482971 ; NM_004006.2(DMD):c.10141C>T ; NM_004006.2(DMD):c.6906G>A ; NM_004006.2(DMD):c.1261C>T ; NM_004006.2(DMD):c.10086+1G>A ; NM_004006.2(DMD):c.10446_10447delCT ; NM_004006.2(DMD):c.2484T>G ; NM_004006.2(DMD):c.4375C>T ; g.251879-35885004 ; g.31745624-31876916 ; g.31121669-33339588 ; g.30093911-34060667 ; c.489G>A ; g.31180370-31206667 ; g.10679-52213731 ; c.4486del ; NM_004006.2(DMD):c.9164-1G>C ; NM_004006.2(DMD):c.9854_9863delTGAGACTGGA ; g.31632068-31954142 ; NM_004006.2(DMD):c.1371delG ; NM_004006.2(DMD):c.2281_2285delGAAAA ; c.5570_5571dup ; c.2929dup ; c.6964del ; NM_004006.2(DMD):c.6391_6392delCA ; c.1900A>T ; NM_004006.2(DMD):c.615T>A ; g.32631403-32907656 ; c.530+1del ; NM_004006.2(DMD):c.1048G>T ; NM_004006.2(DMD):c.2755A>T ; c.2479del ; NM_004006.2(DMD):c.3747delG ; NM_004006.2(DMD):c.2815_2816delTT ; c.4409_4412dup ; c.6943G>T ; c.977-1G>T ; NM_004006.2(DMD):c.6182delC ; NM_004006.2(DMD):c.4518+5G>A ; g.10701-49071220 ; g.251880-51643625 ; NM_004006.2(DMD):c.1529_1530delTC ; NM_004006.2(DMD):c.6373C>T ; g.32380341-32412502 ; NM_004006.2(DMD):c.2803+1G>T ; c.6340A>T ; NM_004006.2(DMD):c.5773G>T ; c.3697del ; g.32341945-32816915 ; c.6763-2A>G ; c.4735G>T ; c.5671A>T ; c.5807T>A ; g.31744863-31846787 ; g.31627435-31774446 ; g.31679229-31968838 ; NM_004006.2(DMD):c.1306dupG ; g.32697662-32699472 ; NM_004006.2(DMD):c.7682G>A ; c.4500del ; NM_004006.2(DMD):c.6392_6393insCA ; c.1159C>T ; NM_004006.2(DMD):c.137_138dupAT ; g.31444405-31806767 ; g.32452761-32645074 ; NM_004006.2(DMD):c.5530C>T ; NM_004006.2(DMD):c.6982A>T ; c.3022A>T ; c.2523del ; NM_004006.2(DMD):c.9568C>T ; g.31819658-31932544 ; NM_004006.2(DMD):c.583C>T ; c.8086del ; NM_004006.2(DMD):c.5363C>G ; g.31898812-32022323 ; NM_004006.2(DMD):c.4405C>T ; NM_004006.2(DMD):c.2332C>T ; NM_004006.2(DMD):c.4117C>T ; g.31679229-31932544 ; g.32662366-32758964 ; NM_004006.2(DMD):c.8656C>T ; NM_004006.2(DMD):c.2302C>T ; NM_004006.2(DMD):c.2380+1G>C ; c.6014_6017del ; c.204dup ; NM_004006.2(DMD):c.5353C>T ; NM_004006.2(DMD):c.6292C>T ; c.2137C>T ; NM_004006.2(DMD):c.2294_2297delCCAT ; c.5313dup ; c.199G>T ; g.32432957-32823439 ; g.32267823-32372572 ; NM_004006.2(DMD):c.3639dupA ; g.31147275-31173604 ; c.1193C>G ; c.6226G>T ; c.6834del ; g.13020141-143473520 ; NM_004006.2(DMD):c.10454delT ; g.31870708-32353592 ; NM_004006.2(DMD):c.8944C>T ; g.10701-53131191 ; NM_004006.2(DMD):c.7894C>T ; NM_004006.2(DMD):c.412_413delAA ; NM_004006.2(DMD):c.4843A>T ; NM_004006.2(DMD):c.1332-9A>G ; NM_004006.2(DMD):c.2650C>T ; NM_004006.2(DMD):c.8713C>T ; g.31874956-31932544 ; NM_004006.2(DMD):c.8374_8375delAA ; NM_004006.2(DMD):c.5554C>T ; NM_004006.2(DMD):c.7683G>A ; g.31518752-31636035 ; g.31609490-32699472 ; NM_004006.2(DMD):c.1070delC ; NM_004006.2(DMD):c.9361+1G>C ; g.31929292-31968838 ; g.32364355-32390415 ; NM_004006.2(DMD):c.133C>T ; g.32216645-32651039 ; NM_004006.2:c.3246_3247insTTTCTAAAAA ; NM_004006.2(DMD):c.1489C>T ; g.32275729-32353585 ; g.31695292-31840818 ; NM_004006.2(DMD):c.9564-1G>A ; NM_004006.2(DMD):c.3779_3785delCTTTGGAinsGG ; g.31773859-31932544 ; g.31627435-31932544 ; g.31836597-31932544 ; NM_004006.2(DMD):c.3121C>T ; NM_004006.2(DMD):c.5697delA ; NM_004006.2(DMD):c.7771G>T ; NM_004006.2(DMD):c.7922delA ; g.31640772-31665565 ; g.31431098-31525874 ; g.32411633-33020588 ; g.31121669-31134568 ; NM_004006.2(DMD):c.1886C>A ; g.31931923-31932544 ; g.31965009-31968838 ; g.33019769-33020588 ; NM_004006.2(DMD):c.5287C>T ; g.31189847-31945183 ; NM_004006.2(DMD):c.5640T>A ; g.31133877-31134568 ; g.32380341-32380904 ; c.3087G>A ; g.26102-57302794 ; NM_004006.2(DMD):c.8608C>T ; NM_004006.2(DMD):c.2804-1G>A ; NM_004006.2(DMD):c.8069T>G ; g.31645986-31773985 ; c.1664G>A ; NM_004006.2(DMD):c.4471_4472delAA ; NM_004006.2(DMD):c.5899C>T ; c.3076G>T ; NM_004006.2(DMD):c.9337C>T ; NM_004006.2(DMD):c.3432+3A>G ; NM_004006.2(DMD):c.4806A>T ; NM_004006.2(DMD):c.9361+1G>A ; c.171G>A ; NM_004006.2(DMD):c.2816T>A ; NM_004006.2(DMD):c.627delA ; NM_004006.2(DMD):c.10033C>T ; c.2380+2T>C ; NM_004006.2(DMD):c.2804-2A>T ; c.6936del ; NM_004006.2(DMD):c.2547delT ; c.2758C>T ; NM_004006.2(DMD):c.6000T>A ; c.220del ; g.32557406-32754551 ; c.1900_1903dup ; c.1734del ; NM_004006.2(DMD):c.1286C>A ; NM_004006.2(DMD):c.676_678delAAG ; NM_004006.2(DMD):c.3295C>T ; NM_004006.2(DMD):c.2125delC ; g.31540244-32059446 ; NM_004006.2(DMD):c.6986dupA ; NM_004006.2(DMD):c.8443C>T ; c.2803+1G>A ; c.2587del ; g.32341945-32596022 ; NM_004006.2(DMD):c.3432+1G>A ; c.2266_2267del ; c.2866C>T ; NM_004006.2(DMD):c.6238delC ; NM_004006.2(DMD):c.9650-2A>G ; g.31724913-31806626 ; NM_004006.2(DMD):c.9862G>T ; g.10679-36186635 ; NM_004006.2(DMD):c.8064_8065delTA ; NM_004006.2(DMD):c.1341_1342dupAG ; g.32203741-32353533 ; g.31744885-32562211 ; NM_004006.2(DMD):c.1012G>T ; c.3124A>T ; NM_004006.2(DMD):c.8652_8653delCT ; NM_004006.2(DMD):c.433C>T ; c.277C>T ; NM_004006.2:c.2169-3_2169-1delinsAA ; c.7764dup ; NM_004006.2(DMD):c.3276+1G>A ; g.32501716-32932295 ; g.31856886-32482971 ; NM_004006.2(DMD):c.10141C>T ; NM_004006.2(DMD):c.6906G>A ; NM_004006.2(DMD):c.1261C>T ; NM_004006.2(DMD):c.10086+1G>A ; NM_004006.2(DMD):c.10446_10447delCT ; NM_004006.2(DMD):c.2484T>G ; NM_004006.2(DMD):c.4375C>T ; g.251879-35885004 ; g.31745624-31876916 ; g.31121669-33339588 ; g.30093911-34060667 ; c.489G>A ; g.31180370-31206667 ; g.10679-52213731 ; c.4486del ; NM_004006.2(DMD):c.9164-1G>C ; NM_004006.2(DMD):c.9854_9863delTGAGACTGGA ; g.31632068-31954142 ; NM_004006.2(DMD):c.1371delG ; NM_004006.2(DMD):c.2281_2285delGAAAA ; c.5570_5571dup ; c.2929dup ; c.6964del ; NM_004006.2(DMD):c.6391_6392delCA ; c.1900A>T ; NM_004006.2(DMD):c.615T>A ; g.32631403-32907656 ; c.530+1del ; NM_004006.2(DMD):c.1048G>T ; NM_004006.2(DMD):c.2755A>T ; c.2479del ; NM_004006.2(DMD):c.3747delG ; NM_004006.2(DMD):c.2815_2816delTT ; c.4409_4412dup ; c.6943G>T ; c.977-1G>T ; NM_004006.2(DMD):c.6182delC ; NM_004006.2(DMD):c.4518+5G>A ; g.10701-49071220 ; g.251880-51643625 ; NM_004006.2(DMD):c.1529_1530delTC ; NM_004006.2(DMD):c.6373C>T ; g.32380341-32412502 ; NM_004006.2(DMD):c.2803+1G>T ; c.6340A>T ; NM_004006.2(DMD):c.5773G>T ; c.3697del ; g.32341945-32816915 ; c.6763-2A>G ; c.4735G>T ; c.5671A>T ; c.5807T>A ; g.31744863-31846787 ; g.31627435-31774446 ; g.31679229-31968838 ; NM_004006.2(DMD):c.1306dupG ; g.32697662-32699472 ; NM_004006.2(DMD):c.7682G>A ; c.4500del ; NM_004006.2(DMD):c.6392_6393insCA ; c.1159C>T ; NM_004006.2(DMD):c.137_138dupAT ; g.31444405-31806767 ; g.32452761-32645074 ; NM_004006.2(DMD):c.5530C>T ; NM_004006.2(DMD):c.6982A>T ; c.3022A>T ; c.2523del ; NM_004006.2(DMD):c.9568C>T ; g.31819658-31932544 ; NM_004006.2(DMD):c.583C>T ; c.8086del ; NM_004006.2(DMD):c.5363C>G ; g.31898812-32022323 ; NM_004006.2(DMD):c.4405C>T ; NM_004006.2(DMD):c.2332C>T ; NM_004006.2(DMD):c.4117C>T ; g.31679229-31932544 ; g.32662366-32758964 ; NM_004006.2(DMD):c.8656C>T ; NM_004006.2(DMD):c.2302C>T ; NM_004006.2(DMD):c.2380+1G>C ; c.6014_6017del ; c.204dup ; NM_004006.2(DMD):c.5353C>T ; NM_004006.2(DMD):c.6292C>T ; c.2137C>T ; NM_004006.2(DMD):c.2294_2297delCCAT ; c.5313dup ; c.199G>T ; g.32432957-32823439 ; g.32267823-32372572 ; NM_004006.2(DMD):c.3639dupA ; g.31147275-31173604 ; c.1193C>G ; c.6226G>T ; c.6834del ; g.13020141-143473520 ; NM_004006.2(DMD):c.10454delT ; g.31870708-32353592 ; NM_004006.2(DMD):c.8944C>T ; g.10701-53131191 ; NM_004006.2(DMD):c.7894C>T ; NM_004006.2(DMD):c.412_413delAA ; NM_004006.2(DMD):c.4843A>T ; NM_004006.2(DMD):c.1332-9A>G ; NM_004006.2(DMD):c.2650C>T ; NM_004006.2(DMD):c.8713C>T ; g.31874956-31932544 ; NM_004006.2(DMD):c.8374_8375delAA ; NM_004006.2(DMD):c.5554C>T ; NM_004006.2(DMD):c.7683G>A ; g.31518752-31636035 ; g.31609490-32699472 ; NM_004006.2(DMD):c.1070delC ; NM_004006.2(DMD):c.9361+1G>C ; g.31929292-31968838 ; g.32364355-32390415 ; NM_004006.2(DMD):c.133C>T ; g.32216645-32651039 ; NM_004006.2:c.3246_3247insTTTCTAAAAA ; NM_004006.2(DMD):c.1489C>T ; g.32275729-32353585 ; g.31695292-31840818 ; NM_004006.2(DMD):c.9564-1G>A ; NM_004006.2(DMD):c.3779_3785delCTTTGGAinsGG ; g.31773859-31932544 ; g.31627435-31932544 ; g.31836597-31932544 ; NM_004006.2(DMD):c.3121C>T ; NM_004006.2(DMD):c.5697delA ; NM_004006.2(DMD):c.7771G>T ; NM_004006.2(DMD):c.7922delA ; g.31640772-31665565 ; g.31431098-31525874 ; g.32411633-33020588 ; g.31121669-31134568 ; NM_004006.2(DMD):c.1886C>A ; g.31931923-31932544 ; g.31965009-31968838 ; g.33019769-33020588 ; NM_004006.2(DMD):c.5287C>T ; g.31189847-31945183 ; NM_004006.2(DMD):c.5640T>A ; g.31133877-31134568 ; g.32380341-32380904

DMD	Familial isolated dilated cardiomyopathy	A rare familial cardiomyopathy characterized by the dilation of left ventricle and progressively impairing of systolic ventricular function, in the absence of abnormal loading conditions or coronary artery disease sufficient to cause global systolic impairment. The disease may cause heart failure or arrhythmia. The disease is isolated when no additional atypical cardiac or extracardiac manifestations are present.	The disease is defined by the presence of two major clinical criteria: left ventricular (LV) fractional shortening less than 25% and/or LV ejection fraction less than 45% with LV end diastolic diameter greater than 117% of the predicted value (corrected for age and body surface area based on Henry's formula), in the absence of abnormal loading conditions or coronary artery disease sufficient to cause global systolic impairment. The disease can develop at any age, in either sex. LV mass is often greatly increased in this disorder but LV wall thickness is normal. Symptoms of heart failure may be present as well as arrhythmias. Other presentations include the incidental detection of asymptomatic cardiomegaly and symptoms related to coexisting conduction disturbance or thromboembolic complications. Typically, there is a history of DCM in the family.	c.3087G>A ; g.26102-57302794 ; NM_004006.2(DMD):c.8608C>T ; NM_004006.2(DMD):c.2804-1G>A ; NM_004006.2(DMD):c.8069T>G ; g.31645986-31773985 ; c.1664G>A ; NM_004006.2(DMD):c.4471_4472delAA ; NM_004006.2(DMD):c.5899C>T ; c.3076G>T ; NM_004006.2(DMD):c.9337C>T ; NM_004006.2(DMD):c.3432+3A>G ; NM_004006.2(DMD):c.4806A>T ; NM_004006.2(DMD):c.9361+1G>A ; c.171G>A ; NM_004006.2(DMD):c.2816T>A ; NM_004006.2(DMD):c.627delA ; NM_004006.2(DMD):c.10033C>T ; c.2380+2T>C ; NM_004006.2(DMD):c.2804-2A>T ; c.6936del ; NM_004006.2(DMD):c.2547delT ; c.2758C>T ; NM_004006.2(DMD):c.6000T>A ; c.220del ; g.32557406-32754551 ; c.1900_1903dup ; c.1734del ; NM_004006.2(DMD):c.1286C>A ; NM_004006.2(DMD):c.676_678delAAG ; NM_004006.2(DMD):c.3295C>T ; NM_004006.2(DMD):c.2125delC ; g.31540244-32059446 ; NM_004006.2(DMD):c.6986dupA ; NM_004006.2(DMD):c.8443C>T ; c.2803+1G>A ; c.2587del ; g.32341945-32596022 ; NM_004006.2(DMD):c.3432+1G>A ; c.2266_2267del ; c.2866C>T ; NM_004006.2(DMD):c.6238delC ; NM_004006.2(DMD):c.9650-2A>G ; g.31724913-31806626 ; NM_004006.2(DMD):c.9862G>T ; g.10679-36186635 ; NM_004006.2(DMD):c.8064_8065delTA ; NM_004006.2(DMD):c.1341_1342dupAG ; g.32203741-32353533 ; g.31744885-32562211 ; NM_004006.2(DMD):c.1012G>T ; c.3124A>T ; NM_004006.2(DMD):c.8652_8653delCT ; NM_004006.2(DMD):c.433C>T ; c.277C>T ; NM_004006.2:c.2169-3_2169-1delinsAA ; c.7764dup ; NM_004006.2(DMD):c.3276+1G>A ; g.32501716-32932295 ; g.31856886-32482971 ; NM_004006.2(DMD):c.10141C>T ; NM_004006.2(DMD):c.6906G>A ; NM_004006.2(DMD):c.1261C>T ; NM_004006.2(DMD):c.10086+1G>A ; NM_004006.2(DMD):c.10446_10447delCT ; NM_004006.2(DMD):c.2484T>G ; NM_004006.2(DMD):c.4375C>T ; g.251879-35885004 ; g.31745624-31876916 ; g.31121669-33339588 ; g.30093911-34060667 ; c.489G>A ; g.31180370-31206667 ; g.10679-52213731 ; c.4486del ; NM_004006.2(DMD):c.9164-1G>C ; NM_004006.2(DMD):c.9854_9863delTGAGACTGGA ; g.31632068-31954142 ; NM_004006.2(DMD):c.1371delG ; NM_004006.2(DMD):c.2281_2285delGAAAA ; c.5570_5571dup ; c.2929dup ; c.6964del ; NM_004006.2(DMD):c.6391_6392delCA ; c.1900A>T ; NM_004006.2(DMD):c.615T>A ; g.32631403-32907656 ; c.530+1del ; NM_004006.2(DMD):c.1048G>T ; NM_004006.2(DMD):c.2755A>T ; c.2479del ; NM_004006.2(DMD):c.3747delG ; NM_004006.2(DMD):c.2815_2816delTT ; c.4409_4412dup ; c.6943G>T ; c.977-1G>T ; NM_004006.2(DMD):c.6182delC ; NM_004006.2(DMD):c.4518+5G>A ; g.10701-49071220 ; g.251880-51643625 ; NM_004006.2(DMD):c.1529_1530delTC ; NM_004006.2(DMD):c.6373C>T ; g.32380341-32412502 ; NM_004006.2(DMD):c.2803+1G>T ; c.6340A>T ; NM_004006.2(DMD):c.5773G>T ; c.3697del ; g.32341945-32816915 ; c.6763-2A>G ; c.4735G>T ; c.5671A>T ; c.5807T>A ; g.31744863-31846787 ; g.31627435-31774446 ; g.31679229-31968838 ; NM_004006.2(DMD):c.1306dupG ; g.32697662-32699472 ; NM_004006.2(DMD):c.7682G>A ; c.4500del ; NM_004006.2(DMD):c.6392_6393insCA ; c.1159C>T ; NM_004006.2(DMD):c.137_138dupAT ; g.31444405-31806767 ; g.32452761-32645074 ; NM_004006.2(DMD):c.5530C>T ; NM_004006.2(DMD):c.6982A>T ; c.3022A>T ; c.2523del ; NM_004006.2(DMD):c.9568C>T ; g.31819658-31932544 ; NM_004006.2(DMD):c.583C>T ; c.8086del ; NM_004006.2(DMD):c.5363C>G ; g.31898812-32022323 ; NM_004006.2(DMD):c.4405C>T ; NM_004006.2(DMD):c.2332C>T ; NM_004006.2(DMD):c.4117C>T ; g.31679229-31932544 ; g.32662366-32758964 ; NM_004006.2(DMD):c.8656C>T ; NM_004006.2(DMD):c.2302C>T ; NM_004006.2(DMD):c.2380+1G>C ; c.6014_6017del ; c.204dup ; NM_004006.2(DMD):c.5353C>T ; NM_004006.2(DMD):c.6292C>T ; c.2137C>T ; NM_004006.2(DMD):c.2294_2297delCCAT ; c.5313dup ; c.199G>T ; g.32432957-32823439 ; g.32267823-32372572 ; NM_004006.2(DMD):c.3639dupA ; g.31147275-31173604 ; c.1193C>G ; c.6226G>T ; c.6834del ; g.13020141-143473520 ; NM_004006.2(DMD):c.10454delT ; g.31870708-32353592 ; NM_004006.2(DMD):c.8944C>T ; g.10701-53131191 ; NM_004006.2(DMD):c.7894C>T ; NM_004006.2(DMD):c.412_413delAA ; NM_004006.2(DMD):c.4843A>T ; NM_004006.2(DMD):c.1332-9A>G ; NM_004006.2(DMD):c.2650C>T ; NM_004006.2(DMD):c.8713C>T ; g.31874956-31932544 ; NM_004006.2(DMD):c.8374_8375delAA ; NM_004006.2(DMD):c.5554C>T ; NM_004006.2(DMD):c.7683G>A ; g.31518752-31636035 ; g.31609490-32699472 ; NM_004006.2(DMD):c.1070delC ; NM_004006.2(DMD):c.9361+1G>C ; g.31929292-31968838 ; g.32364355-32390415 ; NM_004006.2(DMD):c.133C>T ; g.32216645-32651039 ; NM_004006.2:c.3246_3247insTTTCTAAAAA ; NM_004006.2(DMD):c.1489C>T ; g.32275729-32353585 ; g.31695292-31840818 ; NM_004006.2(DMD):c.9564-1G>A ; NM_004006.2(DMD):c.3779_3785delCTTTGGAinsGG ; g.31773859-31932544 ; g.31627435-31932544 ; g.31836597-31932544 ; NM_004006.2(DMD):c.3121C>T ; NM_004006.2(DMD):c.5697delA ; NM_004006.2(DMD):c.7771G>T ; NM_004006.2(DMD):c.7922delA ; g.31640772-31665565 ; g.31431098-31525874 ; g.32411633-33020588 ; g.31121669-31134568 ; NM_004006.2(DMD):c.1886C>A ; g.31931923-31932544 ; g.31965009-31968838 ; g.33019769-33020588 ; NM_004006.2(DMD):c.5287C>T ; g.31189847-31945183 ; NM_004006.2(DMD):c.5640T>A ; g.31133877-31134568 ; g.32380341-32380904 ; c.3087G>A ; g.26102-57302794 ; NM_004006.2(DMD):c.8608C>T ; NM_004006.2(DMD):c.2804-1G>A ; NM_004006.2(DMD):c.8069T>G ; g.31645986-31773985 ; c.1664G>A ; NM_004006.2(DMD):c.4471_4472delAA ; NM_004006.2(DMD):c.5899C>T ; c.3076G>T ; NM_004006.2(DMD):c.9337C>T ; NM_004006.2(DMD):c.3432+3A>G ; NM_004006.2(DMD):c.4806A>T ; NM_004006.2(DMD):c.9361+1G>A ; c.171G>A ; NM_004006.2(DMD):c.2816T>A ; NM_004006.2(DMD):c.627delA ; NM_004006.2(DMD):c.10033C>T ; c.2380+2T>C ; NM_004006.2(DMD):c.2804-2A>T ; c.6936del ; NM_004006.2(DMD):c.2547delT ; c.2758C>T ; NM_004006.2(DMD):c.6000T>A ; c.220del ; g.32557406-32754551 ; c.1900_1903dup ; c.1734del ; NM_004006.2(DMD):c.1286C>A ; NM_004006.2(DMD):c.676_678delAAG ; NM_004006.2(DMD):c.3295C>T ; NM_004006.2(DMD):c.2125delC ; g.31540244-32059446 ; NM_004006.2(DMD):c.6986dupA ; NM_004006.2(DMD):c.8443C>T ; c.2803+1G>A ; c.2587del ; g.32341945-32596022 ; NM_004006.2(DMD):c.3432+1G>A ; c.2266_2267del ; c.2866C>T ; NM_004006.2(DMD):c.6238delC ; NM_004006.2(DMD):c.9650-2A>G ; g.31724913-31806626 ; NM_004006.2(DMD):c.9862G>T ; g.10679-36186635 ; NM_004006.2(DMD):c.8064_8065delTA ; NM_004006.2(DMD):c.1341_1342dupAG ; g.32203741-32353533 ; g.31744885-32562211 ; NM_004006.2(DMD):c.1012G>T ; c.3124A>T ; NM_004006.2(DMD):c.8652_8653delCT ; NM_004006.2(DMD):c.433C>T ; c.277C>T ; NM_004006.2:c.2169-3_2169-1delinsAA ; c.7764dup ; NM_004006.2(DMD):c.3276+1G>A ; g.32501716-32932295 ; g.31856886-32482971 ; NM_004006.2(DMD):c.10141C>T ; NM_004006.2(DMD):c.6906G>A ; NM_004006.2(DMD):c.1261C>T ; NM_004006.2(DMD):c.10086+1G>A ; NM_004006.2(DMD):c.10446_10447delCT ; NM_004006.2(DMD):c.2484T>G ; NM_004006.2(DMD):c.4375C>T ; g.251879-35885004 ; g.31745624-31876916 ; g.31121669-33339588 ; g.30093911-34060667 ; c.489G>A ; g.31180370-31206667 ; g.10679-52213731 ; c.4486del ; NM_004006.2(DMD):c.9164-1G>C ; NM_004006.2(DMD):c.9854_9863delTGAGACTGGA ; g.31632068-31954142 ; NM_004006.2(DMD):c.1371delG ; NM_004006.2(DMD):c.2281_2285delGAAAA ; c.5570_5571dup ; c.2929dup ; c.6964del ; NM_004006.2(DMD):c.6391_6392delCA ; c.1900A>T ; NM_004006.2(DMD):c.615T>A ; g.32631403-32907656 ; c.530+1del ; NM_004006.2(DMD):c.1048G>T ; NM_004006.2(DMD):c.2755A>T ; c.2479del ; NM_004006.2(DMD):c.3747delG ; NM_004006.2(DMD):c.2815_2816delTT ; c.4409_4412dup ; c.6943G>T ; c.977-1G>T ; NM_004006.2(DMD):c.6182delC ; NM_004006.2(DMD):c.4518+5G>A ; g.10701-49071220 ; g.251880-51643625 ; NM_004006.2(DMD):c.1529_1530delTC ; NM_004006.2(DMD):c.6373C>T ; g.32380341-32412502 ; NM_004006.2(DMD):c.2803+1G>T ; c.6340A>T ; NM_004006.2(DMD):c.5773G>T ; c.3697del ; g.32341945-32816915 ; c.6763-2A>G ; c.4735G>T ; c.5671A>T ; c.5807T>A ; g.31744863-31846787 ; g.31627435-31774446 ; g.31679229-31968838 ; NM_004006.2(DMD):c.1306dupG ; g.32697662-32699472 ; NM_004006.2(DMD):c.7682G>A ; c.4500del ; NM_004006.2(DMD):c.6392_6393insCA ; c.1159C>T ; NM_004006.2(DMD):c.137_138dupAT ; g.31444405-31806767 ; g.32452761-32645074 ; NM_004006.2(DMD):c.5530C>T ; NM_004006.2(DMD):c.6982A>T ; c.3022A>T ; c.2523del ; NM_004006.2(DMD):c.9568C>T ; g.31819658-31932544 ; NM_004006.2(DMD):c.583C>T ; c.8086del ; NM_004006.2(DMD):c.5363C>G ; g.31898812-32022323 ; NM_004006.2(DMD):c.4405C>T ; NM_004006.2(DMD):c.2332C>T ; NM_004006.2(DMD):c.4117C>T ; g.31679229-31932544 ; g.32662366-32758964 ; NM_004006.2(DMD):c.8656C>T ; NM_004006.2(DMD):c.2302C>T ; NM_004006.2(DMD):c.2380+1G>C ; c.6014_6017del ; c.204dup ; NM_004006.2(DMD):c.5353C>T ; NM_004006.2(DMD):c.6292C>T ; c.2137C>T ; NM_004006.2(DMD):c.2294_2297delCCAT ; c.5313dup ; c.199G>T ; g.32432957-32823439 ; g.32267823-32372572 ; NM_004006.2(DMD):c.3639dupA ; g.31147275-31173604 ; c.1193C>G ; c.6226G>T ; c.6834del ; g.13020141-143473520 ; NM_004006.2(DMD):c.10454delT ; g.31870708-32353592 ; NM_004006.2(DMD):c.8944C>T ; g.10701-53131191 ; NM_004006.2(DMD):c.7894C>T ; NM_004006.2(DMD):c.412_413delAA ; NM_004006.2(DMD):c.4843A>T ; NM_004006.2(DMD):c.1332-9A>G ; NM_004006.2(DMD):c.2650C>T ; NM_004006.2(DMD):c.8713C>T ; g.31874956-31932544 ; NM_004006.2(DMD):c.8374_8375delAA ; NM_004006.2(DMD):c.5554C>T ; NM_004006.2(DMD):c.7683G>A ; g.31518752-31636035 ; g.31609490-32699472 ; NM_004006.2(DMD):c.1070delC ; NM_004006.2(DMD):c.9361+1G>C ; g.31929292-31968838 ; g.32364355-32390415 ; NM_004006.2(DMD):c.133C>T ; g.32216645-32651039 ; NM_004006.2:c.3246_3247insTTTCTAAAAA ; NM_004006.2(DMD):c.1489C>T ; g.32275729-32353585 ; g.31695292-31840818 ; NM_004006.2(DMD):c.9564-1G>A ; NM_004006.2(DMD):c.3779_3785delCTTTGGAinsGG ; g.31773859-31932544 ; g.31627435-31932544 ; g.31836597-31932544 ; NM_004006.2(DMD):c.3121C>T ; NM_004006.2(DMD):c.5697delA ; NM_004006.2(DMD):c.7771G>T ; NM_004006.2(DMD):c.7922delA ; g.31640772-31665565 ; g.31431098-31525874 ; g.32411633-33020588 ; g.31121669-31134568 ; NM_004006.2(DMD):c.1886C>A ; g.31931923-31932544 ; g.31965009-31968838 ; g.33019769-33020588 ; NM_004006.2(DMD):c.5287C>T ; g.31189847-31945183 ; NM_004006.2(DMD):c.5640T>A ; g.31133877-31134568 ; g.32380341-32380904

DMD	Symptomatic form of muscular dystrophy of Duchenne and Becker in female carriers	A rare, genetic muscular dystrophy affecting female carriers and characterized by variable degrees of muscle weakness due to progressive skeletal myopathy, sometimes associated with dilated cardiomyopathy or left ventricle dilation.	Symptomatic female carriers usually present later than males with DMD or BMD. The muscle weakness is generally less severe than in affected males and is usually proximal and, unlike males, has an asymmetric distribution. The upper limbs may be weaker than the lower limbs. Myalgia and cramps have also been reported. The serum creatine kinase level is raised. Some patients may present with cardiac manifestations alone.	c.3087G>A ; g.26102-57302794 ; NM_004006.2(DMD):c.8608C>T ; NM_004006.2(DMD):c.2804-1G>A ; NM_004006.2(DMD):c.8069T>G ; g.31645986-31773985 ; c.1664G>A ; NM_004006.2(DMD):c.4471_4472delAA ; NM_004006.2(DMD):c.5899C>T ; c.3076G>T ; NM_004006.2(DMD):c.9337C>T ; NM_004006.2(DMD):c.3432+3A>G ; NM_004006.2(DMD):c.4806A>T ; NM_004006.2(DMD):c.9361+1G>A ; c.171G>A ; NM_004006.2(DMD):c.2816T>A ; NM_004006.2(DMD):c.627delA ; NM_004006.2(DMD):c.10033C>T ; c.2380+2T>C ; NM_004006.2(DMD):c.2804-2A>T ; c.6936del ; NM_004006.2(DMD):c.2547delT ; c.2758C>T ; NM_004006.2(DMD):c.6000T>A ; c.220del ; g.32557406-32754551 ; c.1900_1903dup ; c.1734del ; NM_004006.2(DMD):c.1286C>A ; NM_004006.2(DMD):c.676_678delAAG ; NM_004006.2(DMD):c.3295C>T ; NM_004006.2(DMD):c.2125delC ; g.31540244-32059446 ; NM_004006.2(DMD):c.6986dupA ; NM_004006.2(DMD):c.8443C>T ; c.2803+1G>A ; c.2587del ; g.32341945-32596022 ; NM_004006.2(DMD):c.3432+1G>A ; c.2266_2267del ; c.2866C>T ; NM_004006.2(DMD):c.6238delC ; NM_004006.2(DMD):c.9650-2A>G ; g.31724913-31806626 ; NM_004006.2(DMD):c.9862G>T ; g.10679-36186635 ; NM_004006.2(DMD):c.8064_8065delTA ; NM_004006.2(DMD):c.1341_1342dupAG ; g.32203741-32353533 ; g.31744885-32562211 ; NM_004006.2(DMD):c.1012G>T ; c.3124A>T ; NM_004006.2(DMD):c.8652_8653delCT ; NM_004006.2(DMD):c.433C>T ; c.277C>T ; NM_004006.2:c.2169-3_2169-1delinsAA ; c.7764dup ; NM_004006.2(DMD):c.3276+1G>A ; g.32501716-32932295 ; g.31856886-32482971 ; NM_004006.2(DMD):c.10141C>T ; NM_004006.2(DMD):c.6906G>A ; NM_004006.2(DMD):c.1261C>T ; NM_004006.2(DMD):c.10086+1G>A ; NM_004006.2(DMD):c.10446_10447delCT ; NM_004006.2(DMD):c.2484T>G ; NM_004006.2(DMD):c.4375C>T ; g.251879-35885004 ; g.31745624-31876916 ; g.31121669-33339588 ; g.30093911-34060667 ; c.489G>A ; g.31180370-31206667 ; g.10679-52213731 ; c.4486del ; NM_004006.2(DMD):c.9164-1G>C ; NM_004006.2(DMD):c.9854_9863delTGAGACTGGA ; g.31632068-31954142 ; NM_004006.2(DMD):c.1371delG ; NM_004006.2(DMD):c.2281_2285delGAAAA ; c.5570_5571dup ; c.2929dup ; c.6964del ; NM_004006.2(DMD):c.6391_6392delCA ; c.1900A>T ; NM_004006.2(DMD):c.615T>A ; g.32631403-32907656 ; c.530+1del ; NM_004006.2(DMD):c.1048G>T ; NM_004006.2(DMD):c.2755A>T ; c.2479del ; NM_004006.2(DMD):c.3747delG ; NM_004006.2(DMD):c.2815_2816delTT ; c.4409_4412dup ; c.6943G>T ; c.977-1G>T ; NM_004006.2(DMD):c.6182delC ; NM_004006.2(DMD):c.4518+5G>A ; g.10701-49071220 ; g.251880-51643625 ; NM_004006.2(DMD):c.1529_1530delTC ; NM_004006.2(DMD):c.6373C>T ; g.32380341-32412502 ; NM_004006.2(DMD):c.2803+1G>T ; c.6340A>T ; NM_004006.2(DMD):c.5773G>T ; c.3697del ; g.32341945-32816915 ; c.6763-2A>G ; c.4735G>T ; c.5671A>T ; c.5807T>A ; g.31744863-31846787 ; g.31627435-31774446 ; g.31679229-31968838 ; NM_004006.2(DMD):c.1306dupG ; g.32697662-32699472 ; NM_004006.2(DMD):c.7682G>A ; c.4500del ; NM_004006.2(DMD):c.6392_6393insCA ; c.1159C>T ; NM_004006.2(DMD):c.137_138dupAT ; g.31444405-31806767 ; g.32452761-32645074 ; NM_004006.2(DMD):c.5530C>T ; NM_004006.2(DMD):c.6982A>T ; c.3022A>T ; c.2523del ; NM_004006.2(DMD):c.9568C>T ; g.31819658-31932544 ; NM_004006.2(DMD):c.583C>T ; c.8086del ; NM_004006.2(DMD):c.5363C>G ; g.31898812-32022323 ; NM_004006.2(DMD):c.4405C>T ; NM_004006.2(DMD):c.2332C>T ; NM_004006.2(DMD):c.4117C>T ; g.31679229-31932544 ; g.32662366-32758964 ; NM_004006.2(DMD):c.8656C>T ; NM_004006.2(DMD):c.2302C>T ; NM_004006.2(DMD):c.2380+1G>C ; c.6014_6017del ; c.204dup ; NM_004006.2(DMD):c.5353C>T ; NM_004006.2(DMD):c.6292C>T ; c.2137C>T ; NM_004006.2(DMD):c.2294_2297delCCAT ; c.5313dup ; c.199G>T ; g.32432957-32823439 ; g.32267823-32372572 ; NM_004006.2(DMD):c.3639dupA ; g.31147275-31173604 ; c.1193C>G ; c.6226G>T ; c.6834del ; g.13020141-143473520 ; NM_004006.2(DMD):c.10454delT ; g.31870708-32353592 ; NM_004006.2(DMD):c.8944C>T ; g.10701-53131191 ; NM_004006.2(DMD):c.7894C>T ; NM_004006.2(DMD):c.412_413delAA ; NM_004006.2(DMD):c.4843A>T ; NM_004006.2(DMD):c.1332-9A>G ; NM_004006.2(DMD):c.2650C>T ; NM_004006.2(DMD):c.8713C>T ; g.31874956-31932544 ; NM_004006.2(DMD):c.8374_8375delAA ; NM_004006.2(DMD):c.5554C>T ; NM_004006.2(DMD):c.7683G>A ; g.31518752-31636035 ; g.31609490-32699472 ; NM_004006.2(DMD):c.1070delC ; NM_004006.2(DMD):c.9361+1G>C ; g.31929292-31968838 ; g.32364355-32390415 ; NM_004006.2(DMD):c.133C>T ; g.32216645-32651039 ; NM_004006.2:c.3246_3247insTTTCTAAAAA ; NM_004006.2(DMD):c.1489C>T ; g.32275729-32353585 ; g.31695292-31840818 ; NM_004006.2(DMD):c.9564-1G>A ; NM_004006.2(DMD):c.3779_3785delCTTTGGAinsGG ; g.31773859-31932544 ; g.31627435-31932544 ; g.31836597-31932544 ; NM_004006.2(DMD):c.3121C>T ; NM_004006.2(DMD):c.5697delA ; NM_004006.2(DMD):c.7771G>T ; NM_004006.2(DMD):c.7922delA ; g.31640772-31665565 ; g.31431098-31525874 ; g.32411633-33020588 ; g.31121669-31134568 ; NM_004006.2(DMD):c.1886C>A ; g.31931923-31932544 ; g.31965009-31968838 ; g.33019769-33020588 ; NM_004006.2(DMD):c.5287C>T ; g.31189847-31945183 ; NM_004006.2(DMD):c.5640T>A ; g.31133877-31134568 ; g.32380341-32380904 ; c.3087G>A ; g.26102-57302794 ; NM_004006.2(DMD):c.8608C>T ; NM_004006.2(DMD):c.2804-1G>A ; NM_004006.2(DMD):c.8069T>G ; g.31645986-31773985 ; c.1664G>A ; NM_004006.2(DMD):c.4471_4472delAA ; NM_004006.2(DMD):c.5899C>T ; c.3076G>T ; NM_004006.2(DMD):c.9337C>T ; NM_004006.2(DMD):c.3432+3A>G ; NM_004006.2(DMD):c.4806A>T ; NM_004006.2(DMD):c.9361+1G>A ; c.171G>A ; NM_004006.2(DMD):c.2816T>A ; NM_004006.2(DMD):c.627delA ; NM_004006.2(DMD):c.10033C>T ; c.2380+2T>C ; NM_004006.2(DMD):c.2804-2A>T ; c.6936del ; NM_004006.2(DMD):c.2547delT ; c.2758C>T ; NM_004006.2(DMD):c.6000T>A ; c.220del ; g.32557406-32754551 ; c.1900_1903dup ; c.1734del ; NM_004006.2(DMD):c.1286C>A ; NM_004006.2(DMD):c.676_678delAAG ; NM_004006.2(DMD):c.3295C>T ; NM_004006.2(DMD):c.2125delC ; g.31540244-32059446 ; NM_004006.2(DMD):c.6986dupA ; NM_004006.2(DMD):c.8443C>T ; c.2803+1G>A ; c.2587del ; g.32341945-32596022 ; NM_004006.2(DMD):c.3432+1G>A ; c.2266_2267del ; c.2866C>T ; NM_004006.2(DMD):c.6238delC ; NM_004006.2(DMD):c.9650-2A>G ; g.31724913-31806626 ; NM_004006.2(DMD):c.9862G>T ; g.10679-36186635 ; NM_004006.2(DMD):c.8064_8065delTA ; NM_004006.2(DMD):c.1341_1342dupAG ; g.32203741-32353533 ; g.31744885-32562211 ; NM_004006.2(DMD):c.1012G>T ; c.3124A>T ; NM_004006.2(DMD):c.8652_8653delCT ; NM_004006.2(DMD):c.433C>T ; c.277C>T ; NM_004006.2:c.2169-3_2169-1delinsAA ; c.7764dup ; NM_004006.2(DMD):c.3276+1G>A ; g.32501716-32932295 ; g.31856886-32482971 ; NM_004006.2(DMD):c.10141C>T ; NM_004006.2(DMD):c.6906G>A ; NM_004006.2(DMD):c.1261C>T ; NM_004006.2(DMD):c.10086+1G>A ; NM_004006.2(DMD):c.10446_10447delCT ; NM_004006.2(DMD):c.2484T>G ; NM_004006.2(DMD):c.4375C>T ; g.251879-35885004 ; g.31745624-31876916 ; g.31121669-33339588 ; g.30093911-34060667 ; c.489G>A ; g.31180370-31206667 ; g.10679-52213731 ; c.4486del ; NM_004006.2(DMD):c.9164-1G>C ; NM_004006.2(DMD):c.9854_9863delTGAGACTGGA ; g.31632068-31954142 ; NM_004006.2(DMD):c.1371delG ; NM_004006.2(DMD):c.2281_2285delGAAAA ; c.5570_5571dup ; c.2929dup ; c.6964del ; NM_004006.2(DMD):c.6391_6392delCA ; c.1900A>T ; NM_004006.2(DMD):c.615T>A ; g.32631403-32907656 ; c.530+1del ; NM_004006.2(DMD):c.1048G>T ; NM_004006.2(DMD):c.2755A>T ; c.2479del ; NM_004006.2(DMD):c.3747delG ; NM_004006.2(DMD):c.2815_2816delTT ; c.4409_4412dup ; c.6943G>T ; c.977-1G>T ; NM_004006.2(DMD):c.6182delC ; NM_004006.2(DMD):c.4518+5G>A ; g.10701-49071220 ; g.251880-51643625 ; NM_004006.2(DMD):c.1529_1530delTC ; NM_004006.2(DMD):c.6373C>T ; g.32380341-32412502 ; NM_004006.2(DMD):c.2803+1G>T ; c.6340A>T ; NM_004006.2(DMD):c.5773G>T ; c.3697del ; g.32341945-32816915 ; c.6763-2A>G ; c.4735G>T ; c.5671A>T ; c.5807T>A ; g.31744863-31846787 ; g.31627435-31774446 ; g.31679229-31968838 ; NM_004006.2(DMD):c.1306dupG ; g.32697662-32699472 ; NM_004006.2(DMD):c.7682G>A ; c.4500del ; NM_004006.2(DMD):c.6392_6393insCA ; c.1159C>T ; NM_004006.2(DMD):c.137_138dupAT ; g.31444405-31806767 ; g.32452761-32645074 ; NM_004006.2(DMD):c.5530C>T ; NM_004006.2(DMD):c.6982A>T ; c.3022A>T ; c.2523del ; NM_004006.2(DMD):c.9568C>T ; g.31819658-31932544 ; NM_004006.2(DMD):c.583C>T ; c.8086del ; NM_004006.2(DMD):c.5363C>G ; g.31898812-32022323 ; NM_004006.2(DMD):c.4405C>T ; NM_004006.2(DMD):c.2332C>T ; NM_004006.2(DMD):c.4117C>T ; g.31679229-31932544 ; g.32662366-32758964 ; NM_004006.2(DMD):c.8656C>T ; NM_004006.2(DMD):c.2302C>T ; NM_004006.2(DMD):c.2380+1G>C ; c.6014_6017del ; c.204dup ; NM_004006.2(DMD):c.5353C>T ; NM_004006.2(DMD):c.6292C>T ; c.2137C>T ; NM_004006.2(DMD):c.2294_2297delCCAT ; c.5313dup ; c.199G>T ; g.32432957-32823439 ; g.32267823-32372572 ; NM_004006.2(DMD):c.3639dupA ; g.31147275-31173604 ; c.1193C>G ; c.6226G>T ; c.6834del ; g.13020141-143473520 ; NM_004006.2(DMD):c.10454delT ; g.31870708-32353592 ; NM_004006.2(DMD):c.8944C>T ; g.10701-53131191 ; NM_004006.2(DMD):c.7894C>T ; NM_004006.2(DMD):c.412_413delAA ; NM_004006.2(DMD):c.4843A>T ; NM_004006.2(DMD):c.1332-9A>G ; NM_004006.2(DMD):c.2650C>T ; NM_004006.2(DMD):c.8713C>T ; g.31874956-31932544 ; NM_004006.2(DMD):c.8374_8375delAA ; NM_004006.2(DMD):c.5554C>T ; NM_004006.2(DMD):c.7683G>A ; g.31518752-31636035 ; g.31609490-32699472 ; NM_004006.2(DMD):c.1070delC ; NM_004006.2(DMD):c.9361+1G>C ; g.31929292-31968838 ; g.32364355-32390415 ; NM_004006.2(DMD):c.133C>T ; g.32216645-32651039 ; NM_004006.2:c.3246_3247insTTTCTAAAAA ; NM_004006.2(DMD):c.1489C>T ; g.32275729-32353585 ; g.31695292-31840818 ; NM_004006.2(DMD):c.9564-1G>A ; NM_004006.2(DMD):c.3779_3785delCTTTGGAinsGG ; g.31773859-31932544 ; g.31627435-31932544 ; g.31836597-31932544 ; NM_004006.2(DMD):c.3121C>T ; NM_004006.2(DMD):c.5697delA ; NM_004006.2(DMD):c.7771G>T ; NM_004006.2(DMD):c.7922delA ; g.31640772-31665565 ; g.31431098-31525874 ; g.32411633-33020588 ; g.31121669-31134568 ; NM_004006.2(DMD):c.1886C>A ; g.31931923-31932544 ; g.31965009-31968838 ; g.33019769-33020588 ; NM_004006.2(DMD):c.5287C>T ; g.31189847-31945183 ; NM_004006.2(DMD):c.5640T>A ; g.31133877-31134568 ; g.32380341-32380904

DMD	X-linked non-syndromic intellectual disability	MECP2 duplication syndrome is an X-linked neurodevelopmental disorder characterized by severe to profound mental retardation, infantile hypotonia, mild dysmorphic features, poor speech development, autistic features, seizures, progressive spasticity, and recurrent infections. Only males are affected, although female carriers may have some mild neuropsychiatric features, such as anxiety. Submicroscopic Xq28 duplications encompassing MECP2 are considered nonrecurrent events, because the breakpoint locations and rearrangement sizes vary among affected individuals.		c.3087G>A ; g.26102-57302794 ; NM_004006.2(DMD):c.8608C>T ; NM_004006.2(DMD):c.2804-1G>A ; NM_004006.2(DMD):c.8069T>G ; g.31645986-31773985 ; c.1664G>A ; NM_004006.2(DMD):c.4471_4472delAA ; NM_004006.2(DMD):c.5899C>T ; c.3076G>T ; NM_004006.2(DMD):c.9337C>T ; NM_004006.2(DMD):c.3432+3A>G ; NM_004006.2(DMD):c.4806A>T ; NM_004006.2(DMD):c.9361+1G>A ; c.171G>A ; NM_004006.2(DMD):c.2816T>A ; NM_004006.2(DMD):c.627delA ; NM_004006.2(DMD):c.10033C>T ; c.2380+2T>C ; NM_004006.2(DMD):c.2804-2A>T ; c.6936del ; NM_004006.2(DMD):c.2547delT ; c.2758C>T ; NM_004006.2(DMD):c.6000T>A ; c.220del ; g.32557406-32754551 ; c.1900_1903dup ; c.1734del ; NM_004006.2(DMD):c.1286C>A ; NM_004006.2(DMD):c.676_678delAAG ; NM_004006.2(DMD):c.3295C>T ; NM_004006.2(DMD):c.2125delC ; g.31540244-32059446 ; NM_004006.2(DMD):c.6986dupA ; NM_004006.2(DMD):c.8443C>T ; c.2803+1G>A ; c.2587del ; g.32341945-32596022 ; NM_004006.2(DMD):c.3432+1G>A ; c.2266_2267del ; c.2866C>T ; NM_004006.2(DMD):c.6238delC ; NM_004006.2(DMD):c.9650-2A>G ; g.31724913-31806626 ; NM_004006.2(DMD):c.9862G>T ; g.10679-36186635 ; NM_004006.2(DMD):c.8064_8065delTA ; NM_004006.2(DMD):c.1341_1342dupAG ; g.32203741-32353533 ; g.31744885-32562211 ; NM_004006.2(DMD):c.1012G>T ; c.3124A>T ; NM_004006.2(DMD):c.8652_8653delCT ; NM_004006.2(DMD):c.433C>T ; c.277C>T ; NM_004006.2:c.2169-3_2169-1delinsAA ; c.7764dup ; NM_004006.2(DMD):c.3276+1G>A ; g.32501716-32932295 ; g.31856886-32482971 ; NM_004006.2(DMD):c.10141C>T ; NM_004006.2(DMD):c.6906G>A ; NM_004006.2(DMD):c.1261C>T ; NM_004006.2(DMD):c.10086+1G>A ; NM_004006.2(DMD):c.10446_10447delCT ; NM_004006.2(DMD):c.2484T>G ; NM_004006.2(DMD):c.4375C>T ; g.251879-35885004 ; g.31745624-31876916 ; g.31121669-33339588 ; g.30093911-34060667 ; c.489G>A ; g.31180370-31206667 ; g.10679-52213731 ; c.4486del ; NM_004006.2(DMD):c.9164-1G>C ; NM_004006.2(DMD):c.9854_9863delTGAGACTGGA ; g.31632068-31954142 ; NM_004006.2(DMD):c.1371delG ; NM_004006.2(DMD):c.2281_2285delGAAAA ; c.5570_5571dup ; c.2929dup ; c.6964del ; NM_004006.2(DMD):c.6391_6392delCA ; c.1900A>T ; NM_004006.2(DMD):c.615T>A ; g.32631403-32907656 ; c.530+1del ; NM_004006.2(DMD):c.1048G>T ; NM_004006.2(DMD):c.2755A>T ; c.2479del ; NM_004006.2(DMD):c.3747delG ; NM_004006.2(DMD):c.2815_2816delTT ; c.4409_4412dup ; c.6943G>T ; c.977-1G>T ; NM_004006.2(DMD):c.6182delC ; NM_004006.2(DMD):c.4518+5G>A ; g.10701-49071220 ; g.251880-51643625 ; NM_004006.2(DMD):c.1529_1530delTC ; NM_004006.2(DMD):c.6373C>T ; g.32380341-32412502 ; NM_004006.2(DMD):c.2803+1G>T ; c.6340A>T ; NM_004006.2(DMD):c.5773G>T ; c.3697del ; g.32341945-32816915 ; c.6763-2A>G ; c.4735G>T ; c.5671A>T ; c.5807T>A ; g.31744863-31846787 ; g.31627435-31774446 ; g.31679229-31968838 ; NM_004006.2(DMD):c.1306dupG ; g.32697662-32699472 ; NM_004006.2(DMD):c.7682G>A ; c.4500del ; NM_004006.2(DMD):c.6392_6393insCA ; c.1159C>T ; NM_004006.2(DMD):c.137_138dupAT ; g.31444405-31806767 ; g.32452761-32645074 ; NM_004006.2(DMD):c.5530C>T ; NM_004006.2(DMD):c.6982A>T ; c.3022A>T ; c.2523del ; NM_004006.2(DMD):c.9568C>T ; g.31819658-31932544 ; NM_004006.2(DMD):c.583C>T ; c.8086del ; NM_004006.2(DMD):c.5363C>G ; g.31898812-32022323 ; NM_004006.2(DMD):c.4405C>T ; NM_004006.2(DMD):c.2332C>T ; NM_004006.2(DMD):c.4117C>T ; g.31679229-31932544 ; g.32662366-32758964 ; NM_004006.2(DMD):c.8656C>T ; NM_004006.2(DMD):c.2302C>T ; NM_004006.2(DMD):c.2380+1G>C ; c.6014_6017del ; c.204dup ; NM_004006.2(DMD):c.5353C>T ; NM_004006.2(DMD):c.6292C>T ; c.2137C>T ; NM_004006.2(DMD):c.2294_2297delCCAT ; c.5313dup ; c.199G>T ; g.32432957-32823439 ; g.32267823-32372572 ; NM_004006.2(DMD):c.3639dupA ; g.31147275-31173604 ; c.1193C>G ; c.6226G>T ; c.6834del ; g.13020141-143473520 ; NM_004006.2(DMD):c.10454delT ; g.31870708-32353592 ; NM_004006.2(DMD):c.8944C>T ; g.10701-53131191 ; NM_004006.2(DMD):c.7894C>T ; NM_004006.2(DMD):c.412_413delAA ; NM_004006.2(DMD):c.4843A>T ; NM_004006.2(DMD):c.1332-9A>G ; NM_004006.2(DMD):c.2650C>T ; NM_004006.2(DMD):c.8713C>T ; g.31874956-31932544 ; NM_004006.2(DMD):c.8374_8375delAA ; NM_004006.2(DMD):c.5554C>T ; NM_004006.2(DMD):c.7683G>A ; g.31518752-31636035 ; g.31609490-32699472 ; NM_004006.2(DMD):c.1070delC ; NM_004006.2(DMD):c.9361+1G>C ; g.31929292-31968838 ; g.32364355-32390415 ; NM_004006.2(DMD):c.133C>T ; g.32216645-32651039 ; NM_004006.2:c.3246_3247insTTTCTAAAAA ; NM_004006.2(DMD):c.1489C>T ; g.32275729-32353585 ; g.31695292-31840818 ; NM_004006.2(DMD):c.9564-1G>A ; NM_004006.2(DMD):c.3779_3785delCTTTGGAinsGG ; g.31773859-31932544 ; g.31627435-31932544 ; g.31836597-31932544 ; NM_004006.2(DMD):c.3121C>T ; NM_004006.2(DMD):c.5697delA ; NM_004006.2(DMD):c.7771G>T ; NM_004006.2(DMD):c.7922delA ; g.31640772-31665565 ; g.31431098-31525874 ; g.32411633-33020588 ; g.31121669-31134568 ; NM_004006.2(DMD):c.1886C>A ; g.31931923-31932544 ; g.31965009-31968838 ; g.33019769-33020588 ; NM_004006.2(DMD):c.5287C>T ; g.31189847-31945183 ; NM_004006.2(DMD):c.5640T>A ; g.31133877-31134568 ; g.32380341-32380904 ; c.3087G>A ; g.26102-57302794 ; NM_004006.2(DMD):c.8608C>T ; NM_004006.2(DMD):c.2804-1G>A ; NM_004006.2(DMD):c.8069T>G ; g.31645986-31773985 ; c.1664G>A ; NM_004006.2(DMD):c.4471_4472delAA ; NM_004006.2(DMD):c.5899C>T ; c.3076G>T ; NM_004006.2(DMD):c.9337C>T ; NM_004006.2(DMD):c.3432+3A>G ; NM_004006.2(DMD):c.4806A>T ; NM_004006.2(DMD):c.9361+1G>A ; c.171G>A ; NM_004006.2(DMD):c.2816T>A ; NM_004006.2(DMD):c.627delA ; NM_004006.2(DMD):c.10033C>T ; c.2380+2T>C ; NM_004006.2(DMD):c.2804-2A>T ; c.6936del ; NM_004006.2(DMD):c.2547delT ; c.2758C>T ; NM_004006.2(DMD):c.6000T>A ; c.220del ; g.32557406-32754551 ; c.1900_1903dup ; c.1734del ; NM_004006.2(DMD):c.1286C>A ; NM_004006.2(DMD):c.676_678delAAG ; NM_004006.2(DMD):c.3295C>T ; NM_004006.2(DMD):c.2125delC ; g.31540244-32059446 ; NM_004006.2(DMD):c.6986dupA ; NM_004006.2(DMD):c.8443C>T ; c.2803+1G>A ; c.2587del ; g.32341945-32596022 ; NM_004006.2(DMD):c.3432+1G>A ; c.2266_2267del ; c.2866C>T ; NM_004006.2(DMD):c.6238delC ; NM_004006.2(DMD):c.9650-2A>G ; g.31724913-31806626 ; NM_004006.2(DMD):c.9862G>T ; g.10679-36186635 ; NM_004006.2(DMD):c.8064_8065delTA ; NM_004006.2(DMD):c.1341_1342dupAG ; g.32203741-32353533 ; g.31744885-32562211 ; NM_004006.2(DMD):c.1012G>T ; c.3124A>T ; NM_004006.2(DMD):c.8652_8653delCT ; NM_004006.2(DMD):c.433C>T ; c.277C>T ; NM_004006.2:c.2169-3_2169-1delinsAA ; c.7764dup ; NM_004006.2(DMD):c.3276+1G>A ; g.32501716-32932295 ; g.31856886-32482971 ; NM_004006.2(DMD):c.10141C>T ; NM_004006.2(DMD):c.6906G>A ; NM_004006.2(DMD):c.1261C>T ; NM_004006.2(DMD):c.10086+1G>A ; NM_004006.2(DMD):c.10446_10447delCT ; NM_004006.2(DMD):c.2484T>G ; NM_004006.2(DMD):c.4375C>T ; g.251879-35885004 ; g.31745624-31876916 ; g.31121669-33339588 ; g.30093911-34060667 ; c.489G>A ; g.31180370-31206667 ; g.10679-52213731 ; c.4486del ; NM_004006.2(DMD):c.9164-1G>C ; NM_004006.2(DMD):c.9854_9863delTGAGACTGGA ; g.31632068-31954142 ; NM_004006.2(DMD):c.1371delG ; NM_004006.2(DMD):c.2281_2285delGAAAA ; c.5570_5571dup ; c.2929dup ; c.6964del ; NM_004006.2(DMD):c.6391_6392delCA ; c.1900A>T ; NM_004006.2(DMD):c.615T>A ; g.32631403-32907656 ; c.530+1del ; NM_004006.2(DMD):c.1048G>T ; NM_004006.2(DMD):c.2755A>T ; c.2479del ; NM_004006.2(DMD):c.3747delG ; NM_004006.2(DMD):c.2815_2816delTT ; c.4409_4412dup ; c.6943G>T ; c.977-1G>T ; NM_004006.2(DMD):c.6182delC ; NM_004006.2(DMD):c.4518+5G>A ; g.10701-49071220 ; g.251880-51643625 ; NM_004006.2(DMD):c.1529_1530delTC ; NM_004006.2(DMD):c.6373C>T ; g.32380341-32412502 ; NM_004006.2(DMD):c.2803+1G>T ; c.6340A>T ; NM_004006.2(DMD):c.5773G>T ; c.3697del ; g.32341945-32816915 ; c.6763-2A>G ; c.4735G>T ; c.5671A>T ; c.5807T>A ; g.31744863-31846787 ; g.31627435-31774446 ; g.31679229-31968838 ; NM_004006.2(DMD):c.1306dupG ; g.32697662-32699472 ; NM_004006.2(DMD):c.7682G>A ; c.4500del ; NM_004006.2(DMD):c.6392_6393insCA ; c.1159C>T ; NM_004006.2(DMD):c.137_138dupAT ; g.31444405-31806767 ; g.32452761-32645074 ; NM_004006.2(DMD):c.5530C>T ; NM_004006.2(DMD):c.6982A>T ; c.3022A>T ; c.2523del ; NM_004006.2(DMD):c.9568C>T ; g.31819658-31932544 ; NM_004006.2(DMD):c.583C>T ; c.8086del ; NM_004006.2(DMD):c.5363C>G ; g.31898812-32022323 ; NM_004006.2(DMD):c.4405C>T ; NM_004006.2(DMD):c.2332C>T ; NM_004006.2(DMD):c.4117C>T ; g.31679229-31932544 ; g.32662366-32758964 ; NM_004006.2(DMD):c.8656C>T ; NM_004006.2(DMD):c.2302C>T ; NM_004006.2(DMD):c.2380+1G>C ; c.6014_6017del ; c.204dup ; NM_004006.2(DMD):c.5353C>T ; NM_004006.2(DMD):c.6292C>T ; c.2137C>T ; NM_004006.2(DMD):c.2294_2297delCCAT ; c.5313dup ; c.199G>T ; g.32432957-32823439 ; g.32267823-32372572 ; NM_004006.2(DMD):c.3639dupA ; g.31147275-31173604 ; c.1193C>G ; c.6226G>T ; c.6834del ; g.13020141-143473520 ; NM_004006.2(DMD):c.10454delT ; g.31870708-32353592 ; NM_004006.2(DMD):c.8944C>T ; g.10701-53131191 ; NM_004006.2(DMD):c.7894C>T ; NM_004006.2(DMD):c.412_413delAA ; NM_004006.2(DMD):c.4843A>T ; NM_004006.2(DMD):c.1332-9A>G ; NM_004006.2(DMD):c.2650C>T ; NM_004006.2(DMD):c.8713C>T ; g.31874956-31932544 ; NM_004006.2(DMD):c.8374_8375delAA ; NM_004006.2(DMD):c.5554C>T ; NM_004006.2(DMD):c.7683G>A ; g.31518752-31636035 ; g.31609490-32699472 ; NM_004006.2(DMD):c.1070delC ; NM_004006.2(DMD):c.9361+1G>C ; g.31929292-31968838 ; g.32364355-32390415 ; NM_004006.2(DMD):c.133C>T ; g.32216645-32651039 ; NM_004006.2:c.3246_3247insTTTCTAAAAA ; NM_004006.2(DMD):c.1489C>T ; g.32275729-32353585 ; g.31695292-31840818 ; NM_004006.2(DMD):c.9564-1G>A ; NM_004006.2(DMD):c.3779_3785delCTTTGGAinsGG ; g.31773859-31932544 ; g.31627435-31932544 ; g.31836597-31932544 ; NM_004006.2(DMD):c.3121C>T ; NM_004006.2(DMD):c.5697delA ; NM_004006.2(DMD):c.7771G>T ; NM_004006.2(DMD):c.7922delA ; g.31640772-31665565 ; g.31431098-31525874 ; g.32411633-33020588 ; g.31121669-31134568 ; NM_004006.2(DMD):c.1886C>A ; g.31931923-31932544 ; g.31965009-31968838 ; g.33019769-33020588 ; NM_004006.2(DMD):c.5287C>T ; g.31189847-31945183 ; NM_004006.2(DMD):c.5640T>A ; g.31133877-31134568 ; g.32380341-32380904

DPYD	1p21.3 microdeletion syndrome	1p21.3 microdeletion syndrome is an extremely rare chromosomal anomaly characterized by severe speech and language delay, intellectual deficiency, autism spectrum disorder(see this term).	1p21.3 microdeletion syndrome is characterized by severe speech and language delay, a borderline-mild to mild-moderate intellectual deficiency, autism spectrum disorder (see this term) features, and minor dysmorphic facial features such as long ears, deep set eyes, a broad nasal tip and a thick lower lip. Affected individuals have normal gross motor development without major abnormalities, they are often very shy and friendly with a tendency to overeat.	NM_000110.3(DPYD):c.1109_1110delTA ; NM_000110.3(DPYD):c.1109_1110delTA
DPYD	Dihydropyrimidine dehydrogenase deficiency	Dihyropyrimidine dehydrogenase deficiency shows large phenotypic variability, ranging from no symptoms to a convulsive disorder with motor and mental retardation in homozygous patients. In addition, homozygous and heterozygous mutation carriers can develop severe toxicity after the administration of the antineoplastic drug 5-fluorouracil (5FU), which is also catabolized by the DPYD enzyme.	A rare disorder of pyrimidine metabolism characterized by a variable phenotype ranging from absence of symptoms to severe neurological involvement with developmental delay, intellectual disability, and seizures. Additional signs and symptoms may include hypotonia, microcephaly, ocular abnormalities (such as microphthalmia, nystagmus, and strabismus), and autistic behavior, among others. Analysis of urine typically shows high levels of uracil and thymine. Patients are at risk of suffering from severe toxicity after the administration of the anti-neoplastic agent 5-fluorouracil.	NM_000110.3(DPYD):c.1109_1110delTA ; NM_000110.3(DPYD):c.1109_1110delTA

DYSF	Congenital myopathy, Paradas type	A rare congenital muscular dystrophy characterized by early onset of hypotonia, delayed motor development, and variably progressive generalized muscle weakness. Predominant involvement of pelvic and neck flexor muscles has been reported, as well as early involvement of hamstrings and medial gastrocnemius visible on muscle MRI. Serum creatine kinase levels are markedly elevated (in some cases already from early childhood). Muscle biopsy shows absence of dysferlin.		NM_003494.3(DYSF):c.610C>T ; c.5992G>T ; NM_003494.3(DYSF):c.3641delC ; c.3175-2A>T ; NM_001130978.1(DYSF):c.5264A>G ; NM_003494.3(DYSF):c.3444_3445delTGinsAA ; NM_003494.3(DYSF):c.1053+1G>A ; NM_003494.3(DYSF):c.937+1G>A ; c.3957del ; NM_003494.3(DYSF):c.5341-2A>C ; c.3477C>A ; NM_003494.3(DYSF):c.2870_2874delAGACC ; NM_001130987.1(DYSF):c.1372G>A ; c.4108_4109del ; NM_003494.3(DYSF):c.3041A>G ; c.1620del ; NM_001130978.1(DYSF):c.1813C>T ; NM_003494.3(DYSF):c.5836_5839delCAGC ; NM_001130987.1(DYSF):c.853C>T ; NM_003494.3(DYSF):c.5509G>A ; NM_003494.3(DYSF):c.1368C>A ; NM_003494.3(DYSF):c.5644C>T ; NM_003494.3(DYSF):c.5525+1G>A ; NM_003494.3(DYSF):c.2997G>T ; c.3708del ; NM_001130978.1(DYSF):c.1873G>T ; NM_003494.3(DYSF):c.1398-2A>G ; NM_003494.3(DYSF):c.4253G>A ; c.1861G>C ; NM_003494.3(DYSF):c.1481-1G>A ; NM_003494.3(DYSF):c.5077C>T ; NM_003494.3(DYSF):c.5266C>T ; NM_003494.3(DYSF):c.1392dupA ; NM_003494.3(DYSF):c.895G>A ; NM_003494.3(DYSF):c.5429G>A ; NM_003494.3(DYSF):c.5698_5699delAG ; NM_001130978.1(DYSF):c.895G>T ; c.3903+1del ; NM_003494.3(DYSF):c.663+1G>C ; NM_001130978.1(DYSF):c.200_201delTGinsAT ; NM_003494.3(DYSF):c.1398-1G>A ; NM_003494.3(DYSF):c.3112C>T ; NM_003494.3(DYSF):c.6124C>T ; NM_003494.3(DYSF):c.3805G>T ; NM_003494.3(DYSF):c.1663C>T ; NM_003494.4:c.4872_4876delGCCCGinsCCCC ; NM_003494.3(DYSF):c.3478C>T ; NM_003494.3(DYSF):c.701G>A ; NM_003494.3(DYSF):c.1284+2T>C ; NM_003494.3(DYSF):c.4090C>T ; NM_003494.3(DYSF):c.4756C>T ; NM_003494.3(DYSF):c.1638+2T>A ; NM_003494.3(DYSF):c.2869C>T ; NM_003494.3(DYSF):c.5497G>T ; NM_003494.3(DYSF):c.5594delG ; NM_003494.3(DYSF):c.5429+1G>T ; NM_003494.3(DYSF):c.5979dupA ; NM_003494.3(DYSF):c.5713C>T ; NM_003494.3(DYSF):c.1834C>T ; NM_003494.3(DYSF):c.393_394delCC ; NM_003494.3(DYSF):c.610C>T ; c.5992G>T ; NM_003494.3(DYSF):c.3641delC ; c.3175-2A>T ; NM_001130978.1(DYSF):c.5264A>G ; NM_003494.3(DYSF):c.3444_3445delTGinsAA ; NM_003494.3(DYSF):c.1053+1G>A ; NM_003494.3(DYSF):c.937+1G>A ; c.3957del ; NM_003494.3(DYSF):c.5341-2A>C ; c.3477C>A ; NM_003494.3(DYSF):c.2870_2874delAGACC ; NM_001130987.1(DYSF):c.1372G>A ; c.4108_4109del ; NM_003494.3(DYSF):c.3041A>G ; c.1620del ; NM_001130978.1(DYSF):c.1813C>T ; NM_003494.3(DYSF):c.5836_5839delCAGC ; NM_001130987.1(DYSF):c.853C>T ; NM_003494.3(DYSF):c.5509G>A ; NM_003494.3(DYSF):c.1368C>A ; NM_003494.3(DYSF):c.5644C>T ; NM_003494.3(DYSF):c.5525+1G>A ; NM_003494.3(DYSF):c.2997G>T ; c.3708del ; NM_001130978.1(DYSF):c.1873G>T ; NM_003494.3(DYSF):c.1398-2A>G ; NM_003494.3(DYSF):c.4253G>A ; c.1861G>C ; NM_003494.3(DYSF):c.1481-1G>A ; NM_003494.3(DYSF):c.5077C>T ; NM_003494.3(DYSF):c.5266C>T ; NM_003494.3(DYSF):c.1392dupA ; NM_003494.3(DYSF):c.895G>A ; NM_003494.3(DYSF):c.5429G>A ; NM_003494.3(DYSF):c.5698_5699delAG ; NM_001130978.1(DYSF):c.895G>T ; c.3903+1del ; NM_003494.3(DYSF):c.663+1G>C ; NM_001130978.1(DYSF):c.200_201delTGinsAT ; NM_003494.3(DYSF):c.1398-1G>A ; NM_003494.3(DYSF):c.3112C>T ; NM_003494.3(DYSF):c.6124C>T ; NM_003494.3(DYSF):c.3805G>T ; NM_003494.3(DYSF):c.1663C>T ; NM_003494.4:c.4872_4876delGCCCGinsCCCC ; NM_003494.3(DYSF):c.3478C>T ; NM_003494.3(DYSF):c.701G>A ; NM_003494.3(DYSF):c.1284+2T>C ; NM_003494.3(DYSF):c.4090C>T ; NM_003494.3(DYSF):c.4756C>T ; NM_003494.3(DYSF):c.1638+2T>A ; NM_003494.3(DYSF):c.2869C>T ; NM_003494.3(DYSF):c.5497G>T ; NM_003494.3(DYSF):c.5594delG ; NM_003494.3(DYSF):c.5429+1G>T ; NM_003494.3(DYSF):c.5979dupA ; NM_003494.3(DYSF):c.5713C>T ; NM_003494.3(DYSF):c.1834C>T ; NM_003494.3(DYSF):c.393_394delCC
DYSF	Distal myopathy with anterior tibial onset	Distal myopathy with anterior tibial onset is a rare, genetic neuromuscular disease characterized by a progressive muscle weakness starting in the anterior tibial muscles, later involving lower and upper limb muscles, associated with an increased serum creatine kinase levels and absence of dysferlin on muscle biopsy. Patients become wheelchair dependent.	Onset of the disorder is between 14 and 28 years of age and the anterior tibial muscles are the first muscle group to be involved. The disorder has a rapidly progressive course successively involving the lower and upper proximal muscles, with patients being confined to a wheelchair 11 to 22 years from onset. The cranial muscles are spared. Serum creatine kinase level is increased 20 to 70 times the normal value and muscle histopathologic studies show moderate myopathic changes without vacuoles.	NM_003494.3(DYSF):c.610C>T ; c.5992G>T ; NM_003494.3(DYSF):c.3641delC ; c.3175-2A>T ; NM_001130978.1(DYSF):c.5264A>G ; NM_003494.3(DYSF):c.3444_3445delTGinsAA ; NM_003494.3(DYSF):c.1053+1G>A ; NM_003494.3(DYSF):c.937+1G>A ; c.3957del ; NM_003494.3(DYSF):c.5341-2A>C ; c.3477C>A ; NM_003494.3(DYSF):c.2870_2874delAGACC ; NM_001130987.1(DYSF):c.1372G>A ; c.4108_4109del ; NM_003494.3(DYSF):c.3041A>G ; c.1620del ; NM_001130978.1(DYSF):c.1813C>T ; NM_003494.3(DYSF):c.5836_5839delCAGC ; NM_001130987.1(DYSF):c.853C>T ; NM_003494.3(DYSF):c.5509G>A ; NM_003494.3(DYSF):c.1368C>A ; NM_003494.3(DYSF):c.5644C>T ; NM_003494.3(DYSF):c.5525+1G>A ; NM_003494.3(DYSF):c.2997G>T ; c.3708del ; NM_001130978.1(DYSF):c.1873G>T ; NM_003494.3(DYSF):c.1398-2A>G ; NM_003494.3(DYSF):c.4253G>A ; c.1861G>C ; NM_003494.3(DYSF):c.1481-1G>A ; NM_003494.3(DYSF):c.5077C>T ; NM_003494.3(DYSF):c.5266C>T ; NM_003494.3(DYSF):c.1392dupA ; NM_003494.3(DYSF):c.895G>A ; NM_003494.3(DYSF):c.5429G>A ; NM_003494.3(DYSF):c.5698_5699delAG ; NM_001130978.1(DYSF):c.895G>T ; c.3903+1del ; NM_003494.3(DYSF):c.663+1G>C ; NM_001130978.1(DYSF):c.200_201delTGinsAT ; NM_003494.3(DYSF):c.1398-1G>A ; NM_003494.3(DYSF):c.3112C>T ; NM_003494.3(DYSF):c.6124C>T ; NM_003494.3(DYSF):c.3805G>T ; NM_003494.3(DYSF):c.1663C>T ; NM_003494.4:c.4872_4876delGCCCGinsCCCC ; NM_003494.3(DYSF):c.3478C>T ; NM_003494.3(DYSF):c.701G>A ; NM_003494.3(DYSF):c.1284+2T>C ; NM_003494.3(DYSF):c.4090C>T ; NM_003494.3(DYSF):c.4756C>T ; NM_003494.3(DYSF):c.1638+2T>A ; NM_003494.3(DYSF):c.2869C>T ; NM_003494.3(DYSF):c.5497G>T ; NM_003494.3(DYSF):c.5594delG ; NM_003494.3(DYSF):c.5429+1G>T ; NM_003494.3(DYSF):c.5979dupA ; NM_003494.3(DYSF):c.5713C>T ; NM_003494.3(DYSF):c.1834C>T ; NM_003494.3(DYSF):c.393_394delCC

DYSF	Dysferlin-related limb-girdle muscular dystrophy R2	A subtype of autosomal recessive limb-girdle muscular dystrophy characterized by an onset in late adolescence or early adulthood of slowly progressive, proximal weakness and atrophy of shoulder and pelvic girdle muscles. Cardiac and respiratory muscles are not involved. Hypertrophy of the calf muscles and highly elevated serum creatine kinase levels are frequently observed.	Age at onset ranges from 15 to 25 years with difficulty in climbing stairs, fatigue, weakness, and markedly elevated serum creatine kinase. EMG showed myopathic changes and skeletal muscle biopsies showed severe myopathic changes with variation of fiber size, fiber splitting, increased connective tissue, and some necrotic changes. Disease progression was relatively slow.	NM_003494.3(DYSF):c.610C>T ; c.5992G>T ; NM_003494.3(DYSF):c.3641delC ; c.3175-2A>T ; NM_001130978.1(DYSF):c.5264A>G ; NM_003494.3(DYSF):c.3444_3445delTGinsAA ; NM_003494.3(DYSF):c.1053+1G>A ; NM_003494.3(DYSF):c.937+1G>A ; c.3957del ; NM_003494.3(DYSF):c.5341-2A>C ; c.3477C>A ; NM_003494.3(DYSF):c.2870_2874delAGACC ; NM_001130987.1(DYSF):c.1372G>A ; c.4108_4109del ; NM_003494.3(DYSF):c.3041A>G ; c.1620del ; NM_001130978.1(DYSF):c.1813C>T ; NM_003494.3(DYSF):c.5836_5839delCAGC ; NM_001130987.1(DYSF):c.853C>T ; NM_003494.3(DYSF):c.5509G>A ; NM_003494.3(DYSF):c.1368C>A ; NM_003494.3(DYSF):c.5644C>T ; NM_003494.3(DYSF):c.5525+1G>A ; NM_003494.3(DYSF):c.2997G>T ; c.3708del ; NM_001130978.1(DYSF):c.1873G>T ; NM_003494.3(DYSF):c.1398-2A>G ; NM_003494.3(DYSF):c.4253G>A ; c.1861G>C ; NM_003494.3(DYSF):c.1481-1G>A ; NM_003494.3(DYSF):c.5077C>T ; NM_003494.3(DYSF):c.5266C>T ; NM_003494.3(DYSF):c.1392dupA ; NM_003494.3(DYSF):c.895G>A ; NM_003494.3(DYSF):c.5429G>A ; NM_003494.3(DYSF):c.5698_5699delAG ; NM_001130978.1(DYSF):c.895G>T ; c.3903+1del ; NM_003494.3(DYSF):c.663+1G>C ; NM_001130978.1(DYSF):c.200_201delTGinsAT ; NM_003494.3(DYSF):c.1398-1G>A ; NM_003494.3(DYSF):c.3112C>T ; NM_003494.3(DYSF):c.6124C>T ; NM_003494.3(DYSF):c.3805G>T ; NM_003494.3(DYSF):c.1663C>T ; NM_003494.4:c.4872_4876delGCCCGinsCCCC ; NM_003494.3(DYSF):c.3478C>T ; NM_003494.3(DYSF):c.701G>A ; NM_003494.3(DYSF):c.1284+2T>C ; NM_003494.3(DYSF):c.4090C>T ; NM_003494.3(DYSF):c.4756C>T ; NM_003494.3(DYSF):c.1638+2T>A ; NM_003494.3(DYSF):c.2869C>T ; NM_003494.3(DYSF):c.5497G>T ; NM_003494.3(DYSF):c.5594delG ; NM_003494.3(DYSF):c.5429+1G>T ; NM_003494.3(DYSF):c.5979dupA ; NM_003494.3(DYSF):c.5713C>T ; NM_003494.3(DYSF):c.1834C>T ; NM_003494.3(DYSF):c.393_394delCC ; NM_003494.3(DYSF):c.610C>T ; c.5992G>T ; NM_003494.3(DYSF):c.3641delC ; c.3175-2A>T ; NM_001130978.1(DYSF):c.5264A>G ; NM_003494.3(DYSF):c.3444_3445delTGinsAA ; NM_003494.3(DYSF):c.1053+1G>A ; NM_003494.3(DYSF):c.937+1G>A ; c.3957del ; NM_003494.3(DYSF):c.5341-2A>C ; c.3477C>A ; NM_003494.3(DYSF):c.2870_2874delAGACC ; NM_001130987.1(DYSF):c.1372G>A ; c.4108_4109del ; NM_003494.3(DYSF):c.3041A>G ; c.1620del ; NM_001130978.1(DYSF):c.1813C>T ; NM_003494.3(DYSF):c.5836_5839delCAGC ; NM_001130987.1(DYSF):c.853C>T ; NM_003494.3(DYSF):c.5509G>A ; NM_003494.3(DYSF):c.1368C>A ; NM_003494.3(DYSF):c.5644C>T ; NM_003494.3(DYSF):c.5525+1G>A ; NM_003494.3(DYSF):c.2997G>T ; c.3708del ; NM_001130978.1(DYSF):c.1873G>T ; NM_003494.3(DYSF):c.1398-2A>G ; NM_003494.3(DYSF):c.4253G>A ; c.1861G>C ; NM_003494.3(DYSF):c.1481-1G>A ; NM_003494.3(DYSF):c.5077C>T ; NM_003494.3(DYSF):c.5266C>T ; NM_003494.3(DYSF):c.1392dupA ; NM_003494.3(DYSF):c.895G>A ; NM_003494.3(DYSF):c.5429G>A ; NM_003494.3(DYSF):c.5698_5699delAG ; NM_001130978.1(DYSF):c.895G>T ; c.3903+1del ; NM_003494.3(DYSF):c.663+1G>C ; NM_001130978.1(DYSF):c.200_201delTGinsAT ; NM_003494.3(DYSF):c.1398-1G>A ; NM_003494.3(DYSF):c.3112C>T ; NM_003494.3(DYSF):c.6124C>T ; NM_003494.3(DYSF):c.3805G>T ; NM_003494.3(DYSF):c.1663C>T ; NM_003494.4:c.4872_4876delGCCCGinsCCCC ; NM_003494.3(DYSF):c.3478C>T ; NM_003494.3(DYSF):c.701G>A ; NM_003494.3(DYSF):c.1284+2T>C ; NM_003494.3(DYSF):c.4090C>T ; NM_003494.3(DYSF):c.4756C>T ; NM_003494.3(DYSF):c.1638+2T>A ; NM_003494.3(DYSF):c.2869C>T ; NM_003494.3(DYSF):c.5497G>T ; NM_003494.3(DYSF):c.5594delG ; NM_003494.3(DYSF):c.5429+1G>T ; NM_003494.3(DYSF):c.5979dupA ; NM_003494.3(DYSF):c.5713C>T ; NM_003494.3(DYSF):c.1834C>T ; NM_003494.3(DYSF):c.393_394delCC
DYSF	Miyoshi myopathy	A recessive distal myopathy characterized by weakness in the distal lower extremity posterior compartment (gastrocnemius and soleus muscles) and associated with difficulties in standing on tip toes.	The typical age of onset of MM lies between 15 and 30 years (median 19 years) and the disease is characterized by muscle atrophy usually symmetric especially of the calf muscles (soleus and gastrocnemius). Onset in the anterior tibial muscles has been rarely reported. Ankle muscle stretch reflexes are lost and difficulties for toe walking or climbing stairs are encountered. Exercise-induced myalgia and aching discomfort in the calves can be an early symptom. Anterior compartment muscles of the distal lower extremities eventually become weak as well. As the disease progresses, patients will develop proximal leg and arm weakness to varying degrees. Decrease in respiratory functions have been reported only in few patients with moderate to severe disease. Bulbar or symptoms have not been reported.	NM_003494.3(DYSF):c.610C>T ; c.5992G>T ; NM_003494.3(DYSF):c.3641delC ; c.3175-2A>T ; NM_001130978.1(DYSF):c.5264A>G ; NM_003494.3(DYSF):c.3444_3445delTGinsAA ; NM_003494.3(DYSF):c.1053+1G>A ; NM_003494.3(DYSF):c.937+1G>A ; c.3957del ; NM_003494.3(DYSF):c.5341-2A>C ; c.3477C>A ; NM_003494.3(DYSF):c.2870_2874delAGACC ; NM_001130987.1(DYSF):c.1372G>A ; c.4108_4109del ; NM_003494.3(DYSF):c.3041A>G ; c.1620del ; NM_001130978.1(DYSF):c.1813C>T ; NM_003494.3(DYSF):c.5836_5839delCAGC ; NM_001130987.1(DYSF):c.853C>T ; NM_003494.3(DYSF):c.5509G>A ; NM_003494.3(DYSF):c.1368C>A ; NM_003494.3(DYSF):c.5644C>T ; NM_003494.3(DYSF):c.5525+1G>A ; NM_003494.3(DYSF):c.2997G>T ; c.3708del ; NM_001130978.1(DYSF):c.1873G>T ; NM_003494.3(DYSF):c.1398-2A>G ; NM_003494.3(DYSF):c.4253G>A ; c.1861G>C ; NM_003494.3(DYSF):c.1481-1G>A ; NM_003494.3(DYSF):c.5077C>T ; NM_003494.3(DYSF):c.5266C>T ; NM_003494.3(DYSF):c.1392dupA ; NM_003494.3(DYSF):c.895G>A ; NM_003494.3(DYSF):c.5429G>A ; NM_003494.3(DYSF):c.5698_5699delAG ; NM_001130978.1(DYSF):c.895G>T ; c.3903+1del ; NM_003494.3(DYSF):c.663+1G>C ; NM_001130978.1(DYSF):c.200_201delTGinsAT ; NM_003494.3(DYSF):c.1398-1G>A ; NM_003494.3(DYSF):c.3112C>T ; NM_003494.3(DYSF):c.6124C>T ; NM_003494.3(DYSF):c.3805G>T ; NM_003494.3(DYSF):c.1663C>T ; NM_003494.4:c.4872_4876delGCCCGinsCCCC ; NM_003494.3(DYSF):c.3478C>T ; NM_003494.3(DYSF):c.701G>A ; NM_003494.3(DYSF):c.1284+2T>C ; NM_003494.3(DYSF):c.4090C>T ; NM_003494.3(DYSF):c.4756C>T ; NM_003494.3(DYSF):c.1638+2T>A ; NM_003494.3(DYSF):c.2869C>T ; NM_003494.3(DYSF):c.5497G>T ; NM_003494.3(DYSF):c.5594delG ; NM_003494.3(DYSF):c.5429+1G>T ; NM_003494.3(DYSF):c.5979dupA ; NM_003494.3(DYSF):c.5713C>T ; NM_003494.3(DYSF):c.1834C>T ; NM_003494.3(DYSF):c.393_394delCC

EDA	Oligodontia	Oligodontia is a rare developmental dental anomaly in humans characterized by the absence of six or more teeth.	Clinical features of oligodontia include six or more missing teeth, lack of development of maxillary and mandibular alveolar bone height and reduced lower facial height. Variation in tooth morphology is also observed along with problems in tooth development, eruption and exfoliation.	NM_001399.4(EDA):c.187G>A ; NM_001399.4(EDA):c.183C>G ; NM_001399.4(EDA):c.467G>A ; NM_001399.5(EDA):c.573_574insT ; NM_001399.4(EDA):c.463C>T ; NM_001399.4(EDA):c.466C>T ; NM_001399.4(EDA):c.671G>C ; NM_001399.4(EDA):c.826C>T ; NM_001399.4(EDA):c.1045G>A ; NM_001399.4(EDA):c.181T>C ; NM_001399.4(EDA):c.187G>A ; NM_001399.4(EDA):c.183C>G ; NM_001399.4(EDA):c.467G>A ; NM_001399.5(EDA):c.573_574insT ; NM_001399.4(EDA):c.463C>T ; NM_001399.4(EDA):c.466C>T ; NM_001399.4(EDA):c.671G>C ; NM_001399.4(EDA):c.826C>T ; NM_001399.4(EDA):c.1045G>A ; NM_001399.4(EDA):c.181T>C
EDA	X-linked hypohidrotic ectodermal dysplasia	0	Hypohidrotic, or anhidrotic, ectodermal dysplasia (HED/EDA) is characterized by a triad of signs comprising sparse hair (hypotrichosis), abnormal or missing teeth (anodontia or hypodontia), and inability to sweat (anhidrosis or hypohidrosis). Typical clinical manifestations also include dryness of the skin, eyes, airways, and mucous membranes presumably due to the defective development of several exocrine glands. Hypohidrotic ectodermal dysplasia can be associated with dysmorphic features (forehead bumps, rings under the eyes, everted nose, and prominent lips) and occasionally with absent nipples. Ectodermal dysplasia-1, due to mutation in the EDA gene, is the most frequent form of hypohidrotic ectodermal dysplasia.	NM_001399.4(EDA):c.187G>A ; NM_001399.4(EDA):c.183C>G ; NM_001399.4(EDA):c.467G>A ; NM_001399.5(EDA):c.573_574insT ; NM_001399.4(EDA):c.463C>T ; NM_001399.4(EDA):c.466C>T ; NM_001399.4(EDA):c.671G>C ; NM_001399.4(EDA):c.826C>T ; NM_001399.4(EDA):c.1045G>A ; NM_001399.4(EDA):c.181T>C ; NM_001399.4(EDA):c.187G>A ; NM_001399.4(EDA):c.183C>G ; NM_001399.4(EDA):c.467G>A ; NM_001399.5(EDA):c.573_574insT ; NM_001399.4(EDA):c.463C>T ; NM_001399.4(EDA):c.466C>T ; NM_001399.4(EDA):c.671G>C ; NM_001399.4(EDA):c.826C>T ; NM_001399.4(EDA):c.1045G>A ; NM_001399.4(EDA):c.181T>C
EIF2AK3	Wolcott-Rallison syndrome	Wolcott-Rallison syndrome (WRS) is a very rare genetic disease, characterized by permanent neonatal diabetes mellitus (PNDM) with multiple epiphyseal dysplasia and other clinical manifestations, including recurrent episodes of acute liver failure.	Diabetes occurs early, generally before six months of age, is permanent and insulin-dependent from the onset. Skeletal dysplasia generally manifests within the 1st or 2nd year of life, and is associated with short stature (dwarfism with short trunk). Deficient mineralization or dysplastic changes, affecting the long bones, pelvis and vertebrae, but usually not the skull, may be seen on radiography as early as diabetes onset. Hepatic dysfunction is a 3rd characteristic feature and the most life-threatening complication, and manifests by elevated hepatic enzymes, liver enlargement and recurrent acute liver failure. Other manifestations vary between patients in type and severity and include renal dysfunction, exocrine pancreas insufficiency, intellectual deficit, hypothyroidism, neutropenia and recurrent infections. Clinical course is variable, including within the same sibship.	NM_004836.6(EIF2AK3):c.1763G>A ; NM_004836.6(EIF2AK3):c.994G>T ; NM_004836.6(EIF2AK3):c.1763G>A ; NM_004836.6(EIF2AK3):c.994G>T

EMD	X-linked Emery-Dreifuss muscular dystrophy	A neuromuscular disease that is characterized by muscular weakness and atrophy, with early joint contractures and cardiomyopathy.	The clinical triad is comprised of joint contractures of the Achilles, elbow and posterior neck tendons (beginning during early childhood and worsening to result in limited joint movement). It presents slowly progressive muscle weakness and atrophy (initially and generally with a humeroperoneal distribution but later becoming more diffuse). Cardiac anomalies (conduction defects, rhythm disturbances and dilated cardiomyopathy) that usually manifest at the turn of the 2nd to the 3rd decade of life and may lead to sudden death (sometimes the presenting feature of the disease) and ischemic accidents due to embolism. Disease course and severity vary between families and between patients from the same family.	NM_000117.2(EMD):c.547C>A ; c.631_635del ; NM_000117.2(EMD):c.547C>A ; c.631_635del
ERCC2	COFS syndrome	Cerebrooculofacioskeletal (COFS) syndrome is a rare genetic disorder, belonging to a family of diseases of DNA repair, characterized by a severe sensorineural involvement.	COFS syndrome constitutes the prenatal extreme form of Cockayne syndrome (see this term). Clinically, the following criteria are found: congenital microcephaly, congenital cataract and/or microphthalmia, arthrogryposis, severe psychomotor developmental delay, height-weight growth delay (principally postnatal) and facial dysmorphism (prominent metopic suture, micrognathism). The axial hypotonia contrasts with the peripheral hypertonia and is associated with feeding difficulties. Cutaneous photosensitivity, peripheral neuropathy, sensorineural hearing loss and pigmentary retinopathy can be observed.	c.950-2A>G ; NM_000400.3(ERCC2):c.1454T>C ; c.949+1G>A ; c.1308-1G>A ; NM_000400.3(ERCC2):c.2176C>T ; NM_000400.3(ERCC2):c.1381C>G ; c.567G>A ; c.1354C>T ; c.719-1G>A ; NM_000400.3(ERCC2):c.1621A>C ; c.2230_2233dup ; NM_000400.3(ERCC2):c.2047C>T ; NM_000400.3(ERCC2):c.1972C>T ; NM_000400.3(ERCC2):c.1703_1704delTT ; c.950-2A>G ; NM_000400.3(ERCC2):c.1454T>C ; c.949+1G>A ; c.1308-1G>A ; NM_000400.3(ERCC2):c.2176C>T ; NM_000400.3(ERCC2):c.1381C>G ; c.567G>A ; c.1354C>T ; c.719-1G>A ; NM_000400.3(ERCC2):c.1621A>C ; c.2230_2233dup ; NM_000400.3(ERCC2):c.2047C>T ; NM_000400.3(ERCC2):c.1972C>T ; NM_000400.3(ERCC2):c.1703_1704delTT

ERCC2	Trichothiodystrophy	Trichothiodystrophy or TTD is a heterogeneous group disorders characterized by short, brittle hair with low-sulphur content (due to an abnormal synthesis of the sulphur containing keratins).	Within the spectrum of the TTD syndromes are numerous syndromes affecting mainly organs derived from the neuroectoderm. The clinical appearance is always characterized by brittle and fragile hair, often combined with growth retardation and intellectual deficit, congenital ichthyosis and nail abnormalities, among other symptoms. The abnormalities are usually obvious at birth, with variable clinical expression. The variants of TTD, depending on their different associations, are: BIDS syndrome (or TTD type D or Amish Brittle Hair syndrome), IBIDS syndrome (or Tay syndrome or TTD typeE), PIBIDS syndrome (or TTD type F), Sabinas syndrome (TTD type B), SIBIDS syndrome, ONMRS (Itin syndrome) and Pollitt syndrome (TTD type C).	c.950-2A>G ; NM_000400.3(ERCC2):c.1454T>C ; c.949+1G>A ; c.1308-1G>A ; NM_000400.3(ERCC2):c.2176C>T ; NM_000400.3(ERCC2):c.1381C>G ; c.567G>A ; c.1354C>T ; c.719-1G>A ; NM_000400.3(ERCC2):c.1621A>C ; c.2230_2233dup ; NM_000400.3(ERCC2):c.2047C>T ; NM_000400.3(ERCC2):c.1972C>T ; NM_000400.3(ERCC2):c.1703_1704delTT ; c.950-2A>G ; NM_000400.3(ERCC2):c.1454T>C ; c.949+1G>A ; c.1308-1G>A ; NM_000400.3(ERCC2):c.2176C>T ; NM_000400.3(ERCC2):c.1381C>G ; c.567G>A ; c.1354C>T ; c.719-1G>A ; NM_000400.3(ERCC2):c.1621A>C ; c.2230_2233dup ; NM_000400.3(ERCC2):c.2047C>T ; NM_000400.3(ERCC2):c.1972C>T ; NM_000400.3(ERCC2):c.1703_1704delTT

ERCC2	Xeroderma pigmentosum	Xeroderma pigmentosum (XP) is a rare genodermatosis characterized by extreme sensitivity to ultraviolet (UV)-induced changes in the skin and eyes, and multiple skin cancers. It is subdivided into 8 complementation groups, according to the affected gene: classical XP (XPA to XPG) and XP variant (XPV) (see these terms).	The severity of the clinical manifestations and the age of onset are extremely variable and are in part dependent on exposure to sunlight and the complementation group. Approximately 50% of affected individuals have acute sun sensitivity from the first few months of life, presenting with severe sunburn and/or persistent erythema which takes weeks to resolve. Others do not show any sunburn reaction and gradually develop marked freckling at sun exposed sites. Individuals have dry skin and hypo- or hyperpigmented lesions. There is a greater than 10,000-fold increased risk of non-melanoma skin cancers, and a 2,000 fold increased risk of melanoma under the age of 20 when compared to the general population. Patients with classical XP develop skin cancer generally before the age of 20, while patients with XP variant start to develop skin cancer at about 20-30 years of age. Ocular abnormalities include keratitis resulting in corneal opacification and vascularization. Photophobia is common. Ocular squamous cell carcinoma and melanoma are common. Neurologic abnormalities of varying severity have been reported in about 30% of cases. These include acquired microcephaly, diminished or absent deep tendon stretch reflexes, progressive sensorineural hearing loss, spasticity, ataxia, seizures and progressive cognitive impairment. De Sanctis-Cacchione syndrome is a term that was originally attributed to XP cases with severe neurological abnormalities but it is no longer in general use.	c.950-2A>G ; NM_000400.3(ERCC2):c.1454T>C ; c.949+1G>A ; c.1308-1G>A ; NM_000400.3(ERCC2):c.2176C>T ; NM_000400.3(ERCC2):c.1381C>G ; c.567G>A ; c.1354C>T ; c.719-1G>A ; NM_000400.3(ERCC2):c.1621A>C ; c.2230_2233dup ; NM_000400.3(ERCC2):c.2047C>T ; NM_000400.3(ERCC2):c.1972C>T ; NM_000400.3(ERCC2):c.1703_1704delTT ; c.950-2A>G ; NM_000400.3(ERCC2):c.1454T>C ; c.949+1G>A ; c.1308-1G>A ; NM_000400.3(ERCC2):c.2176C>T ; NM_000400.3(ERCC2):c.1381C>G ; c.567G>A ; c.1354C>T ; c.719-1G>A ; NM_000400.3(ERCC2):c.1621A>C ; c.2230_2233dup ; NM_000400.3(ERCC2):c.2047C>T ; NM_000400.3(ERCC2):c.1972C>T ; NM_000400.3(ERCC2):c.1703_1704delTT

ERCC2	Xeroderma pigmentosum-Cockayne syndrome complex	Xeroderma pigmentosum/Cockayne syndrome complex (XP/CS complex) is characterized by the cutaneous features of xeroderma pigmentosum (XP) (see this term) together with the systemic and neurological features of Cockayne syndrome (CS; see this term).	The disease manifests during infancy. Patients present with cutaneous UV-sensitive lesions that generally develop into skin cancer, and also develop characteristic CS manifestations such as microcephaly, hydrocephalus, cachexia, premature aging, dwarfism, skin atrophy, arteriosclerosis, progressive hearing loss, cognitive deficit, spasticity, ataxia, pigmentary retinopathy and optic atrophy. In contrast to the neurological abnormalities of XP which are predominantly secondary to neuronal degeneration, in XP/CS complex, dysmyelination typical of CS is observed.	c.950-2A>G ; NM_000400.3(ERCC2):c.1454T>C ; c.949+1G>A ; c.1308-1G>A ; NM_000400.3(ERCC2):c.2176C>T ; NM_000400.3(ERCC2):c.1381C>G ; c.567G>A ; c.1354C>T ; c.719-1G>A ; NM_000400.3(ERCC2):c.1621A>C ; c.2230_2233dup ; NM_000400.3(ERCC2):c.2047C>T ; NM_000400.3(ERCC2):c.1972C>T ; NM_000400.3(ERCC2):c.1703_1704delTT ; c.950-2A>G ; NM_000400.3(ERCC2):c.1454T>C ; c.949+1G>A ; c.1308-1G>A ; NM_000400.3(ERCC2):c.2176C>T ; NM_000400.3(ERCC2):c.1381C>G ; c.567G>A ; c.1354C>T ; c.719-1G>A ; NM_000400.3(ERCC2):c.1621A>C ; c.2230_2233dup ; NM_000400.3(ERCC2):c.2047C>T ; NM_000400.3(ERCC2):c.1972C>T ; NM_000400.3(ERCC2):c.1703_1704delTT
ERCC3	Trichothiodystrophy	Trichothiodystrophy or TTD is a heterogeneous group disorders characterized by short, brittle hair with low-sulphur content (due to an abnormal synthesis of the sulphur containing keratins).	Within the spectrum of the TTD syndromes are numerous syndromes affecting mainly organs derived from the neuroectoderm. The clinical appearance is always characterized by brittle and fragile hair, often combined with growth retardation and intellectual deficit, congenital ichthyosis and nail abnormalities, among other symptoms. The abnormalities are usually obvious at birth, with variable clinical expression. The variants of TTD, depending on their different associations, are: BIDS syndrome (or TTD type D or Amish Brittle Hair syndrome), IBIDS syndrome (or Tay syndrome or TTD typeE), PIBIDS syndrome (or TTD type F), Sabinas syndrome (TTD type B), SIBIDS syndrome, ONMRS (Itin syndrome) and Pollitt syndrome (TTD type C).	NM_000122.1(ERCC3):c.1273C>T ; NM_000122.1(ERCC3):c.1633C>T ; NM_000122.1(ERCC3):c.296T>C ; c.1858del ; c.1757del ; NM_000122.1(ERCC3):c.1273C>T ; NM_000122.1(ERCC3):c.1633C>T ; NM_000122.1(ERCC3):c.296T>C ; c.1858del ; c.1757del

ERCC3	Xeroderma pigmentosum	Xeroderma pigmentosum (XP) is a rare genodermatosis characterized by extreme sensitivity to ultraviolet (UV)-induced changes in the skin and eyes, and multiple skin cancers. It is subdivided into 8 complementation groups, according to the affected gene: classical XP (XPA to XPG) and XP variant (XPV) (see these terms).	The severity of the clinical manifestations and the age of onset are extremely variable and are in part dependent on exposure to sunlight and the complementation group. Approximately 50% of affected individuals have acute sun sensitivity from the first few months of life, presenting with severe sunburn and/or persistent erythema which takes weeks to resolve. Others do not show any sunburn reaction and gradually develop marked freckling at sun exposed sites. Individuals have dry skin and hypo- or hyperpigmented lesions. There is a greater than 10,000-fold increased risk of non-melanoma skin cancers, and a 2,000 fold increased risk of melanoma under the age of 20 when compared to the general population. Patients with classical XP develop skin cancer generally before the age of 20, while patients with XP variant start to develop skin cancer at about 20-30 years of age. Ocular abnormalities include keratitis resulting in corneal opacification and vascularization. Photophobia is common. Ocular squamous cell carcinoma and melanoma are common. Neurologic abnormalities of varying severity have been reported in about 30% of cases. These include acquired microcephaly, diminished or absent deep tendon stretch reflexes, progressive sensorineural hearing loss, spasticity, ataxia, seizures and progressive cognitive impairment. De Sanctis-Cacchione syndrome is a term that was originally attributed to XP cases with severe neurological abnormalities but it is no longer in general use.	NM_000122.1(ERCC3):c.1273C>T ; NM_000122.1(ERCC3):c.1633C>T ; NM_000122.1(ERCC3):c.296T>C ; c.1858del ; c.1757del ; NM_000122.1(ERCC3):c.1273C>T ; NM_000122.1(ERCC3):c.1633C>T ; NM_000122.1(ERCC3):c.296T>C ; c.1858del ; c.1757del

ERCC3	Xeroderma pigmentosum-Cockayne syndrome complex	Xeroderma pigmentosum/Cockayne syndrome complex (XP/CS complex) is characterized by the cutaneous features of xeroderma pigmentosum (XP) (see this term) together with the systemic and neurological features of Cockayne syndrome (CS; see this term).	The disease manifests during infancy. Patients present with cutaneous UV-sensitive lesions that generally develop into skin cancer, and also develop characteristic CS manifestations such as microcephaly, hydrocephalus, cachexia, premature aging, dwarfism, skin atrophy, arteriosclerosis, progressive hearing loss, cognitive deficit, spasticity, ataxia, pigmentary retinopathy and optic atrophy. In contrast to the neurological abnormalities of XP which are predominantly secondary to neuronal degeneration, in XP/CS complex, dysmyelination typical of CS is observed.	NM_000122.1(ERCC3):c.1273C>T ; NM_000122.1(ERCC3):c.1633C>T ; NM_000122.1(ERCC3):c.296T>C ; c.1858del ; c.1757del ; NM_000122.1(ERCC3):c.1273C>T ; NM_000122.1(ERCC3):c.1633C>T ; NM_000122.1(ERCC3):c.296T>C ; c.1858del ; c.1757del
ERCC4	Cockayne syndrome type 1	Cockayne syndrome (CS) is a multisystem condition characterized by short stature, a characteristic facial appearance, premature aging, photosensitivity, progressive neurological dysfunction, and intellectual deficit.	Disease severity and the age of onset are variable. In classical type I CS, the first symptoms usually appear during the first year of life. Early-onset cases with more severe symptoms (type II) and late-onset cases with milder symptoms (type III) have also been described. Common signs of the disease include progressive growth failure, intellectual deficit, cerebellar ataxia, spasticity, peripheral demyelinating neuropathy, pigmentary retinopathy, sensorineural hearing loss and dental anomalies (presence of caries). The typical facial appearance includes microcephaly, large ears, a thin nose, and enophthalmia. Cataracts and cutaneous photosensitivity are observed in some patients. Subcutaneous lipoatrophy is present and can lead to signs of premature aging of the skin. COFS syndrome (see this term) is the extreme prenatal form of the CS clinical spectrum characterized by congenital microphthalmia and arthrogryposis.	c.1467dup ; c.2T>C ; c.2281_2284del ; c.540_541del ; NM_005236.2(ERCC4):c.706T>C ; c.49G>T ; c.1467dup ; c.2T>C ; c.2281_2284del ; c.540_541del ; NM_005236.2(ERCC4):c.706T>C ; c.49G>T

ERCC4	Fanconi anemia	A rare genetic multisystem disorder characterized by progressive pancytopenia with bone marrow failure, variable congenital malformations and predisposition to develop hematological or solid tumors.	The first signs of Fanconi anemia (FA) are typically non-hematological features. Limb anomalies typically affect the extremities, are unilateral or (usually asymmetric) bilateral. Minor anomalies can also be present such as low birth length and weight, microcephaly and/or microphthalmia. Skin pigmentation abnormalities (cafÃ©-au-lait spots) and hypoplastic thenar eminence are frequent. Almost 20% of patients have ear malformations with or without hearing loss. Congenital malformations may involve other organ systems and vary within families. Short stature is syndromic and/or associated to endocrinopathies. Fertility is frequently impaired in males, and is highly disturbed in half of females. When congenital malformations are not prominent, diagnosis may be delayed until the onset of hematological anomalies. Bone marrow failure (BMF) occurs at a median age of 7 years, developing in 90% of patients by 40 years of age. The first manifestations are macrocytosis (very early) and thrombocytopenia. In patients with somatic mosaÃ¯cism, blood counts may stay normal until occurrence of hematological malignancy. In general, patients are highly predisposed to solid tumors (most frequently head and neck or anogenital regions).	c.1467dup ; c.2T>C ; c.2281_2284del ; c.540_541del ; NM_005236.2(ERCC4):c.706T>C ; c.49G>T ; c.1467dup ; c.2T>C ; c.2281_2284del ; c.540_541del ; NM_005236.2(ERCC4):c.706T>C ; c.49G>T

ERCC4	Xeroderma pigmentosum	Xeroderma pigmentosum (XP) is a rare genodermatosis characterized by extreme sensitivity to ultraviolet (UV)-induced changes in the skin and eyes, and multiple skin cancers. It is subdivided into 8 complementation groups, according to the affected gene: classical XP (XPA to XPG) and XP variant (XPV) (see these terms).	The severity of the clinical manifestations and the age of onset are extremely variable and are in part dependent on exposure to sunlight and the complementation group. Approximately 50% of affected individuals have acute sun sensitivity from the first few months of life, presenting with severe sunburn and/or persistent erythema which takes weeks to resolve. Others do not show any sunburn reaction and gradually develop marked freckling at sun exposed sites. Individuals have dry skin and hypo- or hyperpigmented lesions. There is a greater than 10,000-fold increased risk of non-melanoma skin cancers, and a 2,000 fold increased risk of melanoma under the age of 20 when compared to the general population. Patients with classical XP develop skin cancer generally before the age of 20, while patients with XP variant start to develop skin cancer at about 20-30 years of age. Ocular abnormalities include keratitis resulting in corneal opacification and vascularization. Photophobia is common. Ocular squamous cell carcinoma and melanoma are common. Neurologic abnormalities of varying severity have been reported in about 30% of cases. These include acquired microcephaly, diminished or absent deep tendon stretch reflexes, progressive sensorineural hearing loss, spasticity, ataxia, seizures and progressive cognitive impairment. De Sanctis-Cacchione syndrome is a term that was originally attributed to XP cases with severe neurological abnormalities but it is no longer in general use.	c.1467dup ; c.2T>C ; c.2281_2284del ; c.540_541del ; NM_005236.2(ERCC4):c.706T>C ; c.49G>T ; c.1467dup ; c.2T>C ; c.2281_2284del ; c.540_541del ; NM_005236.2(ERCC4):c.706T>C ; c.49G>T

ERCC4	Xeroderma pigmentosum-Cockayne syndrome complex	Xeroderma pigmentosum/Cockayne syndrome complex (XP/CS complex) is characterized by the cutaneous features of xeroderma pigmentosum (XP) (see this term) together with the systemic and neurological features of Cockayne syndrome (CS; see this term).	The disease manifests during infancy. Patients present with cutaneous UV-sensitive lesions that generally develop into skin cancer, and also develop characteristic CS manifestations such as microcephaly, hydrocephalus, cachexia, premature aging, dwarfism, skin atrophy, arteriosclerosis, progressive hearing loss, cognitive deficit, spasticity, ataxia, pigmentary retinopathy and optic atrophy. In contrast to the neurological abnormalities of XP which are predominantly secondary to neuronal degeneration, in XP/CS complex, dysmyelination typical of CS is observed.	c.1467dup ; c.2T>C ; c.2281_2284del ; c.540_541del ; NM_005236.2(ERCC4):c.706T>C ; c.49G>T ; c.1467dup ; c.2T>C ; c.2281_2284del ; c.540_541del ; NM_005236.2(ERCC4):c.706T>C ; c.49G>T
ERCC5	COFS syndrome	Cerebrooculofacioskeletal (COFS) syndrome is a rare genetic disorder, belonging to a family of diseases of DNA repair, characterized by a severe sensorineural involvement.	COFS syndrome constitutes the prenatal extreme form of Cockayne syndrome (see this term). Clinically, the following criteria are found: congenital microcephaly, congenital cataract and/or microphthalmia, arthrogryposis, severe psychomotor developmental delay, height-weight growth delay (principally postnatal) and facial dysmorphism (prominent metopic suture, micrognathism). The axial hypotonia contrasts with the peripheral hypertonia and is associated with feeding difficulties. Cutaneous photosensitivity, peripheral neuropathy, sensorineural hearing loss and pigmentary retinopathy can be observed.	NM_000123.3(ERCC5):c.526C>T ; c.464dup ; c.381-2A>G ; NM_000123.3(ERCC5):c.787C>T ; NM_000123.3(ERCC5):c.215C>A ; NM_000123.3(ERCC5):c.2573T>C ; NM_000123.3(ERCC5):c.406C>T ; c.88+2T>C ; c.2144dup ; NM_000123.3(ERCC5):c.2751del ; NM_000123.3(ERCC5):c.526C>T ; c.464dup ; c.381-2A>G ; NM_000123.3(ERCC5):c.787C>T ; NM_000123.3(ERCC5):c.215C>A ; NM_000123.3(ERCC5):c.2573T>C ; NM_000123.3(ERCC5):c.406C>T ; c.88+2T>C ; c.2144dup ; NM_000123.3(ERCC5):c.2751del

ERCC5	Xeroderma pigmentosum	Xeroderma pigmentosum (XP) is a rare genodermatosis characterized by extreme sensitivity to ultraviolet (UV)-induced changes in the skin and eyes, and multiple skin cancers. It is subdivided into 8 complementation groups, according to the affected gene: classical XP (XPA to XPG) and XP variant (XPV) (see these terms).	The severity of the clinical manifestations and the age of onset are extremely variable and are in part dependent on exposure to sunlight and the complementation group. Approximately 50% of affected individuals have acute sun sensitivity from the first few months of life, presenting with severe sunburn and/or persistent erythema which takes weeks to resolve. Others do not show any sunburn reaction and gradually develop marked freckling at sun exposed sites. Individuals have dry skin and hypo- or hyperpigmented lesions. There is a greater than 10,000-fold increased risk of non-melanoma skin cancers, and a 2,000 fold increased risk of melanoma under the age of 20 when compared to the general population. Patients with classical XP develop skin cancer generally before the age of 20, while patients with XP variant start to develop skin cancer at about 20-30 years of age. Ocular abnormalities include keratitis resulting in corneal opacification and vascularization. Photophobia is common. Ocular squamous cell carcinoma and melanoma are common. Neurologic abnormalities of varying severity have been reported in about 30% of cases. These include acquired microcephaly, diminished or absent deep tendon stretch reflexes, progressive sensorineural hearing loss, spasticity, ataxia, seizures and progressive cognitive impairment. De Sanctis-Cacchione syndrome is a term that was originally attributed to XP cases with severe neurological abnormalities but it is no longer in general use.	NM_000123.3(ERCC5):c.526C>T ; c.464dup ; c.381-2A>G ; NM_000123.3(ERCC5):c.787C>T ; NM_000123.3(ERCC5):c.215C>A ; NM_000123.3(ERCC5):c.2573T>C ; NM_000123.3(ERCC5):c.406C>T ; c.88+2T>C ; c.2144dup ; NM_000123.3(ERCC5):c.2751del ; NM_000123.3(ERCC5):c.526C>T ; c.464dup ; c.381-2A>G ; NM_000123.3(ERCC5):c.787C>T ; NM_000123.3(ERCC5):c.215C>A ; NM_000123.3(ERCC5):c.2573T>C ; NM_000123.3(ERCC5):c.406C>T ; c.88+2T>C ; c.2144dup ; NM_000123.3(ERCC5):c.2751del

ERCC5	Xeroderma pigmentosum-Cockayne syndrome complex	Xeroderma pigmentosum/Cockayne syndrome complex (XP/CS complex) is characterized by the cutaneous features of xeroderma pigmentosum (XP) (see this term) together with the systemic and neurological features of Cockayne syndrome (CS; see this term).	The disease manifests during infancy. Patients present with cutaneous UV-sensitive lesions that generally develop into skin cancer, and also develop characteristic CS manifestations such as microcephaly, hydrocephalus, cachexia, premature aging, dwarfism, skin atrophy, arteriosclerosis, progressive hearing loss, cognitive deficit, spasticity, ataxia, pigmentary retinopathy and optic atrophy. In contrast to the neurological abnormalities of XP which are predominantly secondary to neuronal degeneration, in XP/CS complex, dysmyelination typical of CS is observed.	NM_000123.3(ERCC5):c.526C>T ; c.464dup ; c.381-2A>G ; NM_000123.3(ERCC5):c.787C>T ; NM_000123.3(ERCC5):c.215C>A ; NM_000123.3(ERCC5):c.2573T>C ; NM_000123.3(ERCC5):c.406C>T ; c.88+2T>C ; c.2144dup ; NM_000123.3(ERCC5):c.2751del ; NM_000123.3(ERCC5):c.526C>T ; c.464dup ; c.381-2A>G ; NM_000123.3(ERCC5):c.787C>T ; NM_000123.3(ERCC5):c.215C>A ; NM_000123.3(ERCC5):c.2573T>C ; NM_000123.3(ERCC5):c.406C>T ; c.88+2T>C ; c.2144dup ; NM_000123.3(ERCC5):c.2751del
ERCC6	Cockayne syndrome type 1	Cockayne syndrome (CS) is a multisystem condition characterized by short stature, a characteristic facial appearance, premature aging, photosensitivity, progressive neurological dysfunction, and intellectual deficit.	Disease severity and the age of onset are variable. In classical type I CS, the first symptoms usually appear during the first year of life. Early-onset cases with more severe symptoms (type II) and late-onset cases with milder symptoms (type III) have also been described. Common signs of the disease include progressive growth failure, intellectual deficit, cerebellar ataxia, spasticity, peripheral demyelinating neuropathy, pigmentary retinopathy, sensorineural hearing loss and dental anomalies (presence of caries). The typical facial appearance includes microcephaly, large ears, a thin nose, and enophthalmia. Cataracts and cutaneous photosensitivity are observed in some patients. Subcutaneous lipoatrophy is present and can lead to signs of premature aging of the skin. COFS syndrome (see this term) is the extreme prenatal form of the CS clinical spectrum characterized by congenital microphthalmia and arthrogryposis.	NM_000124.3(ERCC6):c.207dup ; NM_000124.3(ERCC6):c.1550G>A ; NM_000124.3(ERCC6):c.3862C>T ; c.2587C>T ; NM_000124.3(ERCC6):c.422+1G>A ; NM_000124.3(ERCC6):c.1357C>T ; NM_000124.3(ERCC6):c.2203C>T ; NM_000124.3(ERCC6):c.3591_3592dup ; NM_000124.3(ERCC6):c.2047C>T ; c.48_49del ; NM_000124.3(ERCC6):c.207dup ; NM_000124.3(ERCC6):c.1550G>A ; NM_000124.3(ERCC6):c.3862C>T ; c.2587C>T ; NM_000124.3(ERCC6):c.422+1G>A ; NM_000124.3(ERCC6):c.1357C>T ; NM_000124.3(ERCC6):c.2203C>T ; NM_000124.3(ERCC6):c.3591_3592dup ; NM_000124.3(ERCC6):c.2047C>T ; c.48_49del

ERCC6	Cockayne syndrome type 2	Cockayne syndrome (CS) is a multisystem condition characterized by short stature, a characteristic facial appearance, premature aging, photosensitivity, progressive neurological dysfunction, and intellectual deficit.	Disease severity and the age of onset are variable. In classical type I CS, the first symptoms usually appear during the first year of life. Early-onset cases with more severe symptoms (type II) and late-onset cases with milder symptoms (type III) have also been described. Common signs of the disease include progressive growth failure, intellectual deficit, cerebellar ataxia, spasticity, peripheral demyelinating neuropathy, pigmentary retinopathy, sensorineural hearing loss and dental anomalies (presence of caries). The typical facial appearance includes microcephaly, large ears, a thin nose, and enophthalmia. Cataracts and cutaneous photosensitivity are observed in some patients. Subcutaneous lipoatrophy is present and can lead to signs of premature aging of the skin. COFS syndrome (see this term) is the extreme prenatal form of the CS clinical spectrum characterized by congenital microphthalmia and arthrogryposis.	NM_000124.3(ERCC6):c.207dup ; NM_000124.3(ERCC6):c.1550G>A ; NM_000124.3(ERCC6):c.3862C>T ; c.2587C>T ; NM_000124.3(ERCC6):c.422+1G>A ; NM_000124.3(ERCC6):c.1357C>T ; NM_000124.3(ERCC6):c.2203C>T ; NM_000124.3(ERCC6):c.3591_3592dup ; NM_000124.3(ERCC6):c.2047C>T ; c.48_49del ; NM_000124.3(ERCC6):c.207dup ; NM_000124.3(ERCC6):c.1550G>A ; NM_000124.3(ERCC6):c.3862C>T ; c.2587C>T ; NM_000124.3(ERCC6):c.422+1G>A ; NM_000124.3(ERCC6):c.1357C>T ; NM_000124.3(ERCC6):c.2203C>T ; NM_000124.3(ERCC6):c.3591_3592dup ; NM_000124.3(ERCC6):c.2047C>T ; c.48_49del
ERCC6	Cockayne syndrome type 3	Cockayne syndrome (CS) is a multisystem condition characterized by short stature, a characteristic facial appearance, premature aging, photosensitivity, progressive neurological dysfunction, and intellectual deficit.	Disease severity and the age of onset are variable. In classical type I CS, the first symptoms usually appear during the first year of life. Early-onset cases with more severe symptoms (type II) and late-onset cases with milder symptoms (type III) have also been described. Common signs of the disease include progressive growth failure, intellectual deficit, cerebellar ataxia, spasticity, peripheral demyelinating neuropathy, pigmentary retinopathy, sensorineural hearing loss and dental anomalies (presence of caries). The typical facial appearance includes microcephaly, large ears, a thin nose, and enophthalmia. Cataracts and cutaneous photosensitivity are observed in some patients. Subcutaneous lipoatrophy is present and can lead to signs of premature aging of the skin. COFS syndrome (see this term) is the extreme prenatal form of the CS clinical spectrum characterized by congenital microphthalmia and arthrogryposis.	NM_000124.3(ERCC6):c.207dup ; NM_000124.3(ERCC6):c.1550G>A ; NM_000124.3(ERCC6):c.3862C>T ; c.2587C>T ; NM_000124.3(ERCC6):c.422+1G>A ; NM_000124.3(ERCC6):c.1357C>T ; NM_000124.3(ERCC6):c.2203C>T ; NM_000124.3(ERCC6):c.3591_3592dup ; NM_000124.3(ERCC6):c.2047C>T ; c.48_49del ; NM_000124.3(ERCC6):c.207dup ; NM_000124.3(ERCC6):c.1550G>A ; NM_000124.3(ERCC6):c.3862C>T ; c.2587C>T ; NM_000124.3(ERCC6):c.422+1G>A ; NM_000124.3(ERCC6):c.1357C>T ; NM_000124.3(ERCC6):c.2203C>T ; NM_000124.3(ERCC6):c.3591_3592dup ; NM_000124.3(ERCC6):c.2047C>T ; c.48_49del

ERCC6	COFS syndrome	Cerebrooculofacioskeletal (COFS) syndrome is a rare genetic disorder, belonging to a family of diseases of DNA repair, characterized by a severe sensorineural involvement.	COFS syndrome constitutes the prenatal extreme form of Cockayne syndrome (see this term). Clinically, the following criteria are found: congenital microcephaly, congenital cataract and/or microphthalmia, arthrogryposis, severe psychomotor developmental delay, height-weight growth delay (principally postnatal) and facial dysmorphism (prominent metopic suture, micrognathism). The axial hypotonia contrasts with the peripheral hypertonia and is associated with feeding difficulties. Cutaneous photosensitivity, peripheral neuropathy, sensorineural hearing loss and pigmentary retinopathy can be observed.	NM_000124.3(ERCC6):c.207dup ; NM_000124.3(ERCC6):c.1550G>A ; NM_000124.3(ERCC6):c.3862C>T ; c.2587C>T ; NM_000124.3(ERCC6):c.422+1G>A ; NM_000124.3(ERCC6):c.1357C>T ; NM_000124.3(ERCC6):c.2203C>T ; NM_000124.3(ERCC6):c.3591_3592dup ; NM_000124.3(ERCC6):c.2047C>T ; c.48_49del ; NM_000124.3(ERCC6):c.207dup ; NM_000124.3(ERCC6):c.1550G>A ; NM_000124.3(ERCC6):c.3862C>T ; c.2587C>T ; NM_000124.3(ERCC6):c.422+1G>A ; NM_000124.3(ERCC6):c.1357C>T ; NM_000124.3(ERCC6):c.2203C>T ; NM_000124.3(ERCC6):c.3591_3592dup ; NM_000124.3(ERCC6):c.2047C>T ; c.48_49del
ERCC6	NON RARE IN EUROPE: Primary ovarian failure	Premature ovarian failure is a heterogeneous disorder. The terms 'hypergonadotropic ovarian failure' and 'hypergonadotropic ovarian dysgenesis' have been used to indicate a group of disorders in which amenorrhea associated with elevated levels of serum gonadotropins occurs long before the age of 40 years.	Premature ovarian failure-11 (POF11) is characterized by secondary amenorrhea and hypergonadotropic ovarian insufficiency, with elevated serum follicle-stimulating hormone (FSH) levels before age 40 years.	NM_000124.3(ERCC6):c.207dup ; NM_000124.3(ERCC6):c.1550G>A ; NM_000124.3(ERCC6):c.3862C>T ; c.2587C>T ; NM_000124.3(ERCC6):c.422+1G>A ; NM_000124.3(ERCC6):c.1357C>T ; NM_000124.3(ERCC6):c.2203C>T ; NM_000124.3(ERCC6):c.3591_3592dup ; NM_000124.3(ERCC6):c.2047C>T ; c.48_49del ; NM_000124.3(ERCC6):c.207dup ; NM_000124.3(ERCC6):c.1550G>A ; NM_000124.3(ERCC6):c.3862C>T ; c.2587C>T ; NM_000124.3(ERCC6):c.422+1G>A ; NM_000124.3(ERCC6):c.1357C>T ; NM_000124.3(ERCC6):c.2203C>T ; NM_000124.3(ERCC6):c.3591_3592dup ; NM_000124.3(ERCC6):c.2047C>T ; c.48_49del
ERCC6	UV-sensitive syndrome	A rare photodermatosis characterized by cutaneous photosensitivity and slight dyspigmentation, without an increased risk of developing skin tumors. Telangiectasia may also be observed, but no other clinical abnormalities. Patients present in infancy or childhood, mode of inheritance is autosomal recessive.	UV-sensitive syndrome-1 is an autosomal recessive disorder characterized by cutaneous photosensitivity and mild freckling, without an increased risk of skin tumors. Patient cells show impaired recovery of RNA synthesis (RRS) after UV irradiation due to defective preferential repair of DNA damage in actively transcribing genes, although unscheduled DNA repair is normal. The cellular findings are consistent with a defect in transcription-coupled nucleotide excision repair (TC-NER) of UV damage.	NM_000124.3(ERCC6):c.207dup ; NM_000124.3(ERCC6):c.1550G>A ; NM_000124.3(ERCC6):c.3862C>T ; c.2587C>T ; NM_000124.3(ERCC6):c.422+1G>A ; NM_000124.3(ERCC6):c.1357C>T ; NM_000124.3(ERCC6):c.2203C>T ; NM_000124.3(ERCC6):c.3591_3592dup ; NM_000124.3(ERCC6):c.2047C>T ; c.48_49del ; NM_000124.3(ERCC6):c.207dup ; NM_000124.3(ERCC6):c.1550G>A ; NM_000124.3(ERCC6):c.3862C>T ; c.2587C>T ; NM_000124.3(ERCC6):c.422+1G>A ; NM_000124.3(ERCC6):c.1357C>T ; NM_000124.3(ERCC6):c.2203C>T ; NM_000124.3(ERCC6):c.3591_3592dup ; NM_000124.3(ERCC6):c.2047C>T ; c.48_49del

ERCC8	Cockayne syndrome type 1	Cockayne syndrome (CS) is a multisystem condition characterized by short stature, a characteristic facial appearance, premature aging, photosensitivity, progressive neurological dysfunction, and intellectual deficit.	Disease severity and the age of onset are variable. In classical type I CS, the first symptoms usually appear during the first year of life. Early-onset cases with more severe symptoms (type II) and late-onset cases with milder symptoms (type III) have also been described. Common signs of the disease include progressive growth failure, intellectual deficit, cerebellar ataxia, spasticity, peripheral demyelinating neuropathy, pigmentary retinopathy, sensorineural hearing loss and dental anomalies (presence of caries). The typical facial appearance includes microcephaly, large ears, a thin nose, and enophthalmia. Cataracts and cutaneous photosensitivity are observed in some patients. Subcutaneous lipoatrophy is present and can lead to signs of premature aging of the skin. COFS syndrome (see this term) is the extreme prenatal form of the CS clinical spectrum characterized by congenital microphthalmia and arthrogryposis.	NM_000082.3(ERCC8):c.37G>T ; NM_000082.3:c.966C>A ; c.593_594dup ; NM_000082.3(ERCC8):c.618-1G>A ; NM_000082.3(ERCC8):c.37G>T ; NM_000082.3:c.966C>A ; c.593_594dup ; NM_000082.3(ERCC8):c.618-1G>A
ERCC8	Cockayne syndrome type 2	Cockayne syndrome (CS) is a multisystem condition characterized by short stature, a characteristic facial appearance, premature aging, photosensitivity, progressive neurological dysfunction, and intellectual deficit.	Disease severity and the age of onset are variable. In classical type I CS, the first symptoms usually appear during the first year of life. Early-onset cases with more severe symptoms (type II) and late-onset cases with milder symptoms (type III) have also been described. Common signs of the disease include progressive growth failure, intellectual deficit, cerebellar ataxia, spasticity, peripheral demyelinating neuropathy, pigmentary retinopathy, sensorineural hearing loss and dental anomalies (presence of caries). The typical facial appearance includes microcephaly, large ears, a thin nose, and enophthalmia. Cataracts and cutaneous photosensitivity are observed in some patients. Subcutaneous lipoatrophy is present and can lead to signs of premature aging of the skin. COFS syndrome (see this term) is the extreme prenatal form of the CS clinical spectrum characterized by congenital microphthalmia and arthrogryposis.	NM_000082.3(ERCC8):c.37G>T ; NM_000082.3:c.966C>A ; c.593_594dup ; NM_000082.3(ERCC8):c.618-1G>A ; NM_000082.3(ERCC8):c.37G>T ; NM_000082.3:c.966C>A ; c.593_594dup ; NM_000082.3(ERCC8):c.618-1G>A

ERCC8	Cockayne syndrome type 3	Cockayne syndrome (CS) is a multisystem condition characterized by short stature, a characteristic facial appearance, premature aging, photosensitivity, progressive neurological dysfunction, and intellectual deficit.	Disease severity and the age of onset are variable. In classical type I CS, the first symptoms usually appear during the first year of life. Early-onset cases with more severe symptoms (type II) and late-onset cases with milder symptoms (type III) have also been described. Common signs of the disease include progressive growth failure, intellectual deficit, cerebellar ataxia, spasticity, peripheral demyelinating neuropathy, pigmentary retinopathy, sensorineural hearing loss and dental anomalies (presence of caries). The typical facial appearance includes microcephaly, large ears, a thin nose, and enophthalmia. Cataracts and cutaneous photosensitivity are observed in some patients. Subcutaneous lipoatrophy is present and can lead to signs of premature aging of the skin. COFS syndrome (see this term) is the extreme prenatal form of the CS clinical spectrum characterized by congenital microphthalmia and arthrogryposis.	NM_000082.3(ERCC8):c.37G>T ; NM_000082.3:c.966C>A ; c.593_594dup ; NM_000082.3(ERCC8):c.618-1G>A ; NM_000082.3(ERCC8):c.37G>T ; NM_000082.3:c.966C>A ; c.593_594dup ; NM_000082.3(ERCC8):c.618-1G>A
ERCC8	UV-sensitive syndrome	A rare photodermatosis characterized by cutaneous photosensitivity and slight dyspigmentation, without an increased risk of developing skin tumors. Telangiectasia may also be observed, but no other clinical abnormalities. Patients present in infancy or childhood, mode of inheritance is autosomal recessive.	UV-sensitive syndrome-1 is an autosomal recessive disorder characterized by cutaneous photosensitivity and mild freckling, without an increased risk of skin tumors. Patient cells show impaired recovery of RNA synthesis (RRS) after UV irradiation due to defective preferential repair of DNA damage in actively transcribing genes, although unscheduled DNA repair is normal. The cellular findings are consistent with a defect in transcription-coupled nucleotide excision repair (TC-NER) of UV damage.	NM_000082.3(ERCC8):c.37G>T ; NM_000082.3:c.966C>A ; c.593_594dup ; NM_000082.3(ERCC8):c.618-1G>A ; NM_000082.3(ERCC8):c.37G>T ; NM_000082.3:c.966C>A ; c.593_594dup ; NM_000082.3(ERCC8):c.618-1G>A

ESCO2	Roberts syndrome	Roberts syndrome (RBS) is characterized by pre- and postnatal growth retardation, severe symmetric limb reduction defects, craniofacial anomalies and severe intellectual deficit. SC phocomelia is a milder form of RBS.	Upper limbs are more frequently and severely affected than lower limbs. The defect is mostly mesomelic with the radius being the most affected in the upper limbs, and the fibula in the lower limbs. The most severe defects result in phocomelia. Aplastic or hypoplastic thumbs, oligodactyly, clinodactyly or syndactyly can also occur. Craniofacial anomalies include microcephaly (more severe in males than in females), hypoplastic nasal alae, malar hypoplasia, hypertelorism, micrognathia, capillary hemangioma, exophthalmos, downslanting palpebral fissures, dysplastic or small ears, cloudy cornea or cataracts, and cleft lip and palate. There is a correlation between the degree of limb and facial malformations. Other malformations such as congenital heart defects, cystic kidney and large genitalia (enlarged phallus or clitoris), may occur. Severe intellectual deficit is observed in patients surviving the newborn period.	NM_001017420.2(ESCO2):c.308_309delAA ; NM_001017420.2(ESCO2):c.505C>T ; NM_001017420.2(ESCO2):c.604C>T ; c.296_297dup ; NM_001017420.2(ESCO2):c.1615T>G ; NM_001017420.2(ESCO2):c.875_878delACAG ; NM_001017420.2(ESCO2):c.879_880delAG ; NM_001017420.3(ESCO2):c.1597dup ; NM_001017420.2(ESCO2):c.1269G>A ; NM_001017420.2(ESCO2):c.308_309delAA ; NM_001017420.2(ESCO2):c.505C>T ; NM_001017420.2(ESCO2):c.604C>T ; c.296_297dup ; NM_001017420.2(ESCO2):c.1615T>G ; NM_001017420.2(ESCO2):c.875_878delACAG ; NM_001017420.2(ESCO2):c.879_880delAG ; NM_001017420.3(ESCO2):c.1597dup ; NM_001017420.2(ESCO2):c.1269G>A

ETFA	Multiple acyl-CoA dehydrogenase deficiency, mild type	Multiple acyl-CoA dehydrogenation deficiency (MADD) is a disorder of fatty acid and amino acid oxidation and is a clinically heterogeneous disorder ranging from a severe neonatal presentation with metabolic acidosis, cardiomyopathy and liver disease, to a mild childhood/adult disease with episodic metabolic decompensation, muscle weakness, and respiratory failure.	Patients with MADD fall into 3 broad clinical phenotypes: 1) neonatal onset with congenital anomalies, 2) neonatal onset without anomalies, (together called MADD-severe (S); see this term) and 3) mild and/or late onset (MADD-mild (M); see this term). The first group of MADD-S patients are often premature presenting with severe non-ketotic hypoglycemia, hypotonia, hepatomegaly and severe metabolic acidosis within the first 24 hours of life. They usually have dysplastic kidneys with multiple cysts and may also have facial dysmorphism (low-set ears, high forehead, hypertelorism and hypoplastic midface), rocker-bottom feet and anomalies of external genitalia. Death usually occurs within the first week of life. The second group of patients usually present within the first 24-48 hours of life with hypotonia, tachypnea, hepatomegaly, metabolic acidosis and hypoketotic hypoglycemia. Most die during the first week(s) of life but some have survived for several months, usually dying with severe cardiomyopathy. MADD-M patients show a broad clinical spectrum of disease ranging from onset of intermittent episodes of vomiting, metabolic acidosis and hypoketotic hypoglycaemia (+/- cardiac involvement) during the first few months of life to adolescent/adult presentation with acute Reye-like illness with ketoacidosis and lipid storage myopathy. The latter subgroup often responds to pharmacological doses of riboflavin (rr-MADD).	NM_000126.3(ETFA):c.470T>G ; NM_000126.3(ETFA):c.797C>T ; NM_000126.3(ETFA):c.470T>G ; NM_000126.3(ETFA):c.797C>T

ETFA	Multiple acyl-CoA dehydrogenase deficiency, severe neonatal type	Multiple acyl-CoA dehydrogenation deficiency (MADD) is a disorder of fatty acid and amino acid oxidation and is a clinically heterogeneous disorder ranging from a severe neonatal presentation with metabolic acidosis, cardiomyopathy and liver disease, to a mild childhood/adult disease with episodic metabolic decompensation, muscle weakness, and respiratory failure.	Patients with MADD fall into 3 broad clinical phenotypes: 1) neonatal onset with congenital anomalies, 2) neonatal onset without anomalies, (together called MADD-severe (S); see this term) and 3) mild and/or late onset (MADD-mild (M); see this term). The first group of MADD-S patients are often premature presenting with severe non-ketotic hypoglycemia, hypotonia, hepatomegaly and severe metabolic acidosis within the first 24 hours of life. They usually have dysplastic kidneys with multiple cysts and may also have facial dysmorphism (low-set ears, high forehead, hypertelorism and hypoplastic midface), rocker-bottom feet and anomalies of external genitalia. Death usually occurs within the first week of life. The second group of patients usually present within the first 24-48 hours of life with hypotonia, tachypnea, hepatomegaly, metabolic acidosis and hypoketotic hypoglycemia. Most die during the first week(s) of life but some have survived for several months, usually dying with severe cardiomyopathy. MADD-M patients show a broad clinical spectrum of disease ranging from onset of intermittent episodes of vomiting, metabolic acidosis and hypoketotic hypoglycaemia (+/- cardiac involvement) during the first few months of life to adolescent/adult presentation with acute Reye-like illness with ketoacidosis and lipid storage myopathy. The latter subgroup often responds to pharmacological doses of riboflavin (rr-MADD).	NM_000126.3(ETFA):c.470T>G ; NM_000126.3(ETFA):c.797C>T ; NM_000126.3(ETFA):c.470T>G ; NM_000126.3(ETFA):c.797C>T

ETFB	Multiple acyl-CoA dehydrogenase deficiency, mild type	Multiple acyl-CoA dehydrogenation deficiency (MADD) is a disorder of fatty acid and amino acid oxidation and is a clinically heterogeneous disorder ranging from a severe neonatal presentation with metabolic acidosis, cardiomyopathy and liver disease, to a mild childhood/adult disease with episodic metabolic decompensation, muscle weakness, and respiratory failure.	Patients with MADD fall into 3 broad clinical phenotypes: 1) neonatal onset with congenital anomalies, 2) neonatal onset without anomalies, (together called MADD-severe (S); see this term) and 3) mild and/or late onset (MADD-mild (M); see this term). The first group of MADD-S patients are often premature presenting with severe non-ketotic hypoglycemia, hypotonia, hepatomegaly and severe metabolic acidosis within the first 24 hours of life. They usually have dysplastic kidneys with multiple cysts and may also have facial dysmorphism (low-set ears, high forehead, hypertelorism and hypoplastic midface), rocker-bottom feet and anomalies of external genitalia. Death usually occurs within the first week of life. The second group of patients usually present within the first 24-48 hours of life with hypotonia, tachypnea, hepatomegaly, metabolic acidosis and hypoketotic hypoglycemia. Most die during the first week(s) of life but some have survived for several months, usually dying with severe cardiomyopathy. MADD-M patients show a broad clinical spectrum of disease ranging from onset of intermittent episodes of vomiting, metabolic acidosis and hypoketotic hypoglycaemia (+/- cardiac involvement) during the first few months of life to adolescent/adult presentation with acute Reye-like illness with ketoacidosis and lipid storage myopathy. The latter subgroup often responds to pharmacological doses of riboflavin (rr-MADD).	NM_001985.2:c.278_279insG ; c.61C>T ; NM_001985.2(ETFB):c.382G>A ; NM_001985.2(ETFB):c.491G>A ; NM_001985.2:c.278_279insG ; c.61C>T ; NM_001985.2(ETFB):c.382G>A ; NM_001985.2(ETFB):c.491G>A

ETFB	Multiple acyl-CoA dehydrogenase deficiency, severe neonatal type	Multiple acyl-CoA dehydrogenation deficiency (MADD) is a disorder of fatty acid and amino acid oxidation and is a clinically heterogeneous disorder ranging from a severe neonatal presentation with metabolic acidosis, cardiomyopathy and liver disease, to a mild childhood/adult disease with episodic metabolic decompensation, muscle weakness, and respiratory failure.	Patients with MADD fall into 3 broad clinical phenotypes: 1) neonatal onset with congenital anomalies, 2) neonatal onset without anomalies, (together called MADD-severe (S); see this term) and 3) mild and/or late onset (MADD-mild (M); see this term). The first group of MADD-S patients are often premature presenting with severe non-ketotic hypoglycemia, hypotonia, hepatomegaly and severe metabolic acidosis within the first 24 hours of life. They usually have dysplastic kidneys with multiple cysts and may also have facial dysmorphism (low-set ears, high forehead, hypertelorism and hypoplastic midface), rocker-bottom feet and anomalies of external genitalia. Death usually occurs within the first week of life. The second group of patients usually present within the first 24-48 hours of life with hypotonia, tachypnea, hepatomegaly, metabolic acidosis and hypoketotic hypoglycemia. Most die during the first week(s) of life but some have survived for several months, usually dying with severe cardiomyopathy. MADD-M patients show a broad clinical spectrum of disease ranging from onset of intermittent episodes of vomiting, metabolic acidosis and hypoketotic hypoglycaemia (+/- cardiac involvement) during the first few months of life to adolescent/adult presentation with acute Reye-like illness with ketoacidosis and lipid storage myopathy. The latter subgroup often responds to pharmacological doses of riboflavin (rr-MADD).	NM_001985.2:c.278_279insG ; c.61C>T ; NM_001985.2(ETFB):c.382G>A ; NM_001985.2(ETFB):c.491G>A ; NM_001985.2:c.278_279insG ; c.61C>T ; NM_001985.2(ETFB):c.382G>A ; NM_001985.2(ETFB):c.491G>A

ETFDH	Multiple acyl-CoA dehydrogenase deficiency, mild type	Multiple acyl-CoA dehydrogenation deficiency (MADD) is a disorder of fatty acid and amino acid oxidation and is a clinically heterogeneous disorder ranging from a severe neonatal presentation with metabolic acidosis, cardiomyopathy and liver disease, to a mild childhood/adult disease with episodic metabolic decompensation, muscle weakness, and respiratory failure.	Patients with MADD fall into 3 broad clinical phenotypes: 1) neonatal onset with congenital anomalies, 2) neonatal onset without anomalies, (together called MADD-severe (S); see this term) and 3) mild and/or late onset (MADD-mild (M); see this term). The first group of MADD-S patients are often premature presenting with severe non-ketotic hypoglycemia, hypotonia, hepatomegaly and severe metabolic acidosis within the first 24 hours of life. They usually have dysplastic kidneys with multiple cysts and may also have facial dysmorphism (low-set ears, high forehead, hypertelorism and hypoplastic midface), rocker-bottom feet and anomalies of external genitalia. Death usually occurs within the first week of life. The second group of patients usually present within the first 24-48 hours of life with hypotonia, tachypnea, hepatomegaly, metabolic acidosis and hypoketotic hypoglycemia. Most die during the first week(s) of life but some have survived for several months, usually dying with severe cardiomyopathy. MADD-M patients show a broad clinical spectrum of disease ranging from onset of intermittent episodes of vomiting, metabolic acidosis and hypoketotic hypoglycaemia (+/- cardiac involvement) during the first few months of life to adolescent/adult presentation with acute Reye-like illness with ketoacidosis and lipid storage myopathy. The latter subgroup often responds to pharmacological doses of riboflavin (rr-MADD).	NM_004453.3(ETFDH):c.1001T>C ; NM_004453.3(ETFDH):c.524G>T ; NM_004453.3(ETFDH):c.1832G>A ; NM_004453.3(ETFDH):c.1367C>T ; NM_004453.3(ETFDH):c.2T>C ; NM_004453.3(ETFDH):c.1234G>T ; NM_004453.3(ETFDH):c.1823delG ; NM_004453.3(ETFDH):c.250G>A ; NM_004453.3(ETFDH):c.1570_1571delCT ; NM_004453.3(ETFDH):c.413T>G ; NM_004453.3(ETFDH):c.1001T>C ; NM_004453.3(ETFDH):c.524G>T ; NM_004453.3(ETFDH):c.1832G>A ; NM_004453.3(ETFDH):c.1367C>T ; NM_004453.3(ETFDH):c.2T>C ; NM_004453.3(ETFDH):c.1234G>T ; NM_004453.3(ETFDH):c.1823delG ; NM_004453.3(ETFDH):c.250G>A ; NM_004453.3(ETFDH):c.1570_1571delCT ; NM_004453.3(ETFDH):c.413T>G

ETFDH	Multiple acyl-CoA dehydrogenase deficiency, severe neonatal type	Multiple acyl-CoA dehydrogenation deficiency (MADD) is a disorder of fatty acid and amino acid oxidation and is a clinically heterogeneous disorder ranging from a severe neonatal presentation with metabolic acidosis, cardiomyopathy and liver disease, to a mild childhood/adult disease with episodic metabolic decompensation, muscle weakness, and respiratory failure.	Patients with MADD fall into 3 broad clinical phenotypes: 1) neonatal onset with congenital anomalies, 2) neonatal onset without anomalies, (together called MADD-severe (S); see this term) and 3) mild and/or late onset (MADD-mild (M); see this term). The first group of MADD-S patients are often premature presenting with severe non-ketotic hypoglycemia, hypotonia, hepatomegaly and severe metabolic acidosis within the first 24 hours of life. They usually have dysplastic kidneys with multiple cysts and may also have facial dysmorphism (low-set ears, high forehead, hypertelorism and hypoplastic midface), rocker-bottom feet and anomalies of external genitalia. Death usually occurs within the first week of life. The second group of patients usually present within the first 24-48 hours of life with hypotonia, tachypnea, hepatomegaly, metabolic acidosis and hypoketotic hypoglycemia. Most die during the first week(s) of life but some have survived for several months, usually dying with severe cardiomyopathy. MADD-M patients show a broad clinical spectrum of disease ranging from onset of intermittent episodes of vomiting, metabolic acidosis and hypoketotic hypoglycaemia (+/- cardiac involvement) during the first few months of life to adolescent/adult presentation with acute Reye-like illness with ketoacidosis and lipid storage myopathy. The latter subgroup often responds to pharmacological doses of riboflavin (rr-MADD).	NM_004453.3(ETFDH):c.1001T>C ; NM_004453.3(ETFDH):c.524G>T ; NM_004453.3(ETFDH):c.1832G>A ; NM_004453.3(ETFDH):c.1367C>T ; NM_004453.3(ETFDH):c.2T>C ; NM_004453.3(ETFDH):c.1234G>T ; NM_004453.3(ETFDH):c.1823delG ; NM_004453.3(ETFDH):c.250G>A ; NM_004453.3(ETFDH):c.1570_1571delCT ; NM_004453.3(ETFDH):c.413T>G ; NM_004453.3(ETFDH):c.1001T>C ; NM_004453.3(ETFDH):c.524G>T ; NM_004453.3(ETFDH):c.1832G>A ; NM_004453.3(ETFDH):c.1367C>T ; NM_004453.3(ETFDH):c.2T>C ; NM_004453.3(ETFDH):c.1234G>T ; NM_004453.3(ETFDH):c.1823delG ; NM_004453.3(ETFDH):c.250G>A ; NM_004453.3(ETFDH):c.1570_1571delCT ; NM_004453.3(ETFDH):c.413T>G

ETHE1	Ethylmalonic encephalopathy	Ethylmalonic acid encephalopathy (EE) is defined by elevated excretion of ethylmalonic acid (EMA) with recurrent petechiae, orthostatic acrocyanosis and chronic diarrhoea associated with neurodevelopmental delay, psychomotor regression and hypotonia with brain magnetic resonance imaging (MRI) abnormalities.	The disease manifests at birth or in the first few months of life. Spastic tetraplegia may be present. In addition to increased excretion of EMA, methylsuccinic acid and C4-C6-acylglycines (isobutyryl-, isovaleryl-, 2-methylbutyryl-, hexanoylglycine) may also be found in small, but elevated, amounts in the urine. Blood levels of C4-C6-carnitines (butyryl-, isobutyryl-, isovaleryl- and hexanoylcarnitine) may be elevated.	NM_014297.4(ETHE1):c.604dup ; NM_014297.4(ETHE1):c.440_450delACAGCATGGCC ; NM_014297.3(ETHE1):c.487C>T ; NM_014297.3(ETHE1):c.488G>A ; NM_014297.4(ETHE1):c.221dupA ; NM_014297.4(ETHE1):c.554T>G ; NM_014297.4(ETHE1):c.604dup ; NM_014297.4(ETHE1):c.440_450delACAGCATGGCC ; NM_014297.3(ETHE1):c.487C>T ; NM_014297.3(ETHE1):c.488G>A ; NM_014297.4(ETHE1):c.221dupA ; NM_014297.4(ETHE1):c.554T>G
EYS	Retinitis pigmentosa	Retinitis pigmentosa (RP) is an inherited retinal dystrophy leading to progressive loss of the photoreceptors and retinal pigment epithelium and resulting in blindness usually after several decades.	Retinitis pigmentosa is slowly progressive but relentless. There is however broad variability in age of onset, rate of progression and secondary clinical manifestations. Affected individuals generally first develop night blindness (nyctalopia) due to loss of rod function, often in adolescence or earlier. They then develop peripheral visual field impairment, and over time loss of central vision, usually at late stages, often around midlife. Central visual acuity loss may occur at any age as a result of cystoid macular edema or photoreceptor loss. Posterior subcapsular cataracts are common and severity is age dependent. Reduced color vision may also be found. Fundus examination reveals bone spicule pigment deposits, attenuated retinal vessels, retinal atrophy and waxy optic nerve pallor. Severity is partly correlated with the pattern of inheritance with X-linked cases having the most severe course, autosomal recessive and single occurrence cases having intermediate severity, and autosomal dominant the most favorable course.	c.8692_8695dup ; c.6170del ; NM_001142800.1(EYS):c.9405T>A ; c.6102dup ; c.571dup ; c.8632G>T ; c.7822C>T ; c.4597_4613del ; NM_001142800.1(EYS):c.490C>T ; c.4462_4469dup ; c.9362_9365del ; NM_001142800.1(EYS):c.4350_4356delTATAGCT ; NM_001142800.1(EYS):c.7095T>G ; NM_001142800.1(EYS):c.8648_8655del8 ; NM_001142800.1:c.8408dupA ; c.1211dupA ; NM_001142800.1(EYS):c.5928-2A>G ; NM_001142800.1(EYS):c.103C>T ; c.5757dup ; c.4120C>T ; NC_000006.12:g.65495181del ; c.9099del ; NM_001142800.1(EYS):c.4045C>T ; NM_001142800.1(EYS):c.5857G>T ; NM_001142800.1(EYS):c.2826_2827delAT ; c.8692_8695dup ; c.6170del ; NM_001142800.1(EYS):c.9405T>A ; c.6102dup ; c.571dup ; c.8632G>T ; c.7822C>T ; c.4597_4613del ; NM_001142800.1(EYS):c.490C>T ; c.4462_4469dup ; c.9362_9365del ; NM_001142800.1(EYS):c.4350_4356delTATAGCT ; NM_001142800.1(EYS):c.7095T>G ; NM_001142800.1(EYS):c.8648_8655del8 ; NM_001142800.1:c.8408dupA ; c.1211dupA ; NM_001142800.1(EYS):c.5928-2A>G ; NM_001142800.1(EYS):c.103C>T ; c.5757dup ; c.4120C>T ; NC_000006.12:g.65495181del ; c.9099del ; NM_001142800.1(EYS):c.4045C>T ; NM_001142800.1(EYS):c.5857G>T ; NM_001142800.1(EYS):c.2826_2827delAT

F11	Congenital factor XI deficiency	A rare inherited bleeding disorder characterized by reduced levels and/or activity of factor XI (FXI) resulting in moderate bleeding symptoms, usually occurring after trauma or surgery.	Bleeding may manifest at any age, usually occuring after circumcision, dental extractions, trauma, or surgery (in particular surgery in the otorhinological and urogenital areas). Patients usually do not present spontaneous bleeding but women can present with menorrhagia. Hemorrhages are usually moderate. Undiagnosed and untreated patients can develop significant hematomas after a surgical procedure.	NM_000128.4:c.901T>C ; NM_000128.3(F11):c.1613C>T ; NM_000128.4:c.403G>T ; NM_000128.3(F11):c.1693G>A ; NM_000128.3(F11):c.438C>A ; NM_000128.3(F11):c.1211C>A ; NM_000128.3(F11):c.166T>C ; NM_000128.4:c.901T>C ; NM_000128.3(F11):c.1613C>T ; NM_000128.4:c.403G>T ; NM_000128.3(F11):c.1693G>A ; NM_000128.3(F11):c.438C>A ; NM_000128.3(F11):c.1211C>A ; NM_000128.3(F11):c.166T>C

F8	Mild hemophilia A	Mild hemophilia A is a form of hemophilia A (see this term) characterized by a small deficiency of factor VIII leading to abnormal bleeding as a result of minor injuries, or following surgery or tooth extraction.	The biological activity of factor VIII is between 5 and 40%. Spontaneous hemorrhages do not occur.	NM_000132.3(F8):c.872A>G ; c.788-1G>C ; c.6130del ; c.3251C>G ; c.4339dup ; c.4382_4383del ; c.3152del ; c.1438_1439del ; c.6070dup ; NM_000132.3(F8):c.687_688delAG ; c.889del ; c.415C>T ; c.1941_1944del ; c.3833del ; c.985dup ; c.2373dup ; c.3053del ; c.4619del ; c.4935G>A ; c.446del ; c.355C>T ; NM_000132.3(F8):c.1630G>A ; c.3409_3410del ; c.4999del ; c.5243del ; c.1538-2A>T ; c.1165del ; c.4719_4729del ; c.4662_4663del ; c.3907_3911del ; c.3991_3992del ; c.1653T>G ; NM_000132.3(F8):c.6464_6465delAA ; c.63_64del ; c.4408G>T ; c.3385del ; c.3031A>T ; NM_000132.3(F8):c.5879G>T ; c.4035del ; NM_000132.3(F8):c.1293delG ; c.516del ; c.1904-1G>A ; c.6136dup ; c.3913C>T ; c.4474A>T ; c.616G>T ; c.4934G>A ; c.89del ; c.1990_1991del ; c.420T>A ; c.3735_3744delinsATTTCTTTTTCTTT ; c.3863dup ; c.4969C>T ; NM_000132.3(F8):c.404A>G ; c.5301C>A ; c.6089dup ; c.985del ; c.5348_5357del ; c.1357G>T ; c.5697del ; c.510del ; c.709C>T ; c.3624del ; c.3402del ; NM_000132.3(F8):c.943delG ; c.729del ; c.6120_6135del ; c.3607G>T ; c.566C>A ; c.4450del ; c.5964_5967dup ; c.3421C>T ; c.496-2A>G ; c.3417dup ; c.3298A>T ; c.4942C>T ; c.3982C>T ; c.4156C>T ; NM_000132.3(F8):c.907delG ; c.1996_1999dup ; c.560T>A ; NM_000132.3:c.770_771insCC ; c.628_635del ; c.6115+1G>A ; c.4006C>T ; c.169+1G>T ; NM_000132.3(F8):c.849delT ; c.3827C>G ; c.5343T>A ; c.392del ; c.3967C>T ; c.5254del ; c.120del ; c.1410_1413del ; c.173del ; c.2412_2421del ; c.4492del ; c.974_975del ; c.1925_1928del ; c.1675G>T ; c.6116-2A>G ; c.169+1G>A ; c.850G>T ; c.787+2T>C ; c.4895dup ; NM_000132.3(F8):c.986G>A ; c.4697_4701dup ; c.4430_4431del ; c.4926del ; c.3344del ; c.2409del ; c.3902del ; c.5220-1G>A ; c.3540del ; c.591G>A ; c.1338del ; c.3844A>T ; c.4658del ; NM_000132.3(F8):c.1952A>C ; c.519_523del ; c.6194G>A ; c.2404C>T ; NM_000132.3(F8):c.1988C>T ; c.4199del ; c.4549_4550del ; c.3964C>T ; c.1443+2T>C ; c.5689_5690del ; c.3500dup ; c.788-1G>A ; c.4339del ; c.1394C>G ; c.5010del ; c.4265_4266del ; c.3496A>T ; c.607del ; c.73del ; c.1336dup ; c.195C>A ; c.4922dup ; c.1189dup ; c.948_951del ; c.3631A>T ; c.525C>A ; c.935del ; c.1442_1443dup ; c.3565dup ; c.2058_2059del ; c.160_161del ; c.128dup ; c.4425_4426del ; c.5251A>T ; c.4841del ; c.4072C>T ; c.6078_6079del ; c.3651del ; c.3772del ; c.3302_3303del ; c.6250A>T ; c.4806del ; c.4094_4100del ; NM_000132.3(F8):c.6865C>T ; c.1A>G ; c.3371C>A ; c.3652del ; c.4687del ; c.4492_4496del ; c.4363C>T ; c.3203_3204del ; c.3493G>T ; c.1538-1G>T ; c.2384_2388del ; c.6099del ; c.4318del ; c.92del ; c.201_202dup ; c.335_336del ; c.2032A>T ; c.4694_4697del ; c.4814C>A ; c.2462_2463del ; NM_000132.3:c.3150_3151insTC ; c.4996C>T ; c.6084del ; c.1202G>A ; NM_000132.3(F8):c.3548_3549delAA ; c.3922G>T ; c.3736del ; c.5337del ; c.5675dup ; c.3860del ; c.4446dup ; c.2089_2090del ; c.452_462del ; c.4280del ; c.4345del ; c.4345G>T ; c.4542del ; c.4201C>T ; c.4242dup ; c.333del ; c.185C>G ; c.4460del ; NM_000132.3:c.514_515insTCAAGATA ; c.3300del ; c.871G>T ; NM_000132.3(F8):c.6263C>T ; c.482del ; NM_000132.3(F8):c.7031G>A ; c.4770T>A ; c.72del ; c.1175C>G ; c.1390G>T ; c.6253G>T ; c.3416_3417del ; NM_000132.3(F8):c.1596_1597insG ; c.796G>T ; c.3994_3997del ; c.5953del ; c.4519del ; c.472C>T ; c.2397del ; c.1203G>A ; c.465G>A ; c.5960_5961del ; c.1595G>A ; c.4895del ; c.5766C>A ; c.6116_6117del ; c.5696dup ; c.4561C>T ; c.4272del ; c.224del ; c.2419dup ; c.685_686del ; c.98G>A ; c.471G>A ; NM_000132.3(F8):c.4473C>A ; c.4712_4715del ; NM_000132.3(F8):c.1175C>A ; c.1560del ; NM_000132.3(F8):c.6016G>T ; c.4918G>T ; c.3490del ; c.1311del ; c.5923dup ; c.495+1G>A ; c.5914_5915del ; c.680G>A ; c.4987A>T ; c.6120T>A ; c.3984dup ; c.4483del ; c.4483G>T ; NM_000132.3:c.1440_1441insA ; c.4473C>G ; c.2338del ; c.4686del ; c.4103del ; NM_000132.3(F8):c.2029T>C ; c.1200_1201del ; c.4805_4806del ; c.1947_1950del ; c.4798A>T ; NM_000132.3(F8):c.6912_6916delAAATC ; NM_000132.3(F8):c.4858delC ; c.3224del ; NM_000132.3(F8):c.493C>T ; c.6273+1G>A ; NM_000132.3(F8):c.1214T>G ; c.4899del ; c.60del ; c.5227_5228del ; c.4241C>A ; c.5869C>T ; c.5752del ; c.788-1G>T ; c.96del ; c.2000del ; c.919del ; c.4423C>T ; c.4512del ; c.2360del ; NM_000132.3(F8):c.5719_5720insA ; c.1596G>A ; c.3505del ; c.5271del ; c.6115+2T>C ; c.583del ; c.695_698del ; c.4848del ; c.3887del ; c.3830del ; c.3168_3187del ; NM_000132.3(F8):c.1075_1078delAATG ; c.1996_1999del ; c.3710del ; NM_000132.3(F8):c.832G>A ; c.1331_1332del ; c.3766G>T ; c.514_515del ; c.3851_3852del ; c.1443+1G>A ; NM_000132.3(F8):c.1726G>T ; c.3756del ; NM_000132.3(F8):c.4293_4297delCTCTT ; c.355del ; c.334G>T ; c.4720del ; c.4543_4544delinsA ; c.2102_2106del ; c.4492_4493del ; NM_000132.3(F8):c.1078_1079delGA ; c.421G>T ; c.265+1G>T ; NM_000132.3(F8):c.6533G>A ; c.4672_4675del ; c.3255_3258del ; c.64_65del ; c.3289C>T ; NM_000132.3(F8):c.199_200delAA ; c.143+1G>A ; NM_000132.3(F8):c.822G>A ; c.788-2A>T ; NM_000132.3(F8):c.872A>G ; c.788-1G>C ; c.6130del ; c.3251C>G ; c.4339dup ; c.4382_4383del ; c.3152del ; c.1438_1439del ; c.6070dup ; NM_000132.3(F8):c.687_688delAG ; c.889del ; c.415C>T ; c.1941_1944del ; c.3833del ; c.985dup ; c.2373dup ; c.3053del ; c.4619del ; c.4935G>A ; c.446del ; c.355C>T ; NM_000132.3(F8):c.1630G>A ; c.3409_3410del ; c.4999del ; c.5243del ; c.1538-2A>T ; c.1165del ; c.4719_4729del ; c.4662_4663del ; c.3907_3911del ; c.3991_3992del ; c.1653T>G ; NM_000132.3(F8):c.6464_6465delAA ; c.63_64del ; c.4408G>T ; c.3385del ; c.3031A>T ; NM_000132.3(F8):c.5879G>T ; c.4035del ; NM_000132.3(F8):c.1293delG ; c.516del ; c.1904-1G>A ; c.6136dup ; c.3913C>T ; c.4474A>T ; c.616G>T ; c.4934G>A ; c.89del ; c.1990_1991del ; c.420T>A ; c.3735_3744delinsATTTCTTTTTCTTT ; c.3863dup ; c.4969C>T ; NM_000132.3(F8):c.404A>G ; c.5301C>A ; c.6089dup ; c.985del ; c.5348_5357del ; c.1357G>T ; c.5697del ; c.510del ; c.709C>T ; c.3624del ; c.3402del ; NM_000132.3(F8):c.943delG ; c.729del ; c.6120_6135del ; c.3607G>T ; c.566C>A ; c.4450del ; c.5964_5967dup ; c.3421C>T ; c.496-2A>G ; c.3417dup ; c.3298A>T ; c.4942C>T ; c.3982C>T ; c.4156C>T ; NM_000132.3(F8):c.907delG ; c.1996_1999dup ; c.560T>A ; NM_000132.3:c.770_771insCC ; c.628_635del ; c.6115+1G>A ; c.4006C>T ; c.169+1G>T ; NM_000132.3(F8):c.849delT ; c.3827C>G ; c.5343T>A ; c.392del ; c.3967C>T ; c.5254del ; c.120del ; c.1410_1413del ; c.173del ; c.2412_2421del ; c.4492del ; c.974_975del ; c.1925_1928del ; c.1675G>T ; c.6116-2A>G ; c.169+1G>A ; c.850G>T ; c.787+2T>C ; c.4895dup ; NM_000132.3(F8):c.986G>A ; c.4697_4701dup ; c.4430_4431del ; c.4926del ; c.3344del ; c.2409del ; c.3902del ; c.5220-1G>A ; c.3540del ; c.591G>A ; c.1338del ; c.3844A>T ; c.4658del ; NM_000132.3(F8):c.1952A>C ; c.519_523del ; c.6194G>A ; c.2404C>T ; NM_000132.3(F8):c.1988C>T ; c.4199del ; c.4549_4550del ; c.3964C>T ; c.1443+2T>C ; c.5689_5690del ; c.3500dup ; c.788-1G>A ; c.4339del ; c.1394C>G ; c.5010del ; c.4265_4266del ; c.3496A>T ; c.607del ; c.73del ; c.1336dup ; c.195C>A ; c.4922dup ; c.1189dup ; c.948_951del ; c.3631A>T ; c.525C>A ; c.935del ; c.1442_1443dup ; c.3565dup ; c.2058_2059del ; c.160_161del ; c.128dup ; c.4425_4426del ; c.5251A>T ; c.4841del ; c.4072C>T ; c.6078_6079del ; c.3651del ; c.3772del ; c.3302_3303del ; c.6250A>T ; c.4806del ; c.4094_4100del ; NM_000132.3(F8):c.6865C>T ; c.1A>G ; c.3371C>A ; c.3652del ; c.4687del ; c.4492_4496del ; c.4363C>T ; c.3203_3204del ; c.3493G>T ; c.1538-1G>T ; c.2384_2388del ; c.6099del ; c.4318del ; c.92del ; c.201_202dup ; c.335_336del ; c.2032A>T ; c.4694_4697del ; c.4814C>A ; c.2462_2463del ; NM_000132.3:c.3150_3151insTC ; c.4996C>T ; c.6084del ; c.1202G>A ; NM_000132.3(F8):c.3548_3549delAA ; c.3922G>T ; c.3736del ; c.5337del ; c.5675dup ; c.3860del ; c.4446dup ; c.2089_2090del ; c.452_462del ; c.4280del ; c.4345del ; c.4345G>T ; c.4542del ; c.4201C>T ; c.4242dup ; c.333del ; c.185C>G ; c.4460del ; NM_000132.3:c.514_515insTCAAGATA ; c.3300del ; c.871G>T ; NM_000132.3(F8):c.6263C>T ; c.482del ; NM_000132.3(F8):c.7031G>A ; c.4770T>A ; c.72del ; c.1175C>G ; c.1390G>T ; c.6253G>T ; c.3416_3417del ; NM_000132.3(F8):c.1596_1597insG ; c.796G>T ; c.3994_3997del ; c.5953del ; c.4519del ; c.472C>T ; c.2397del ; c.1203G>A ; c.465G>A ; c.5960_5961del ; c.1595G>A ; c.4895del ; c.5766C>A ; c.6116_6117del ; c.5696dup ; c.4561C>T ; c.4272del ; c.224del ; c.2419dup ; c.685_686del ; c.98G>A ; c.471G>A ; NM_000132.3(F8):c.4473C>A ; c.4712_4715del ; NM_000132.3(F8):c.1175C>A ; c.1560del ; NM_000132.3(F8):c.6016G>T ; c.4918G>T ; c.3490del ; c.1311del ; c.5923dup ; c.495+1G>A ; c.5914_5915del ; c.680G>A ; c.4987A>T ; c.6120T>A ; c.3984dup ; c.4483del ; c.4483G>T ; NM_000132.3:c.1440_1441insA ; c.4473C>G ; c.2338del ; c.4686del ; c.4103del ; NM_000132.3(F8):c.2029T>C ; c.1200_1201del ; c.4805_4806del ; c.1947_1950del ; c.4798A>T ; NM_000132.3(F8):c.6912_6916delAAATC ; NM_000132.3(F8):c.4858delC ; c.3224del ; NM_000132.3(F8):c.493C>T ; c.6273+1G>A ; NM_000132.3(F8):c.1214T>G ; c.4899del ; c.60del ; c.5227_5228del ; c.4241C>A ; c.5869C>T ; c.5752del ; c.788-1G>T ; c.96del ; c.2000del ; c.919del ; c.4423C>T ; c.4512del ; c.2360del ; NM_000132.3(F8):c.5719_5720insA ; c.1596G>A ; c.3505del ; c.5271del ; c.6115+2T>C ; c.583del ; c.695_698del ; c.4848del ; c.3887del ; c.3830del ; c.3168_3187del ; NM_000132.3(F8):c.1075_1078delAATG ; c.1996_1999del ; c.3710del ; NM_000132.3(F8):c.832G>A ; c.1331_1332del ; c.3766G>T ; c.514_515del ; c.3851_3852del ; c.1443+1G>A ; NM_000132.3(F8):c.1726G>T ; c.3756del ; NM_000132.3(F8):c.4293_4297delCTCTT ; c.355del ; c.334G>T ; c.4720del ; c.4543_4544delinsA ; c.2102_2106del ; c.4492_4493del ; NM_000132.3(F8):c.1078_1079delGA ; c.421G>T ; c.265+1G>T ; NM_000132.3(F8):c.6533G>A ; c.4672_4675del ; c.3255_3258del ; c.64_65del ; c.3289C>T ; NM_000132.3(F8):c.199_200delAA ; c.143+1G>A ; NM_000132.3(F8):c.822G>A ; c.788-2A>T

F8	Moderately severe hemophilia A	Moderately severe hemophilia A is a form of hemophilia A (see this term) characterized by factor VIII deficiency leading to abnormal bleeding as a result of minor injuries, or following surgery or tooth extraction.	The biological activity of factor VIII is between 1% and 5%. Spontaneous hemorrhages are rare.	NM_000132.3(F8):c.872A>G ; c.788-1G>C ; c.6130del ; c.3251C>G ; c.4339dup ; c.4382_4383del ; c.3152del ; c.1438_1439del ; c.6070dup ; NM_000132.3(F8):c.687_688delAG ; c.889del ; c.415C>T ; c.1941_1944del ; c.3833del ; c.985dup ; c.2373dup ; c.3053del ; c.4619del ; c.4935G>A ; c.446del ; c.355C>T ; NM_000132.3(F8):c.1630G>A ; c.3409_3410del ; c.4999del ; c.5243del ; c.1538-2A>T ; c.1165del ; c.4719_4729del ; c.4662_4663del ; c.3907_3911del ; c.3991_3992del ; c.1653T>G ; NM_000132.3(F8):c.6464_6465delAA ; c.63_64del ; c.4408G>T ; c.3385del ; c.3031A>T ; NM_000132.3(F8):c.5879G>T ; c.4035del ; NM_000132.3(F8):c.1293delG ; c.516del ; c.1904-1G>A ; c.6136dup ; c.3913C>T ; c.4474A>T ; c.616G>T ; c.4934G>A ; c.89del ; c.1990_1991del ; c.420T>A ; c.3735_3744delinsATTTCTTTTTCTTT ; c.3863dup ; c.4969C>T ; NM_000132.3(F8):c.404A>G ; c.5301C>A ; c.6089dup ; c.985del ; c.5348_5357del ; c.1357G>T ; c.5697del ; c.510del ; c.709C>T ; c.3624del ; c.3402del ; NM_000132.3(F8):c.943delG ; c.729del ; c.6120_6135del ; c.3607G>T ; c.566C>A ; c.4450del ; c.5964_5967dup ; c.3421C>T ; c.496-2A>G ; c.3417dup ; c.3298A>T ; c.4942C>T ; c.3982C>T ; c.4156C>T ; NM_000132.3(F8):c.907delG ; c.1996_1999dup ; c.560T>A ; NM_000132.3:c.770_771insCC ; c.628_635del ; c.6115+1G>A ; c.4006C>T ; c.169+1G>T ; NM_000132.3(F8):c.849delT ; c.3827C>G ; c.5343T>A ; c.392del ; c.3967C>T ; c.5254del ; c.120del ; c.1410_1413del ; c.173del ; c.2412_2421del ; c.4492del ; c.974_975del ; c.1925_1928del ; c.1675G>T ; c.6116-2A>G ; c.169+1G>A ; c.850G>T ; c.787+2T>C ; c.4895dup ; NM_000132.3(F8):c.986G>A ; c.4697_4701dup ; c.4430_4431del ; c.4926del ; c.3344del ; c.2409del ; c.3902del ; c.5220-1G>A ; c.3540del ; c.591G>A ; c.1338del ; c.3844A>T ; c.4658del ; NM_000132.3(F8):c.1952A>C ; c.519_523del ; c.6194G>A ; c.2404C>T ; NM_000132.3(F8):c.1988C>T ; c.4199del ; c.4549_4550del ; c.3964C>T ; c.1443+2T>C ; c.5689_5690del ; c.3500dup ; c.788-1G>A ; c.4339del ; c.1394C>G ; c.5010del ; c.4265_4266del ; c.3496A>T ; c.607del ; c.73del ; c.1336dup ; c.195C>A ; c.4922dup ; c.1189dup ; c.948_951del ; c.3631A>T ; c.525C>A ; c.935del ; c.1442_1443dup ; c.3565dup ; c.2058_2059del ; c.160_161del ; c.128dup ; c.4425_4426del ; c.5251A>T ; c.4841del ; c.4072C>T ; c.6078_6079del ; c.3651del ; c.3772del ; c.3302_3303del ; c.6250A>T ; c.4806del ; c.4094_4100del ; NM_000132.3(F8):c.6865C>T ; c.1A>G ; c.3371C>A ; c.3652del ; c.4687del ; c.4492_4496del ; c.4363C>T ; c.3203_3204del ; c.3493G>T ; c.1538-1G>T ; c.2384_2388del ; c.6099del ; c.4318del ; c.92del ; c.201_202dup ; c.335_336del ; c.2032A>T ; c.4694_4697del ; c.4814C>A ; c.2462_2463del ; NM_000132.3:c.3150_3151insTC ; c.4996C>T ; c.6084del ; c.1202G>A ; NM_000132.3(F8):c.3548_3549delAA ; c.3922G>T ; c.3736del ; c.5337del ; c.5675dup ; c.3860del ; c.4446dup ; c.2089_2090del ; c.452_462del ; c.4280del ; c.4345del ; c.4345G>T ; c.4542del ; c.4201C>T ; c.4242dup ; c.333del ; c.185C>G ; c.4460del ; NM_000132.3:c.514_515insTCAAGATA ; c.3300del ; c.871G>T ; NM_000132.3(F8):c.6263C>T ; c.482del ; NM_000132.3(F8):c.7031G>A ; c.4770T>A ; c.72del ; c.1175C>G ; c.1390G>T ; c.6253G>T ; c.3416_3417del ; NM_000132.3(F8):c.1596_1597insG ; c.796G>T ; c.3994_3997del ; c.5953del ; c.4519del ; c.472C>T ; c.2397del ; c.1203G>A ; c.465G>A ; c.5960_5961del ; c.1595G>A ; c.4895del ; c.5766C>A ; c.6116_6117del ; c.5696dup ; c.4561C>T ; c.4272del ; c.224del ; c.2419dup ; c.685_686del ; c.98G>A ; c.471G>A ; NM_000132.3(F8):c.4473C>A ; c.4712_4715del ; NM_000132.3(F8):c.1175C>A ; c.1560del ; NM_000132.3(F8):c.6016G>T ; c.4918G>T ; c.3490del ; c.1311del ; c.5923dup ; c.495+1G>A ; c.5914_5915del ; c.680G>A ; c.4987A>T ; c.6120T>A ; c.3984dup ; c.4483del ; c.4483G>T ; NM_000132.3:c.1440_1441insA ; c.4473C>G ; c.2338del ; c.4686del ; c.4103del ; NM_000132.3(F8):c.2029T>C ; c.1200_1201del ; c.4805_4806del ; c.1947_1950del ; c.4798A>T ; NM_000132.3(F8):c.6912_6916delAAATC ; NM_000132.3(F8):c.4858delC ; c.3224del ; NM_000132.3(F8):c.493C>T ; c.6273+1G>A ; NM_000132.3(F8):c.1214T>G ; c.4899del ; c.60del ; c.5227_5228del ; c.4241C>A ; c.5869C>T ; c.5752del ; c.788-1G>T ; c.96del ; c.2000del ; c.919del ; c.4423C>T ; c.4512del ; c.2360del ; NM_000132.3(F8):c.5719_5720insA ; c.1596G>A ; c.3505del ; c.5271del ; c.6115+2T>C ; c.583del ; c.695_698del ; c.4848del ; c.3887del ; c.3830del ; c.3168_3187del ; NM_000132.3(F8):c.1075_1078delAATG ; c.1996_1999del ; c.3710del ; NM_000132.3(F8):c.832G>A ; c.1331_1332del ; c.3766G>T ; c.514_515del ; c.3851_3852del ; c.1443+1G>A ; NM_000132.3(F8):c.1726G>T ; c.3756del ; NM_000132.3(F8):c.4293_4297delCTCTT ; c.355del ; c.334G>T ; c.4720del ; c.4543_4544delinsA ; c.2102_2106del ; c.4492_4493del ; NM_000132.3(F8):c.1078_1079delGA ; c.421G>T ; c.265+1G>T ; NM_000132.3(F8):c.6533G>A ; c.4672_4675del ; c.3255_3258del ; c.64_65del ; c.3289C>T ; NM_000132.3(F8):c.199_200delAA ; c.143+1G>A ; NM_000132.3(F8):c.822G>A ; c.788-2A>T ; NM_000132.3(F8):c.872A>G ; c.788-1G>C ; c.6130del ; c.3251C>G ; c.4339dup ; c.4382_4383del ; c.3152del ; c.1438_1439del ; c.6070dup ; NM_000132.3(F8):c.687_688delAG ; c.889del ; c.415C>T ; c.1941_1944del ; c.3833del ; c.985dup ; c.2373dup ; c.3053del ; c.4619del ; c.4935G>A ; c.446del ; c.355C>T ; NM_000132.3(F8):c.1630G>A ; c.3409_3410del ; c.4999del ; c.5243del ; c.1538-2A>T ; c.1165del ; c.4719_4729del ; c.4662_4663del ; c.3907_3911del ; c.3991_3992del ; c.1653T>G ; NM_000132.3(F8):c.6464_6465delAA ; c.63_64del ; c.4408G>T ; c.3385del ; c.3031A>T ; NM_000132.3(F8):c.5879G>T ; c.4035del ; NM_000132.3(F8):c.1293delG ; c.516del ; c.1904-1G>A ; c.6136dup ; c.3913C>T ; c.4474A>T ; c.616G>T ; c.4934G>A ; c.89del ; c.1990_1991del ; c.420T>A ; c.3735_3744delinsATTTCTTTTTCTTT ; c.3863dup ; c.4969C>T ; NM_000132.3(F8):c.404A>G ; c.5301C>A ; c.6089dup ; c.985del ; c.5348_5357del ; c.1357G>T ; c.5697del ; c.510del ; c.709C>T ; c.3624del ; c.3402del ; NM_000132.3(F8):c.943delG ; c.729del ; c.6120_6135del ; c.3607G>T ; c.566C>A ; c.4450del ; c.5964_5967dup ; c.3421C>T ; c.496-2A>G ; c.3417dup ; c.3298A>T ; c.4942C>T ; c.3982C>T ; c.4156C>T ; NM_000132.3(F8):c.907delG ; c.1996_1999dup ; c.560T>A ; NM_000132.3:c.770_771insCC ; c.628_635del ; c.6115+1G>A ; c.4006C>T ; c.169+1G>T ; NM_000132.3(F8):c.849delT ; c.3827C>G ; c.5343T>A ; c.392del ; c.3967C>T ; c.5254del ; c.120del ; c.1410_1413del ; c.173del ; c.2412_2421del ; c.4492del ; c.974_975del ; c.1925_1928del ; c.1675G>T ; c.6116-2A>G ; c.169+1G>A ; c.850G>T ; c.787+2T>C ; c.4895dup ; NM_000132.3(F8):c.986G>A ; c.4697_4701dup ; c.4430_4431del ; c.4926del ; c.3344del ; c.2409del ; c.3902del ; c.5220-1G>A ; c.3540del ; c.591G>A ; c.1338del ; c.3844A>T ; c.4658del ; NM_000132.3(F8):c.1952A>C ; c.519_523del ; c.6194G>A ; c.2404C>T ; NM_000132.3(F8):c.1988C>T ; c.4199del ; c.4549_4550del ; c.3964C>T ; c.1443+2T>C ; c.5689_5690del ; c.3500dup ; c.788-1G>A ; c.4339del ; c.1394C>G ; c.5010del ; c.4265_4266del ; c.3496A>T ; c.607del ; c.73del ; c.1336dup ; c.195C>A ; c.4922dup ; c.1189dup ; c.948_951del ; c.3631A>T ; c.525C>A ; c.935del ; c.1442_1443dup ; c.3565dup ; c.2058_2059del ; c.160_161del ; c.128dup ; c.4425_4426del ; c.5251A>T ; c.4841del ; c.4072C>T ; c.6078_6079del ; c.3651del ; c.3772del ; c.3302_3303del ; c.6250A>T ; c.4806del ; c.4094_4100del ; NM_000132.3(F8):c.6865C>T ; c.1A>G ; c.3371C>A ; c.3652del ; c.4687del ; c.4492_4496del ; c.4363C>T ; c.3203_3204del ; c.3493G>T ; c.1538-1G>T ; c.2384_2388del ; c.6099del ; c.4318del ; c.92del ; c.201_202dup ; c.335_336del ; c.2032A>T ; c.4694_4697del ; c.4814C>A ; c.2462_2463del ; NM_000132.3:c.3150_3151insTC ; c.4996C>T ; c.6084del ; c.1202G>A ; NM_000132.3(F8):c.3548_3549delAA ; c.3922G>T ; c.3736del ; c.5337del ; c.5675dup ; c.3860del ; c.4446dup ; c.2089_2090del ; c.452_462del ; c.4280del ; c.4345del ; c.4345G>T ; c.4542del ; c.4201C>T ; c.4242dup ; c.333del ; c.185C>G ; c.4460del ; NM_000132.3:c.514_515insTCAAGATA ; c.3300del ; c.871G>T ; NM_000132.3(F8):c.6263C>T ; c.482del ; NM_000132.3(F8):c.7031G>A ; c.4770T>A ; c.72del ; c.1175C>G ; c.1390G>T ; c.6253G>T ; c.3416_3417del ; NM_000132.3(F8):c.1596_1597insG ; c.796G>T ; c.3994_3997del ; c.5953del ; c.4519del ; c.472C>T ; c.2397del ; c.1203G>A ; c.465G>A ; c.5960_5961del ; c.1595G>A ; c.4895del ; c.5766C>A ; c.6116_6117del ; c.5696dup ; c.4561C>T ; c.4272del ; c.224del ; c.2419dup ; c.685_686del ; c.98G>A ; c.471G>A ; NM_000132.3(F8):c.4473C>A ; c.4712_4715del ; NM_000132.3(F8):c.1175C>A ; c.1560del ; NM_000132.3(F8):c.6016G>T ; c.4918G>T ; c.3490del ; c.1311del ; c.5923dup ; c.495+1G>A ; c.5914_5915del ; c.680G>A ; c.4987A>T ; c.6120T>A ; c.3984dup ; c.4483del ; c.4483G>T ; NM_000132.3:c.1440_1441insA ; c.4473C>G ; c.2338del ; c.4686del ; c.4103del ; NM_000132.3(F8):c.2029T>C ; c.1200_1201del ; c.4805_4806del ; c.1947_1950del ; c.4798A>T ; NM_000132.3(F8):c.6912_6916delAAATC ; NM_000132.3(F8):c.4858delC ; c.3224del ; NM_000132.3(F8):c.493C>T ; c.6273+1G>A ; NM_000132.3(F8):c.1214T>G ; c.4899del ; c.60del ; c.5227_5228del ; c.4241C>A ; c.5869C>T ; c.5752del ; c.788-1G>T ; c.96del ; c.2000del ; c.919del ; c.4423C>T ; c.4512del ; c.2360del ; NM_000132.3(F8):c.5719_5720insA ; c.1596G>A ; c.3505del ; c.5271del ; c.6115+2T>C ; c.583del ; c.695_698del ; c.4848del ; c.3887del ; c.3830del ; c.3168_3187del ; NM_000132.3(F8):c.1075_1078delAATG ; c.1996_1999del ; c.3710del ; NM_000132.3(F8):c.832G>A ; c.1331_1332del ; c.3766G>T ; c.514_515del ; c.3851_3852del ; c.1443+1G>A ; NM_000132.3(F8):c.1726G>T ; c.3756del ; NM_000132.3(F8):c.4293_4297delCTCTT ; c.355del ; c.334G>T ; c.4720del ; c.4543_4544delinsA ; c.2102_2106del ; c.4492_4493del ; NM_000132.3(F8):c.1078_1079delGA ; c.421G>T ; c.265+1G>T ; NM_000132.3(F8):c.6533G>A ; c.4672_4675del ; c.3255_3258del ; c.64_65del ; c.3289C>T ; NM_000132.3(F8):c.199_200delAA ; c.143+1G>A ; NM_000132.3(F8):c.822G>A ; c.788-2A>T

F8	Severe hemophilia A	Severe hemophilia A is a form of hemophilia A (see this term) characterized by a large deficiency of factor VIII leading to frequent spontaneous hemorrhage and abnormal bleeding as a result of minor injuries, or following surgery or tooth extraction.	The biological activity of factor VIII is below 1%.	NM_000132.3(F8):c.872A>G ; c.788-1G>C ; c.6130del ; c.3251C>G ; c.4339dup ; c.4382_4383del ; c.3152del ; c.1438_1439del ; c.6070dup ; NM_000132.3(F8):c.687_688delAG ; c.889del ; c.415C>T ; c.1941_1944del ; c.3833del ; c.985dup ; c.2373dup ; c.3053del ; c.4619del ; c.4935G>A ; c.446del ; c.355C>T ; NM_000132.3(F8):c.1630G>A ; c.3409_3410del ; c.4999del ; c.5243del ; c.1538-2A>T ; c.1165del ; c.4719_4729del ; c.4662_4663del ; c.3907_3911del ; c.3991_3992del ; c.1653T>G ; NM_000132.3(F8):c.6464_6465delAA ; c.63_64del ; c.4408G>T ; c.3385del ; c.3031A>T ; NM_000132.3(F8):c.5879G>T ; c.4035del ; NM_000132.3(F8):c.1293delG ; c.516del ; c.1904-1G>A ; c.6136dup ; c.3913C>T ; c.4474A>T ; c.616G>T ; c.4934G>A ; c.89del ; c.1990_1991del ; c.420T>A ; c.3735_3744delinsATTTCTTTTTCTTT ; c.3863dup ; c.4969C>T ; NM_000132.3(F8):c.404A>G ; c.5301C>A ; c.6089dup ; c.985del ; c.5348_5357del ; c.1357G>T ; c.5697del ; c.510del ; c.709C>T ; c.3624del ; c.3402del ; NM_000132.3(F8):c.943delG ; c.729del ; c.6120_6135del ; c.3607G>T ; c.566C>A ; c.4450del ; c.5964_5967dup ; c.3421C>T ; c.496-2A>G ; c.3417dup ; c.3298A>T ; c.4942C>T ; c.3982C>T ; c.4156C>T ; NM_000132.3(F8):c.907delG ; c.1996_1999dup ; c.560T>A ; NM_000132.3:c.770_771insCC ; c.628_635del ; c.6115+1G>A ; c.4006C>T ; c.169+1G>T ; NM_000132.3(F8):c.849delT ; c.3827C>G ; c.5343T>A ; c.392del ; c.3967C>T ; c.5254del ; c.120del ; c.1410_1413del ; c.173del ; c.2412_2421del ; c.4492del ; c.974_975del ; c.1925_1928del ; c.1675G>T ; c.6116-2A>G ; c.169+1G>A ; c.850G>T ; c.787+2T>C ; c.4895dup ; NM_000132.3(F8):c.986G>A ; c.4697_4701dup ; c.4430_4431del ; c.4926del ; c.3344del ; c.2409del ; c.3902del ; c.5220-1G>A ; c.3540del ; c.591G>A ; c.1338del ; c.3844A>T ; c.4658del ; NM_000132.3(F8):c.1952A>C ; c.519_523del ; c.6194G>A ; c.2404C>T ; NM_000132.3(F8):c.1988C>T ; c.4199del ; c.4549_4550del ; c.3964C>T ; c.1443+2T>C ; c.5689_5690del ; c.3500dup ; c.788-1G>A ; c.4339del ; c.1394C>G ; c.5010del ; c.4265_4266del ; c.3496A>T ; c.607del ; c.73del ; c.1336dup ; c.195C>A ; c.4922dup ; c.1189dup ; c.948_951del ; c.3631A>T ; c.525C>A ; c.935del ; c.1442_1443dup ; c.3565dup ; c.2058_2059del ; c.160_161del ; c.128dup ; c.4425_4426del ; c.5251A>T ; c.4841del ; c.4072C>T ; c.6078_6079del ; c.3651del ; c.3772del ; c.3302_3303del ; c.6250A>T ; c.4806del ; c.4094_4100del ; NM_000132.3(F8):c.6865C>T ; c.1A>G ; c.3371C>A ; c.3652del ; c.4687del ; c.4492_4496del ; c.4363C>T ; c.3203_3204del ; c.3493G>T ; c.1538-1G>T ; c.2384_2388del ; c.6099del ; c.4318del ; c.92del ; c.201_202dup ; c.335_336del ; c.2032A>T ; c.4694_4697del ; c.4814C>A ; c.2462_2463del ; NM_000132.3:c.3150_3151insTC ; c.4996C>T ; c.6084del ; c.1202G>A ; NM_000132.3(F8):c.3548_3549delAA ; c.3922G>T ; c.3736del ; c.5337del ; c.5675dup ; c.3860del ; c.4446dup ; c.2089_2090del ; c.452_462del ; c.4280del ; c.4345del ; c.4345G>T ; c.4542del ; c.4201C>T ; c.4242dup ; c.333del ; c.185C>G ; c.4460del ; NM_000132.3:c.514_515insTCAAGATA ; c.3300del ; c.871G>T ; NM_000132.3(F8):c.6263C>T ; c.482del ; NM_000132.3(F8):c.7031G>A ; c.4770T>A ; c.72del ; c.1175C>G ; c.1390G>T ; c.6253G>T ; c.3416_3417del ; NM_000132.3(F8):c.1596_1597insG ; c.796G>T ; c.3994_3997del ; c.5953del ; c.4519del ; c.472C>T ; c.2397del ; c.1203G>A ; c.465G>A ; c.5960_5961del ; c.1595G>A ; c.4895del ; c.5766C>A ; c.6116_6117del ; c.5696dup ; c.4561C>T ; c.4272del ; c.224del ; c.2419dup ; c.685_686del ; c.98G>A ; c.471G>A ; NM_000132.3(F8):c.4473C>A ; c.4712_4715del ; NM_000132.3(F8):c.1175C>A ; c.1560del ; NM_000132.3(F8):c.6016G>T ; c.4918G>T ; c.3490del ; c.1311del ; c.5923dup ; c.495+1G>A ; c.5914_5915del ; c.680G>A ; c.4987A>T ; c.6120T>A ; c.3984dup ; c.4483del ; c.4483G>T ; NM_000132.3:c.1440_1441insA ; c.4473C>G ; c.2338del ; c.4686del ; c.4103del ; NM_000132.3(F8):c.2029T>C ; c.1200_1201del ; c.4805_4806del ; c.1947_1950del ; c.4798A>T ; NM_000132.3(F8):c.6912_6916delAAATC ; NM_000132.3(F8):c.4858delC ; c.3224del ; NM_000132.3(F8):c.493C>T ; c.6273+1G>A ; NM_000132.3(F8):c.1214T>G ; c.4899del ; c.60del ; c.5227_5228del ; c.4241C>A ; c.5869C>T ; c.5752del ; c.788-1G>T ; c.96del ; c.2000del ; c.919del ; c.4423C>T ; c.4512del ; c.2360del ; NM_000132.3(F8):c.5719_5720insA ; c.1596G>A ; c.3505del ; c.5271del ; c.6115+2T>C ; c.583del ; c.695_698del ; c.4848del ; c.3887del ; c.3830del ; c.3168_3187del ; NM_000132.3(F8):c.1075_1078delAATG ; c.1996_1999del ; c.3710del ; NM_000132.3(F8):c.832G>A ; c.1331_1332del ; c.3766G>T ; c.514_515del ; c.3851_3852del ; c.1443+1G>A ; NM_000132.3(F8):c.1726G>T ; c.3756del ; NM_000132.3(F8):c.4293_4297delCTCTT ; c.355del ; c.334G>T ; c.4720del ; c.4543_4544delinsA ; c.2102_2106del ; c.4492_4493del ; NM_000132.3(F8):c.1078_1079delGA ; c.421G>T ; c.265+1G>T ; NM_000132.3(F8):c.6533G>A ; c.4672_4675del ; c.3255_3258del ; c.64_65del ; c.3289C>T ; NM_000132.3(F8):c.199_200delAA ; c.143+1G>A ; NM_000132.3(F8):c.822G>A ; c.788-2A>T ; NM_000132.3(F8):c.872A>G ; c.788-1G>C ; c.6130del ; c.3251C>G ; c.4339dup ; c.4382_4383del ; c.3152del ; c.1438_1439del ; c.6070dup ; NM_000132.3(F8):c.687_688delAG ; c.889del ; c.415C>T ; c.1941_1944del ; c.3833del ; c.985dup ; c.2373dup ; c.3053del ; c.4619del ; c.4935G>A ; c.446del ; c.355C>T ; NM_000132.3(F8):c.1630G>A ; c.3409_3410del ; c.4999del ; c.5243del ; c.1538-2A>T ; c.1165del ; c.4719_4729del ; c.4662_4663del ; c.3907_3911del ; c.3991_3992del ; c.1653T>G ; NM_000132.3(F8):c.6464_6465delAA ; c.63_64del ; c.4408G>T ; c.3385del ; c.3031A>T ; NM_000132.3(F8):c.5879G>T ; c.4035del ; NM_000132.3(F8):c.1293delG ; c.516del ; c.1904-1G>A ; c.6136dup ; c.3913C>T ; c.4474A>T ; c.616G>T ; c.4934G>A ; c.89del ; c.1990_1991del ; c.420T>A ; c.3735_3744delinsATTTCTTTTTCTTT ; c.3863dup ; c.4969C>T ; NM_000132.3(F8):c.404A>G ; c.5301C>A ; c.6089dup ; c.985del ; c.5348_5357del ; c.1357G>T ; c.5697del ; c.510del ; c.709C>T ; c.3624del ; c.3402del ; NM_000132.3(F8):c.943delG ; c.729del ; c.6120_6135del ; c.3607G>T ; c.566C>A ; c.4450del ; c.5964_5967dup ; c.3421C>T ; c.496-2A>G ; c.3417dup ; c.3298A>T ; c.4942C>T ; c.3982C>T ; c.4156C>T ; NM_000132.3(F8):c.907delG ; c.1996_1999dup ; c.560T>A ; NM_000132.3:c.770_771insCC ; c.628_635del ; c.6115+1G>A ; c.4006C>T ; c.169+1G>T ; NM_000132.3(F8):c.849delT ; c.3827C>G ; c.5343T>A ; c.392del ; c.3967C>T ; c.5254del ; c.120del ; c.1410_1413del ; c.173del ; c.2412_2421del ; c.4492del ; c.974_975del ; c.1925_1928del ; c.1675G>T ; c.6116-2A>G ; c.169+1G>A ; c.850G>T ; c.787+2T>C ; c.4895dup ; NM_000132.3(F8):c.986G>A ; c.4697_4701dup ; c.4430_4431del ; c.4926del ; c.3344del ; c.2409del ; c.3902del ; c.5220-1G>A ; c.3540del ; c.591G>A ; c.1338del ; c.3844A>T ; c.4658del ; NM_000132.3(F8):c.1952A>C ; c.519_523del ; c.6194G>A ; c.2404C>T ; NM_000132.3(F8):c.1988C>T ; c.4199del ; c.4549_4550del ; c.3964C>T ; c.1443+2T>C ; c.5689_5690del ; c.3500dup ; c.788-1G>A ; c.4339del ; c.1394C>G ; c.5010del ; c.4265_4266del ; c.3496A>T ; c.607del ; c.73del ; c.1336dup ; c.195C>A ; c.4922dup ; c.1189dup ; c.948_951del ; c.3631A>T ; c.525C>A ; c.935del ; c.1442_1443dup ; c.3565dup ; c.2058_2059del ; c.160_161del ; c.128dup ; c.4425_4426del ; c.5251A>T ; c.4841del ; c.4072C>T ; c.6078_6079del ; c.3651del ; c.3772del ; c.3302_3303del ; c.6250A>T ; c.4806del ; c.4094_4100del ; NM_000132.3(F8):c.6865C>T ; c.1A>G ; c.3371C>A ; c.3652del ; c.4687del ; c.4492_4496del ; c.4363C>T ; c.3203_3204del ; c.3493G>T ; c.1538-1G>T ; c.2384_2388del ; c.6099del ; c.4318del ; c.92del ; c.201_202dup ; c.335_336del ; c.2032A>T ; c.4694_4697del ; c.4814C>A ; c.2462_2463del ; NM_000132.3:c.3150_3151insTC ; c.4996C>T ; c.6084del ; c.1202G>A ; NM_000132.3(F8):c.3548_3549delAA ; c.3922G>T ; c.3736del ; c.5337del ; c.5675dup ; c.3860del ; c.4446dup ; c.2089_2090del ; c.452_462del ; c.4280del ; c.4345del ; c.4345G>T ; c.4542del ; c.4201C>T ; c.4242dup ; c.333del ; c.185C>G ; c.4460del ; NM_000132.3:c.514_515insTCAAGATA ; c.3300del ; c.871G>T ; NM_000132.3(F8):c.6263C>T ; c.482del ; NM_000132.3(F8):c.7031G>A ; c.4770T>A ; c.72del ; c.1175C>G ; c.1390G>T ; c.6253G>T ; c.3416_3417del ; NM_000132.3(F8):c.1596_1597insG ; c.796G>T ; c.3994_3997del ; c.5953del ; c.4519del ; c.472C>T ; c.2397del ; c.1203G>A ; c.465G>A ; c.5960_5961del ; c.1595G>A ; c.4895del ; c.5766C>A ; c.6116_6117del ; c.5696dup ; c.4561C>T ; c.4272del ; c.224del ; c.2419dup ; c.685_686del ; c.98G>A ; c.471G>A ; NM_000132.3(F8):c.4473C>A ; c.4712_4715del ; NM_000132.3(F8):c.1175C>A ; c.1560del ; NM_000132.3(F8):c.6016G>T ; c.4918G>T ; c.3490del ; c.1311del ; c.5923dup ; c.495+1G>A ; c.5914_5915del ; c.680G>A ; c.4987A>T ; c.6120T>A ; c.3984dup ; c.4483del ; c.4483G>T ; NM_000132.3:c.1440_1441insA ; c.4473C>G ; c.2338del ; c.4686del ; c.4103del ; NM_000132.3(F8):c.2029T>C ; c.1200_1201del ; c.4805_4806del ; c.1947_1950del ; c.4798A>T ; NM_000132.3(F8):c.6912_6916delAAATC ; NM_000132.3(F8):c.4858delC ; c.3224del ; NM_000132.3(F8):c.493C>T ; c.6273+1G>A ; NM_000132.3(F8):c.1214T>G ; c.4899del ; c.60del ; c.5227_5228del ; c.4241C>A ; c.5869C>T ; c.5752del ; c.788-1G>T ; c.96del ; c.2000del ; c.919del ; c.4423C>T ; c.4512del ; c.2360del ; NM_000132.3(F8):c.5719_5720insA ; c.1596G>A ; c.3505del ; c.5271del ; c.6115+2T>C ; c.583del ; c.695_698del ; c.4848del ; c.3887del ; c.3830del ; c.3168_3187del ; NM_000132.3(F8):c.1075_1078delAATG ; c.1996_1999del ; c.3710del ; NM_000132.3(F8):c.832G>A ; c.1331_1332del ; c.3766G>T ; c.514_515del ; c.3851_3852del ; c.1443+1G>A ; NM_000132.3(F8):c.1726G>T ; c.3756del ; NM_000132.3(F8):c.4293_4297delCTCTT ; c.355del ; c.334G>T ; c.4720del ; c.4543_4544delinsA ; c.2102_2106del ; c.4492_4493del ; NM_000132.3(F8):c.1078_1079delGA ; c.421G>T ; c.265+1G>T ; NM_000132.3(F8):c.6533G>A ; c.4672_4675del ; c.3255_3258del ; c.64_65del ; c.3289C>T ; NM_000132.3(F8):c.199_200delAA ; c.143+1G>A ; NM_000132.3(F8):c.822G>A ; c.788-2A>T

F8	Symptomatic form of hemophilia A in female carriers	Symptomatic hemophilia A in female carriers is a form of hemophilia A (see this term) that manifests in some women with mutations in the F8 gene (Xq28), encoding coagulation factor VIII.	Symptoms include abnormal bleeding as a result of minor injuries, or following surgery or tooth extraction. Spontaneous hemorrhages may occur occasionally.	NM_000132.3(F8):c.872A>G ; c.788-1G>C ; c.6130del ; c.3251C>G ; c.4339dup ; c.4382_4383del ; c.3152del ; c.1438_1439del ; c.6070dup ; NM_000132.3(F8):c.687_688delAG ; c.889del ; c.415C>T ; c.1941_1944del ; c.3833del ; c.985dup ; c.2373dup ; c.3053del ; c.4619del ; c.4935G>A ; c.446del ; c.355C>T ; NM_000132.3(F8):c.1630G>A ; c.3409_3410del ; c.4999del ; c.5243del ; c.1538-2A>T ; c.1165del ; c.4719_4729del ; c.4662_4663del ; c.3907_3911del ; c.3991_3992del ; c.1653T>G ; NM_000132.3(F8):c.6464_6465delAA ; c.63_64del ; c.4408G>T ; c.3385del ; c.3031A>T ; NM_000132.3(F8):c.5879G>T ; c.4035del ; NM_000132.3(F8):c.1293delG ; c.516del ; c.1904-1G>A ; c.6136dup ; c.3913C>T ; c.4474A>T ; c.616G>T ; c.4934G>A ; c.89del ; c.1990_1991del ; c.420T>A ; c.3735_3744delinsATTTCTTTTTCTTT ; c.3863dup ; c.4969C>T ; NM_000132.3(F8):c.404A>G ; c.5301C>A ; c.6089dup ; c.985del ; c.5348_5357del ; c.1357G>T ; c.5697del ; c.510del ; c.709C>T ; c.3624del ; c.3402del ; NM_000132.3(F8):c.943delG ; c.729del ; c.6120_6135del ; c.3607G>T ; c.566C>A ; c.4450del ; c.5964_5967dup ; c.3421C>T ; c.496-2A>G ; c.3417dup ; c.3298A>T ; c.4942C>T ; c.3982C>T ; c.4156C>T ; NM_000132.3(F8):c.907delG ; c.1996_1999dup ; c.560T>A ; NM_000132.3:c.770_771insCC ; c.628_635del ; c.6115+1G>A ; c.4006C>T ; c.169+1G>T ; NM_000132.3(F8):c.849delT ; c.3827C>G ; c.5343T>A ; c.392del ; c.3967C>T ; c.5254del ; c.120del ; c.1410_1413del ; c.173del ; c.2412_2421del ; c.4492del ; c.974_975del ; c.1925_1928del ; c.1675G>T ; c.6116-2A>G ; c.169+1G>A ; c.850G>T ; c.787+2T>C ; c.4895dup ; NM_000132.3(F8):c.986G>A ; c.4697_4701dup ; c.4430_4431del ; c.4926del ; c.3344del ; c.2409del ; c.3902del ; c.5220-1G>A ; c.3540del ; c.591G>A ; c.1338del ; c.3844A>T ; c.4658del ; NM_000132.3(F8):c.1952A>C ; c.519_523del ; c.6194G>A ; c.2404C>T ; NM_000132.3(F8):c.1988C>T ; c.4199del ; c.4549_4550del ; c.3964C>T ; c.1443+2T>C ; c.5689_5690del ; c.3500dup ; c.788-1G>A ; c.4339del ; c.1394C>G ; c.5010del ; c.4265_4266del ; c.3496A>T ; c.607del ; c.73del ; c.1336dup ; c.195C>A ; c.4922dup ; c.1189dup ; c.948_951del ; c.3631A>T ; c.525C>A ; c.935del ; c.1442_1443dup ; c.3565dup ; c.2058_2059del ; c.160_161del ; c.128dup ; c.4425_4426del ; c.5251A>T ; c.4841del ; c.4072C>T ; c.6078_6079del ; c.3651del ; c.3772del ; c.3302_3303del ; c.6250A>T ; c.4806del ; c.4094_4100del ; NM_000132.3(F8):c.6865C>T ; c.1A>G ; c.3371C>A ; c.3652del ; c.4687del ; c.4492_4496del ; c.4363C>T ; c.3203_3204del ; c.3493G>T ; c.1538-1G>T ; c.2384_2388del ; c.6099del ; c.4318del ; c.92del ; c.201_202dup ; c.335_336del ; c.2032A>T ; c.4694_4697del ; c.4814C>A ; c.2462_2463del ; NM_000132.3:c.3150_3151insTC ; c.4996C>T ; c.6084del ; c.1202G>A ; NM_000132.3(F8):c.3548_3549delAA ; c.3922G>T ; c.3736del ; c.5337del ; c.5675dup ; c.3860del ; c.4446dup ; c.2089_2090del ; c.452_462del ; c.4280del ; c.4345del ; c.4345G>T ; c.4542del ; c.4201C>T ; c.4242dup ; c.333del ; c.185C>G ; c.4460del ; NM_000132.3:c.514_515insTCAAGATA ; c.3300del ; c.871G>T ; NM_000132.3(F8):c.6263C>T ; c.482del ; NM_000132.3(F8):c.7031G>A ; c.4770T>A ; c.72del ; c.1175C>G ; c.1390G>T ; c.6253G>T ; c.3416_3417del ; NM_000132.3(F8):c.1596_1597insG ; c.796G>T ; c.3994_3997del ; c.5953del ; c.4519del ; c.472C>T ; c.2397del ; c.1203G>A ; c.465G>A ; c.5960_5961del ; c.1595G>A ; c.4895del ; c.5766C>A ; c.6116_6117del ; c.5696dup ; c.4561C>T ; c.4272del ; c.224del ; c.2419dup ; c.685_686del ; c.98G>A ; c.471G>A ; NM_000132.3(F8):c.4473C>A ; c.4712_4715del ; NM_000132.3(F8):c.1175C>A ; c.1560del ; NM_000132.3(F8):c.6016G>T ; c.4918G>T ; c.3490del ; c.1311del ; c.5923dup ; c.495+1G>A ; c.5914_5915del ; c.680G>A ; c.4987A>T ; c.6120T>A ; c.3984dup ; c.4483del ; c.4483G>T ; NM_000132.3:c.1440_1441insA ; c.4473C>G ; c.2338del ; c.4686del ; c.4103del ; NM_000132.3(F8):c.2029T>C ; c.1200_1201del ; c.4805_4806del ; c.1947_1950del ; c.4798A>T ; NM_000132.3(F8):c.6912_6916delAAATC ; NM_000132.3(F8):c.4858delC ; c.3224del ; NM_000132.3(F8):c.493C>T ; c.6273+1G>A ; NM_000132.3(F8):c.1214T>G ; c.4899del ; c.60del ; c.5227_5228del ; c.4241C>A ; c.5869C>T ; c.5752del ; c.788-1G>T ; c.96del ; c.2000del ; c.919del ; c.4423C>T ; c.4512del ; c.2360del ; NM_000132.3(F8):c.5719_5720insA ; c.1596G>A ; c.3505del ; c.5271del ; c.6115+2T>C ; c.583del ; c.695_698del ; c.4848del ; c.3887del ; c.3830del ; c.3168_3187del ; NM_000132.3(F8):c.1075_1078delAATG ; c.1996_1999del ; c.3710del ; NM_000132.3(F8):c.832G>A ; c.1331_1332del ; c.3766G>T ; c.514_515del ; c.3851_3852del ; c.1443+1G>A ; NM_000132.3(F8):c.1726G>T ; c.3756del ; NM_000132.3(F8):c.4293_4297delCTCTT ; c.355del ; c.334G>T ; c.4720del ; c.4543_4544delinsA ; c.2102_2106del ; c.4492_4493del ; NM_000132.3(F8):c.1078_1079delGA ; c.421G>T ; c.265+1G>T ; NM_000132.3(F8):c.6533G>A ; c.4672_4675del ; c.3255_3258del ; c.64_65del ; c.3289C>T ; NM_000132.3(F8):c.199_200delAA ; c.143+1G>A ; NM_000132.3(F8):c.822G>A ; c.788-2A>T ; NM_000132.3(F8):c.872A>G ; c.788-1G>C ; c.6130del ; c.3251C>G ; c.4339dup ; c.4382_4383del ; c.3152del ; c.1438_1439del ; c.6070dup ; NM_000132.3(F8):c.687_688delAG ; c.889del ; c.415C>T ; c.1941_1944del ; c.3833del ; c.985dup ; c.2373dup ; c.3053del ; c.4619del ; c.4935G>A ; c.446del ; c.355C>T ; NM_000132.3(F8):c.1630G>A ; c.3409_3410del ; c.4999del ; c.5243del ; c.1538-2A>T ; c.1165del ; c.4719_4729del ; c.4662_4663del ; c.3907_3911del ; c.3991_3992del ; c.1653T>G ; NM_000132.3(F8):c.6464_6465delAA ; c.63_64del ; c.4408G>T ; c.3385del ; c.3031A>T ; NM_000132.3(F8):c.5879G>T ; c.4035del ; NM_000132.3(F8):c.1293delG ; c.516del ; c.1904-1G>A ; c.6136dup ; c.3913C>T ; c.4474A>T ; c.616G>T ; c.4934G>A ; c.89del ; c.1990_1991del ; c.420T>A ; c.3735_3744delinsATTTCTTTTTCTTT ; c.3863dup ; c.4969C>T ; NM_000132.3(F8):c.404A>G ; c.5301C>A ; c.6089dup ; c.985del ; c.5348_5357del ; c.1357G>T ; c.5697del ; c.510del ; c.709C>T ; c.3624del ; c.3402del ; NM_000132.3(F8):c.943delG ; c.729del ; c.6120_6135del ; c.3607G>T ; c.566C>A ; c.4450del ; c.5964_5967dup ; c.3421C>T ; c.496-2A>G ; c.3417dup ; c.3298A>T ; c.4942C>T ; c.3982C>T ; c.4156C>T ; NM_000132.3(F8):c.907delG ; c.1996_1999dup ; c.560T>A ; NM_000132.3:c.770_771insCC ; c.628_635del ; c.6115+1G>A ; c.4006C>T ; c.169+1G>T ; NM_000132.3(F8):c.849delT ; c.3827C>G ; c.5343T>A ; c.392del ; c.3967C>T ; c.5254del ; c.120del ; c.1410_1413del ; c.173del ; c.2412_2421del ; c.4492del ; c.974_975del ; c.1925_1928del ; c.1675G>T ; c.6116-2A>G ; c.169+1G>A ; c.850G>T ; c.787+2T>C ; c.4895dup ; NM_000132.3(F8):c.986G>A ; c.4697_4701dup ; c.4430_4431del ; c.4926del ; c.3344del ; c.2409del ; c.3902del ; c.5220-1G>A ; c.3540del ; c.591G>A ; c.1338del ; c.3844A>T ; c.4658del ; NM_000132.3(F8):c.1952A>C ; c.519_523del ; c.6194G>A ; c.2404C>T ; NM_000132.3(F8):c.1988C>T ; c.4199del ; c.4549_4550del ; c.3964C>T ; c.1443+2T>C ; c.5689_5690del ; c.3500dup ; c.788-1G>A ; c.4339del ; c.1394C>G ; c.5010del ; c.4265_4266del ; c.3496A>T ; c.607del ; c.73del ; c.1336dup ; c.195C>A ; c.4922dup ; c.1189dup ; c.948_951del ; c.3631A>T ; c.525C>A ; c.935del ; c.1442_1443dup ; c.3565dup ; c.2058_2059del ; c.160_161del ; c.128dup ; c.4425_4426del ; c.5251A>T ; c.4841del ; c.4072C>T ; c.6078_6079del ; c.3651del ; c.3772del ; c.3302_3303del ; c.6250A>T ; c.4806del ; c.4094_4100del ; NM_000132.3(F8):c.6865C>T ; c.1A>G ; c.3371C>A ; c.3652del ; c.4687del ; c.4492_4496del ; c.4363C>T ; c.3203_3204del ; c.3493G>T ; c.1538-1G>T ; c.2384_2388del ; c.6099del ; c.4318del ; c.92del ; c.201_202dup ; c.335_336del ; c.2032A>T ; c.4694_4697del ; c.4814C>A ; c.2462_2463del ; NM_000132.3:c.3150_3151insTC ; c.4996C>T ; c.6084del ; c.1202G>A ; NM_000132.3(F8):c.3548_3549delAA ; c.3922G>T ; c.3736del ; c.5337del ; c.5675dup ; c.3860del ; c.4446dup ; c.2089_2090del ; c.452_462del ; c.4280del ; c.4345del ; c.4345G>T ; c.4542del ; c.4201C>T ; c.4242dup ; c.333del ; c.185C>G ; c.4460del ; NM_000132.3:c.514_515insTCAAGATA ; c.3300del ; c.871G>T ; NM_000132.3(F8):c.6263C>T ; c.482del ; NM_000132.3(F8):c.7031G>A ; c.4770T>A ; c.72del ; c.1175C>G ; c.1390G>T ; c.6253G>T ; c.3416_3417del ; NM_000132.3(F8):c.1596_1597insG ; c.796G>T ; c.3994_3997del ; c.5953del ; c.4519del ; c.472C>T ; c.2397del ; c.1203G>A ; c.465G>A ; c.5960_5961del ; c.1595G>A ; c.4895del ; c.5766C>A ; c.6116_6117del ; c.5696dup ; c.4561C>T ; c.4272del ; c.224del ; c.2419dup ; c.685_686del ; c.98G>A ; c.471G>A ; NM_000132.3(F8):c.4473C>A ; c.4712_4715del ; NM_000132.3(F8):c.1175C>A ; c.1560del ; NM_000132.3(F8):c.6016G>T ; c.4918G>T ; c.3490del ; c.1311del ; c.5923dup ; c.495+1G>A ; c.5914_5915del ; c.680G>A ; c.4987A>T ; c.6120T>A ; c.3984dup ; c.4483del ; c.4483G>T ; NM_000132.3:c.1440_1441insA ; c.4473C>G ; c.2338del ; c.4686del ; c.4103del ; NM_000132.3(F8):c.2029T>C ; c.1200_1201del ; c.4805_4806del ; c.1947_1950del ; c.4798A>T ; NM_000132.3(F8):c.6912_6916delAAATC ; NM_000132.3(F8):c.4858delC ; c.3224del ; NM_000132.3(F8):c.493C>T ; c.6273+1G>A ; NM_000132.3(F8):c.1214T>G ; c.4899del ; c.60del ; c.5227_5228del ; c.4241C>A ; c.5869C>T ; c.5752del ; c.788-1G>T ; c.96del ; c.2000del ; c.919del ; c.4423C>T ; c.4512del ; c.2360del ; NM_000132.3(F8):c.5719_5720insA ; c.1596G>A ; c.3505del ; c.5271del ; c.6115+2T>C ; c.583del ; c.695_698del ; c.4848del ; c.3887del ; c.3830del ; c.3168_3187del ; NM_000132.3(F8):c.1075_1078delAATG ; c.1996_1999del ; c.3710del ; NM_000132.3(F8):c.832G>A ; c.1331_1332del ; c.3766G>T ; c.514_515del ; c.3851_3852del ; c.1443+1G>A ; NM_000132.3(F8):c.1726G>T ; c.3756del ; NM_000132.3(F8):c.4293_4297delCTCTT ; c.355del ; c.334G>T ; c.4720del ; c.4543_4544delinsA ; c.2102_2106del ; c.4492_4493del ; NM_000132.3(F8):c.1078_1079delGA ; c.421G>T ; c.265+1G>T ; NM_000132.3(F8):c.6533G>A ; c.4672_4675del ; c.3255_3258del ; c.64_65del ; c.3289C>T ; NM_000132.3(F8):c.199_200delAA ; c.143+1G>A ; NM_000132.3(F8):c.822G>A ; c.788-2A>T

F9	Mild hemophilia B	Mild hemophilia B is a form of hemophilia B (see this term) characterized by a small deficiency of factor IX leading to abnormal bleeding as a result of minor injuries, or following surgery or tooth extraction.	The biological activity of factor IX is between 5 and 40%. Spontaneous hemorrhages do not occur.	NM_000133.3(F9):c.1031T>C ; NM_000133.3(F9):c.79G>A ; NM_000133.3(F9):c.52T>C ; NM_000133.3(F9):c.1136G>A ; NM_000133.3(F9):c.82T>C ; NM_000133.3(F9):c.1150C>T ; NM_000133.3(F9):c.1031T>C ; NM_000133.3(F9):c.79G>A ; NM_000133.3(F9):c.52T>C ; NM_000133.3(F9):c.1136G>A ; NM_000133.3(F9):c.82T>C ; NM_000133.3(F9):c.1150C>T
F9	Moderately severe hemophilia B	Moderately severe hemophilia B is a form of hemophilia B (see this term) characterized by factor IX deficiency leading to abnormal bleeding as a result of minor injuries, or following surgery or tooth extraction.	The biological activity of factor IX is between 1% and 5%. Spontaneous hemorrhages are rare.	NM_000133.3(F9):c.1031T>C ; NM_000133.3(F9):c.79G>A ; NM_000133.3(F9):c.52T>C ; NM_000133.3(F9):c.1136G>A ; NM_000133.3(F9):c.82T>C ; NM_000133.3(F9):c.1150C>T ; NM_000133.3(F9):c.1031T>C ; NM_000133.3(F9):c.79G>A ; NM_000133.3(F9):c.52T>C ; NM_000133.3(F9):c.1136G>A ; NM_000133.3(F9):c.82T>C ; NM_000133.3(F9):c.1150C>T
F9	Severe hemophilia B	Severe hemophilia B is a form of hemophilia B (see this term) characterized by a large deficiency of factor IX leading to frequent spontaneous hemorrhage and abnormal bleeding as a result of minor injuries, or following surgery or tooth extraction.	The biological activity of factor IX is below 1%.	NM_000133.3(F9):c.1031T>C ; NM_000133.3(F9):c.79G>A ; NM_000133.3(F9):c.52T>C ; NM_000133.3(F9):c.1136G>A ; NM_000133.3(F9):c.82T>C ; NM_000133.3(F9):c.1150C>T ; NM_000133.3(F9):c.1031T>C ; NM_000133.3(F9):c.79G>A ; NM_000133.3(F9):c.52T>C ; NM_000133.3(F9):c.1136G>A ; NM_000133.3(F9):c.82T>C ; NM_000133.3(F9):c.1150C>T
F9	Symptomatic form of hemophilia B in female carriers	Symptomatic hemophilia B in female carriers is a form of hemophilia B (see this term) that manifests in some women with mutations in the F9 gene (Xq28), encoding coagulation factor IX.	Symptoms include abnormal bleeding as a result of minor injuries, or following surgery or tooth extraction. Spontaneous hemorrhages may occur occasionally.	NM_000133.3(F9):c.1031T>C ; NM_000133.3(F9):c.79G>A ; NM_000133.3(F9):c.52T>C ; NM_000133.3(F9):c.1136G>A ; NM_000133.3(F9):c.82T>C ; NM_000133.3(F9):c.1150C>T ; NM_000133.3(F9):c.1031T>C ; NM_000133.3(F9):c.79G>A ; NM_000133.3(F9):c.52T>C ; NM_000133.3(F9):c.1136G>A ; NM_000133.3(F9):c.82T>C ; NM_000133.3(F9):c.1150C>T

FAH	Tyrosinemia type 1	Tyrosinemia type 1 (HTI) is an inborn error of tyrosine catabolism caused by defective activity of fumarylacetoacetate hydrolase (FAH) and is characterized by progressive liver disease, renal tubular dysfunction, porphyria-like crises and a dramatic improvement in prognosis following treatment with nitisinone.	HT1 is clinically heterogenous. Symptoms may start during the first few months (acute type), in second half of the first year (subacute type) or in the following years up to adulthood (chronic type). In the acute type, manifestations of hepatic failure predominate (bleeding diathesis, hypoglycemia, ascites etc) with frequent sepsis and rapid deterioration. Mild proximal tubular disease is usually present. Subacute type manifests a similar but less severe clinical picture presenting usually with hepatomegaly or hypophosphatemic rickets (due to tubular dysfunction). Intercurrent illness may precipitate hepatic crisis. Chronic type presents with hepatomegaly secondary to cirrhosis and often tubulopathy, leading to rickets and renal failure. Neurological crises are infrequent presenting symptoms; however they can complicate any type of the disease when untreated. The crises resemble those of acute intermittent porphyria, manifesting with painful parasthesias (causing patients to assume ophisthotonic position, self mutilation), autonomic signs (hypertension, tachycardia, ileus) and respiratory decompensation. All patients stand a high risk of developing hepatocellular carcinoma (HCC) secondary to cirrhosis.	c.837+1G>A ; c.982C>T ; NM_000137.2(FAH):c.786G>A ; NM_000137.2(FAH):c.707-1G>A ; NM_000137.3:c.782C>T ; NM_000137.2(FAH):c.401C>A ; c.939del ; NM_000137.2(FAH):c.1027G>T ; NM_000137.2(FAH):c.1009G>A ; NM_000137.2(FAH):c.47A>T ; NM_000137.2(FAH):c.192G>T ; NM_000137.2(FAH):c.456G>A ; NM_000137.2(FAH):c.1062+5G>A ; NM_000137.2(FAH):c.554-1G>T ; NM_000137.2(FAH):c.1141A>G ; NM_000137.2(FAH):c.1090G>T ; NM_000137.2(FAH):c.1069G>T ; c.837+1G>A ; c.982C>T ; NM_000137.2(FAH):c.786G>A ; NM_000137.2(FAH):c.707-1G>A ; NM_000137.3:c.782C>T ; NM_000137.2(FAH):c.401C>A ; c.939del ; NM_000137.2(FAH):c.1027G>T ; NM_000137.2(FAH):c.1009G>A ; NM_000137.2(FAH):c.47A>T ; NM_000137.2(FAH):c.192G>T ; NM_000137.2(FAH):c.456G>A ; NM_000137.2(FAH):c.1062+5G>A ; NM_000137.2(FAH):c.554-1G>T ; NM_000137.2(FAH):c.1141A>G ; NM_000137.2(FAH):c.1090G>T ; NM_000137.2(FAH):c.1069G>T

FANCA	Fanconi anemia	A rare genetic multisystem disorder characterized by progressive pancytopenia with bone marrow failure, variable congenital malformations and predisposition to develop hematological or solid tumors.	The first signs of Fanconi anemia (FA) are typically non-hematological features. Limb anomalies typically affect the extremities, are unilateral or (usually asymmetric) bilateral. Minor anomalies can also be present such as low birth length and weight, microcephaly and/or microphthalmia. Skin pigmentation abnormalities (cafÃ©-au-lait spots) and hypoplastic thenar eminence are frequent. Almost 20% of patients have ear malformations with or without hearing loss. Congenital malformations may involve other organ systems and vary within families. Short stature is syndromic and/or associated to endocrinopathies. Fertility is frequently impaired in males, and is highly disturbed in half of females. When congenital malformations are not prominent, diagnosis may be delayed until the onset of hematological anomalies. Bone marrow failure (BMF) occurs at a median age of 7 years, developing in 90% of patients by 40 years of age. The first manifestations are macrocytosis (very early) and thrombocytopenia. In patients with somatic mosaÃ¯cism, blood counts may stay normal until occurrence of hematological malignancy. In general, patients are highly predisposed to solid tumors (most frequently head and neck or anogenital regions).	NM_000135.3(FANCA):c.2303T>C ; NM_000135.3(FANCA):c.3558dup ; NM_000135.4:c.3788_3790delTCT ; c.233_236del ; c.3763G>T ; c.4130C>G ; NM_000135.2(FANCA):c.1115_1118delTTGG ; NM_000135.3(FANCA):c.2303T>C ; NM_000135.3(FANCA):c.3558dup ; NM_000135.4:c.3788_3790delTCT ; c.233_236del ; c.3763G>T ; c.4130C>G ; NM_000135.2(FANCA):c.1115_1118delTTGG

FANCC	Fanconi anemia	A rare genetic multisystem disorder characterized by progressive pancytopenia with bone marrow failure, variable congenital malformations and predisposition to develop hematological or solid tumors.	The first signs of Fanconi anemia (FA) are typically non-hematological features. Limb anomalies typically affect the extremities, are unilateral or (usually asymmetric) bilateral. Minor anomalies can also be present such as low birth length and weight, microcephaly and/or microphthalmia. Skin pigmentation abnormalities (cafÃ©-au-lait spots) and hypoplastic thenar eminence are frequent. Almost 20% of patients have ear malformations with or without hearing loss. Congenital malformations may involve other organ systems and vary within families. Short stature is syndromic and/or associated to endocrinopathies. Fertility is frequently impaired in males, and is highly disturbed in half of females. When congenital malformations are not prominent, diagnosis may be delayed until the onset of hematological anomalies. Bone marrow failure (BMF) occurs at a median age of 7 years, developing in 90% of patients by 40 years of age. The first manifestations are macrocytosis (very early) and thrombocytopenia. In patients with somatic mosaÃ¯cism, blood counts may stay normal until occurrence of hematological malignancy. In general, patients are highly predisposed to solid tumors (most frequently head and neck or anogenital regions).	NM_000136.2(FANCC):c.1642C>T ; c.1015del ; NM_000136.2(FANCC):c.37C>T ; NM_000136.2(FANCC):c.67delG ; NM_000136.2(FANCC):c.1103_1104delTG ; NM_000136.2(FANCC):c.1487T>G ; NM_000136.2(FANCC):c.996+1G>T ; NM_000136.2(FANCC):c.1642C>T ; c.1015del ; NM_000136.2(FANCC):c.37C>T ; NM_000136.2(FANCC):c.67delG ; NM_000136.2(FANCC):c.1103_1104delTG ; NM_000136.2(FANCC):c.1487T>G ; NM_000136.2(FANCC):c.996+1G>T

FANCG	Fanconi anemia	A rare genetic multisystem disorder characterized by progressive pancytopenia with bone marrow failure, variable congenital malformations and predisposition to develop hematological or solid tumors.	The first signs of Fanconi anemia (FA) are typically non-hematological features. Limb anomalies typically affect the extremities, are unilateral or (usually asymmetric) bilateral. Minor anomalies can also be present such as low birth length and weight, microcephaly and/or microphthalmia. Skin pigmentation abnormalities (cafÃ©-au-lait spots) and hypoplastic thenar eminence are frequent. Almost 20% of patients have ear malformations with or without hearing loss. Congenital malformations may involve other organ systems and vary within families. Short stature is syndromic and/or associated to endocrinopathies. Fertility is frequently impaired in males, and is highly disturbed in half of females. When congenital malformations are not prominent, diagnosis may be delayed until the onset of hematological anomalies. Bone marrow failure (BMF) occurs at a median age of 7 years, developing in 90% of patients by 40 years of age. The first manifestations are macrocytosis (very early) and thrombocytopenia. In patients with somatic mosaÃ¯cism, blood counts may stay normal until occurrence of hematological malignancy. In general, patients are highly predisposed to solid tumors (most frequently head and neck or anogenital regions).	c.510+1G>A ; c.907_908dup ; NM_004629.1(FANCG):c.313G>T ; NM_004629.1(FANCG):c.1480+1G>C ; c.1795_1804del ; NM_004629.1(FANCG):c.1077-2A>G ; NM_004629.1(FANCG):c.637_643del ; c.510+1G>A ; c.907_908dup ; NM_004629.1(FANCG):c.313G>T ; NM_004629.1(FANCG):c.1480+1G>C ; c.1795_1804del ; NM_004629.1(FANCG):c.1077-2A>G ; NM_004629.1(FANCG):c.637_643del

FH	Fumaric aciduria	Fumaric aciduria (FA), an autosomal recessive metabolic disorder, is most often characterized by early onset but non-specific clinical signs: hypotonia, severe psychomotor impairment, convulsions, respiratory distress, feeding difficulties and frequent cerebral malformations, along with a distinctive facies. Some patients present with only moderate intellectual impairment.	Newborns are frequently microcephalic and may present with facial dysmorphisms. Severe encephalopathy manifests with poor feeding, failure to thrive, hypotonia, lethargy and epileptic seizures. In the most severe cases APGAR scores are low immediately following birth, and bradycardia and respiratory failure may follow. Most children do not achieve visual fixation and are unable to speak or walk. Less severely affected individuals survive beyond childhood, most nonetheless displaying moderate cognitive impairment. Some patients have been reported to present with only moderate cognitive deficits. An increased risk of certain tumors has also been reported, in particular familial leiomyomatosis (see this term).	NM_000143.3(FH):c.1093A>G ; c.901dup ; NM_000143.3(FH):c.1293delA ; NM_000143.3(FH):c.1067T>A ; NM_000143.3(FH):c.697C>T ; NM_000143.3(FH):c.1236+1G>C ; NM_000143.3(FH):c.1446_1449delAAAG ; NM_000143.3(FH):c.1394A>G ; NM_000143.3(FH):c.760C>T ; NM_000143.3(FH):c.320A>C ; NM_000143.3(FH):c.793G>A ; NM_000143.3(FH):c.1255T>C ; NM_000143.3(FH):c.698G>A ; NM_000143.3(FH):c.1200delT ; NM_000143.3(FH):c.1189G>A ; NM_000143.3(FH):c.1093A>G ; c.901dup ; NM_000143.3(FH):c.1293delA ; NM_000143.3(FH):c.1067T>A ; NM_000143.3(FH):c.697C>T ; NM_000143.3(FH):c.1236+1G>C ; NM_000143.3(FH):c.1446_1449delAAAG ; NM_000143.3(FH):c.1394A>G ; NM_000143.3(FH):c.760C>T ; NM_000143.3(FH):c.320A>C ; NM_000143.3(FH):c.793G>A ; NM_000143.3(FH):c.1255T>C ; NM_000143.3(FH):c.698G>A ; NM_000143.3(FH):c.1200delT ; NM_000143.3(FH):c.1189G>A
FH	Hereditary leiomyomatosis and renal cell cancer	Hereditary leiomyomatosis and renal cell cancer (HLRCC) is a hereditary cancer syndrome characterized by a predisposition to cutaneous and uterine leiomyomas and, in some families, to renal cell cancer.	Disease onset can occur at any age, but is more common in young adults and elderly patients. Multiple or single benign cutaneous leiomyomas are common and usually present at around the age of 25 (range from 10-47 years) as firm papules or nodules that are skin colored to light brown. They are usually localized to the trunk and extremities but sometimes on the face. They tend to increase in size and number with age and are usually sensitive to touch and/or cold temperature and, in some, are painful. Uterine leiomyomas (present in 77% of women with HLRCC), also known as fibroids, usually appear around the age of 30 but age at diagnosis can range from 18-52 years. Symptoms of pelvic pain and irregular or heavy menstrual bleeding often occur before they are discovered. Renal tumors (mean age of presentation: 44) are less commonly seen in this syndrome (10-16% of cases) and may present with back pain, although some may be asymptomatic. They are mainly papillary type II renal cell carcinoma and are usually aggressive, often rapidly progressing to metastatic disease and death.	NM_000143.3(FH):c.1093A>G ; c.901dup ; NM_000143.3(FH):c.1293delA ; NM_000143.3(FH):c.1067T>A ; NM_000143.3(FH):c.697C>T ; NM_000143.3(FH):c.1236+1G>C ; NM_000143.3(FH):c.1446_1449delAAAG ; NM_000143.3(FH):c.1394A>G ; NM_000143.3(FH):c.760C>T ; NM_000143.3(FH):c.320A>C ; NM_000143.3(FH):c.793G>A ; NM_000143.3(FH):c.1255T>C ; NM_000143.3(FH):c.698G>A ; NM_000143.3(FH):c.1200delT ; NM_000143.3(FH):c.1189G>A ; NM_000143.3(FH):c.1093A>G ; c.901dup ; NM_000143.3(FH):c.1293delA ; NM_000143.3(FH):c.1067T>A ; NM_000143.3(FH):c.697C>T ; NM_000143.3(FH):c.1236+1G>C ; NM_000143.3(FH):c.1446_1449delAAAG ; NM_000143.3(FH):c.1394A>G ; NM_000143.3(FH):c.760C>T ; NM_000143.3(FH):c.320A>C ; NM_000143.3(FH):c.793G>A ; NM_000143.3(FH):c.1255T>C ; NM_000143.3(FH):c.698G>A ; NM_000143.3(FH):c.1200delT ; NM_000143.3(FH):c.1189G>A

FH	Hereditary pheochromocytoma-paraganglioma	A rare, hereditary, pheochromocytoma/paraganglioma tumor arising from neuroendocrine chromaffin cells of the adrenal medulla (pheochromocytoma) or from any paraganglia from the skull base to the pelvic floor (paraganglioma). Clinical manifestations are often linked to excess catecholamines production causing sustained or paroxysmal elevations in blood pressure, headache, episodic profuse sweating, palpitations, pallor and apprehension or anxiety. Hereditary pheochromocytoma/paraganglioma tumors tend to present at younger ages, to be multi-focal, bilateral, and recurrent, or to have multiple synchronous neoplasms.	0	NM_000143.3(FH):c.1093A>G ; c.901dup ; NM_000143.3(FH):c.1293delA ; NM_000143.3(FH):c.1067T>A ; NM_000143.3(FH):c.697C>T ; NM_000143.3(FH):c.1236+1G>C ; NM_000143.3(FH):c.1446_1449delAAAG ; NM_000143.3(FH):c.1394A>G ; NM_000143.3(FH):c.760C>T ; NM_000143.3(FH):c.320A>C ; NM_000143.3(FH):c.793G>A ; NM_000143.3(FH):c.1255T>C ; NM_000143.3(FH):c.698G>A ; NM_000143.3(FH):c.1200delT ; NM_000143.3(FH):c.1189G>A ; NM_000143.3(FH):c.1093A>G ; c.901dup ; NM_000143.3(FH):c.1293delA ; NM_000143.3(FH):c.1067T>A ; NM_000143.3(FH):c.697C>T ; NM_000143.3(FH):c.1236+1G>C ; NM_000143.3(FH):c.1446_1449delAAAG ; NM_000143.3(FH):c.1394A>G ; NM_000143.3(FH):c.760C>T ; NM_000143.3(FH):c.320A>C ; NM_000143.3(FH):c.793G>A ; NM_000143.3(FH):c.1255T>C ; NM_000143.3(FH):c.698G>A ; NM_000143.3(FH):c.1200delT ; NM_000143.3(FH):c.1189G>A
FKRP	Congenital muscular dystrophy with cerebellar involvement	Congenital muscular dystrophy with cerebellar involvement is a rare, congenital muscular dystrophy due to dystroglycanopathy characterized by proximal muscule weakness with a tendency for muscle hypertrophy and pseudohypertrophy, variable cognitive impairment, microcephaly, cerebellar hypoplasia with or without cysts, and other structural brain anomalies.	Congenital muscular dystrophy-dystroglycanopathy with brain and eye anomalies (type A), which includes both the more severe Walker-Warburg syndrome (WWS) and the slightly less severe muscle-eye-brain disease (MEB), is an autosomal recessive disorder with characteristic brain and eye malformations, profound mental retardation, congenital muscular dystrophy, and death usually in the first years of life. It represents the most severe end of a phenotypic spectrum of similar disorders resulting from defective glycosylation of DAG1 (128239), collectively known as 'dystroglycanopathies'.	NM_024301.4(FKRP):c.1343C>T ; NM_000352.5:c.160C>T ; NM_024301.4(FKRP):c.1387A>G ; NM_024301.4(FKRP):c.1154C>A ; NM_024301.4(FKRP):c.1343C>T ; NM_000352.5:c.160C>T ; NM_024301.4(FKRP):c.1387A>G ; NM_024301.4(FKRP):c.1154C>A

FKRP	Congenital muscular dystrophy with intellectual disability	MDDGB5 is an autosomal recessive congenital muscular dystrophy with impaired intellectual development and structural brain abnormalities.	Congenital muscular dystrophy with intellectual disability is a rare, genetic, congenital muscular dystrophy due to dystroglycanopathy disorder characterized by a wide phenotypic spectrum which includes hypotonia and muscular weakness present at birth or early infancy and delayed or arrested motor development, associated with mild to severe intellectual disability and variable brain abnormalities on neuroimaging studies. Feeding difficulties, joint and spinal deformities, respiratory insufficiency, and ocular anomalies (e.g. strabismus, retinal dystrophy, oculomotor apraxia) may be associated. Decreased or absent alpha-dystroglycan on immunohistochemical muscle staining and elevated serum creatine kinase are observed.	NM_024301.4(FKRP):c.1343C>T ; NM_000352.5:c.160C>T ; NM_024301.4(FKRP):c.1387A>G ; NM_024301.4(FKRP):c.1154C>A ; NM_024301.4(FKRP):c.1343C>T ; NM_000352.5:c.160C>T ; NM_024301.4(FKRP):c.1387A>G ; NM_024301.4(FKRP):c.1154C>A
FKRP	Congenital muscular dystrophy without intellectual disability	MDDGB5 is an autosomal recessive congenital muscular dystrophy with impaired intellectual development and structural brain abnormalities.	Congenital muscular dystrophy with intellectual disability is a rare, genetic, congenital muscular dystrophy due to dystroglycanopathy disorder characterized by a wide phenotypic spectrum which includes hypotonia and muscular weakness present at birth or early infancy and delayed or arrested motor development, associated with mild to severe intellectual disability and variable brain abnormalities on neuroimaging studies. Feeding difficulties, joint and spinal deformities, respiratory insufficiency, and ocular anomalies (e.g. strabismus, retinal dystrophy, oculomotor apraxia) may be associated. Decreased or absent alpha-dystroglycan on immunohistochemical muscle staining and elevated serum creatine kinase are observed.	NM_024301.4(FKRP):c.1343C>T ; NM_000352.5:c.160C>T ; NM_024301.4(FKRP):c.1387A>G ; NM_024301.4(FKRP):c.1154C>A ; NM_024301.4(FKRP):c.1343C>T ; NM_000352.5:c.160C>T ; NM_024301.4(FKRP):c.1387A>G ; NM_024301.4(FKRP):c.1154C>A

FKRP	FKRP-related limb-girdle muscular dystrophy R9	A form of autosomal recessive limb-girdle muscular dystrophy that presents a highly variable age of onset and phenotypic spectrum typically characterized by slowly progressive proximal weakness of the pelvic and shoulder girdle musculature (predominantly affecting the lower limbs), frequently associated with waddling gait, scapular winging, calf and tongue hypertrophy, exercise-induced myalgia, abdominal muscle weakness, cardiomyopathy, respiratory muscle involvement, and myoglobinuria and/or elevated creatine kinase serum levels.	The age of onset is correlated to the genotype and residual expression of fukutin-related protein. Thus, patients homozygous for the common, mild mutation (c.826C>A) usually have an onset in the third decade, while patients compound heterozygous for this mutation have onset before age 10, and loose ambulation around age 20 and need assisted ventilation 5-10 years after that. The manifesting symptoms start in the lower extremities with difficulties raising from a chair, climbing stairs and running. Later proximal weakness starts in the arms with visible scapular winging. Of note, a third of patients may present with myoglobinuria on physical exertion, before weakness is noticed. Patients may develop a cardiomyopathy that requires medical treatment. In rare cases, a cardiac transplant is required. Left ventricular ejection fraction drops on average 0.4% per year. Patients homozygous for the c.826C>A mutation in FKRP loose ambulation around age 60 and may need assisted ventilation at night, but the timing of these losses is highly variable.	NM_024301.4(FKRP):c.1343C>T ; NM_000352.5:c.160C>T ; NM_024301.4(FKRP):c.1387A>G ; NM_024301.4(FKRP):c.1154C>A ; NM_024301.4(FKRP):c.1343C>T ; NM_000352.5:c.160C>T ; NM_024301.4(FKRP):c.1387A>G ; NM_024301.4(FKRP):c.1154C>A

FKRP	Muscle-eye-brain disease	A rare, congenital muscular dystrophy due to dystroglycanopathy characterized by early onset muscular dystrophy, severe muscular hypotonia, severe mental retardation and typical brain and eye malformations, including pachygyria, polymicrogyria, agyria, brainstem and cerebellar structural anomalies, severe myopia, glaucoma, optic nerve and retinal hypoplasia. Patients may present with seizures, macrocephaly or microcephaly, microphthalmia, and congenital contractures. Depending on the severity, limited motor function is acquired. Less severe cases have been reported.	Congenital muscular dystrophy-dystroglycanopathy with brain and eye anomalies (type A), which includes both the more severe Walker-Warburg syndrome (WWS) and the slightly less severe muscle-eye-brain disease (MEB), is an autosomal recessive disorder with characteristic brain and eye malformations, profound mental retardation, congenital muscular dystrophy, and death usually in the first years of life. It represents the most severe end of a phenotypic spectrum of similar disorders resulting from defective glycosylation of DAG1, collectively known as 'dystroglycanopathies'.	NM_024301.4(FKRP):c.1343C>T ; NM_000352.5:c.160C>T ; NM_024301.4(FKRP):c.1387A>G ; NM_024301.4(FKRP):c.1154C>A ; NM_024301.4(FKRP):c.1343C>T ; NM_000352.5:c.160C>T ; NM_024301.4(FKRP):c.1387A>G ; NM_024301.4(FKRP):c.1154C>A
FKRP	Walker-Warburg syndrome	Walker-Warburg Syndrome (WWS) is a rare form of congenital muscular dystrophy associated with brain and eye abnormalities.	Patients present at birth with generalized severe hypotonia, muscle weakness, absent or very poor psychomotor development, eye involvement and seizures. Brain MRI shows type II cobblestone lissencephaly, hydrocephalus (see these terms), severe brainstem and cerebellar hypoplasia (Dandy-Walker malformation is possible, see this term). White matter abnormalities are also observed.	NM_024301.4(FKRP):c.1343C>T ; NM_000352.5:c.160C>T ; NM_024301.4(FKRP):c.1387A>G ; NM_024301.4(FKRP):c.1154C>A ; NM_024301.4(FKRP):c.1343C>T ; NM_000352.5:c.160C>T ; NM_024301.4(FKRP):c.1387A>G ; NM_024301.4(FKRP):c.1154C>A

FKTN	Congenital muscular dystrophy without intellectual disability	MDDGB5 is an autosomal recessive congenital muscular dystrophy with impaired intellectual development and structural brain abnormalities.	Congenital muscular dystrophy with intellectual disability is a rare, genetic, congenital muscular dystrophy due to dystroglycanopathy disorder characterized by a wide phenotypic spectrum which includes hypotonia and muscular weakness present at birth or early infancy and delayed or arrested motor development, associated with mild to severe intellectual disability and variable brain abnormalities on neuroimaging studies. Feeding difficulties, joint and spinal deformities, respiratory insufficiency, and ocular anomalies (e.g. strabismus, retinal dystrophy, oculomotor apraxia) may be associated. Decreased or absent alpha-dystroglycan on immunohistochemical muscle staining and elevated serum creatine kinase are observed.	NM_001079802.1(FKTN):c.509C>A ; NM_006731.2(FKTN):c.411C>A ; NM_001079802.1(FKTN):c.509C>A ; NM_006731.2(FKTN):c.411C>A
FKTN	Congenital muscular dystrophy, Fukuyama type	Fukuyama type muscular dystrophy (FCMD) is a congenital progressive muscular dystrophy characterized by brain malformation (cobblestone lissencephaly), dystrophic changes in skeletal muscle, severe intellectual deficit, epilepsy and motor impairment.	Disease onset typically occurs in early infancy. Initial symptoms include a poor suck, weak cry, floppiness and developmental delay. Symmetrical generalized muscle weakness and hypotonia are present. Patients have contractures of the hips, knees and interphalangeal joints. Later features include myopathic facial appearance, pseudohypertrophy of the calves and forearms, and ophthalmologic abnormalities (visual impairment and retinal dysplasia). Progressive cardiac involvement, and swallowing and feeding disturbances (leading to recurrent aspiration pneumonia and death) occur in infants with severe FCMD and in patients over ten years of age. Seizures (generalized tonic-clonic convulsions, complex partial seizures and partial seizures with secondary generalization, infantile spasms, tonic seizures and myoclonic seizures) occur in over 50% of affected individuals (median age of seizure onset 1-3 years of age). All patients have severe intellectual deficit and the intelligence quotient (IQ) is usually between 30 and 60.	NM_001079802.1(FKTN):c.509C>A ; NM_006731.2(FKTN):c.411C>A ; NM_001079802.1(FKTN):c.509C>A ; NM_006731.2(FKTN):c.411C>A

FKTN	Familial isolated dilated cardiomyopathy	A rare familial cardiomyopathy characterized by the dilation of left ventricle and progressively impairing of systolic ventricular function, in the absence of abnormal loading conditions or coronary artery disease sufficient to cause global systolic impairment. The disease may cause heart failure or arrhythmia. The disease is isolated when no additional atypical cardiac or extracardiac manifestations are present.	The disease is defined by the presence of two major clinical criteria: left ventricular (LV) fractional shortening less than 25% and/or LV ejection fraction less than 45% with LV end diastolic diameter greater than 117% of the predicted value (corrected for age and body surface area based on Henry's formula), in the absence of abnormal loading conditions or coronary artery disease sufficient to cause global systolic impairment. The disease can develop at any age, in either sex. LV mass is often greatly increased in this disorder but LV wall thickness is normal. Symptoms of heart failure may be present as well as arrhythmias. Other presentations include the incidental detection of asymptomatic cardiomegaly and symptoms related to coexisting conduction disturbance or thromboembolic complications. Typically, there is a history of DCM in the family.	NM_001079802.1(FKTN):c.509C>A ; NM_006731.2(FKTN):c.411C>A ; NM_001079802.1(FKTN):c.509C>A ; NM_006731.2(FKTN):c.411C>A
FKTN	Fukutin-related limb-girdle muscular dystrophy R13	A form of limb-girdle muscular dystrophy characterized by an infantile onset of hypotonia, axial and proximal lower limb weakness (with severe weakness noted after febrile illnesses), cardiomyopathy and normal or reduced intelligence. Hypertrophy of calves, thighs, and triceps have also been reported in some cases.	MDDGA4 is a severe autosomal recessive muscular dystrophy-dystroglycanopathy with characteristic brain and eye malformations, seizures, and mental retardation. Cardiac involvement in FCMD/MEB occurs in the second decade of life in those who survive. FKTN-related Walker-Warburg syndrome is a more severe manifestation of the disorder, with death usually in the first year of life.	NM_001079802.1(FKTN):c.509C>A ; NM_006731.2(FKTN):c.411C>A ; NM_001079802.1(FKTN):c.509C>A ; NM_006731.2(FKTN):c.411C>A

FKTN	Muscle-eye-brain disease	A rare, congenital muscular dystrophy due to dystroglycanopathy characterized by early onset muscular dystrophy, severe muscular hypotonia, severe mental retardation and typical brain and eye malformations, including pachygyria, polymicrogyria, agyria, brainstem and cerebellar structural anomalies, severe myopia, glaucoma, optic nerve and retinal hypoplasia. Patients may present with seizures, macrocephaly or microcephaly, microphthalmia, and congenital contractures. Depending on the severity, limited motor function is acquired. Less severe cases have been reported.	Congenital muscular dystrophy-dystroglycanopathy with brain and eye anomalies (type A), which includes both the more severe Walker-Warburg syndrome (WWS) and the slightly less severe muscle-eye-brain disease (MEB), is an autosomal recessive disorder with characteristic brain and eye malformations, profound mental retardation, congenital muscular dystrophy, and death usually in the first years of life. It represents the most severe end of a phenotypic spectrum of similar disorders resulting from defective glycosylation of DAG1, collectively known as 'dystroglycanopathies'.	NM_001079802.1(FKTN):c.509C>A ; NM_006731.2(FKTN):c.411C>A ; NM_001079802.1(FKTN):c.509C>A ; NM_006731.2(FKTN):c.411C>A
FKTN	Walker-Warburg syndrome	Walker-Warburg Syndrome (WWS) is a rare form of congenital muscular dystrophy associated with brain and eye abnormalities.	Patients present at birth with generalized severe hypotonia, muscle weakness, absent or very poor psychomotor development, eye involvement and seizures. Brain MRI shows type II cobblestone lissencephaly, hydrocephalus (see these terms), severe brainstem and cerebellar hypoplasia (Dandy-Walker malformation is possible, see this term). White matter abnormalities are also observed.	NM_001079802.1(FKTN):c.509C>A ; NM_006731.2(FKTN):c.411C>A ; NM_001079802.1(FKTN):c.509C>A ; NM_006731.2(FKTN):c.411C>A

G6PC	Glycogen storage disease due to glucose-6-phosphatase deficiency type Ia	Glycogenosis due to glucose-6-phosphatase deficiency (G6P) type a, or glycogen storage disease (GSD) type 1a, is a type of glycogenosis due to G6P deficiency (see this term).	The disease may manifest at birth by enlarged liver or, more commonly, between the ages of three to four months by symptoms of fast-induced hypoglycemia (tremors, seizures, cyanosis, and apnea). Patients present disturbed glucose homeostasis usually characterized by poor tolerance to fasting, significant hepatomegaly (sometimes eight to ten cm below the right costal margin), growth retardation (short stature and delayed puberty), generally improved by an appropriate diet, osteopenia and, in some cases, osteoporosis, round doll-like facial appearance with full cheeks, mild hypotonia, nephromegaly, and platelet dysfunction that may lead to frequent epistaxis. Diarrhea may be encountered. Late complications are hepatic (adenomas with rare but possible transformation into hepatocellular carcinoma) and renal (glomerular hyperfiltration leading to proteinuria and sometimes to renal failure), but also include anemia, sometimes severe, and a risk of hypoglycemic brain damage. Pulmonary hypertension has been reported in few cases.	NM_000151.3(G6PC):c.497T>G ; NM_000151.3(G6PC):c.508C>T ; NM_000151.3(G6PC):c.379_380dupTA ; NM_000151.3(G6PC):c.551G>A ; NM_000151.3(G6PC):c.248G>A ; NM_000151.3(G6PC):c.447-1G>A ; NM_000151.4:c.247C>T ; NM_000151.3(G6PC):c.229T>C ; NM_000151.3(G6PC):c.1039C>T ; NM_000151.3(G6PC):c.562G>C ; NM_000151.3(G6PC):c.230+1G>C ; NM_000151.3(G6PC):c.113A>T ; NM_000151.3(G6PC):c.883C>T ; NM_000151.3(G6PC):c.370G>A ; NM_000151.3(G6PC):c.497T>G ; NM_000151.3(G6PC):c.508C>T ; NM_000151.3(G6PC):c.379_380dupTA ; NM_000151.3(G6PC):c.551G>A ; NM_000151.3(G6PC):c.248G>A ; NM_000151.3(G6PC):c.447-1G>A ; NM_000151.4:c.247C>T ; NM_000151.3(G6PC):c.229T>C ; NM_000151.3(G6PC):c.1039C>T ; NM_000151.3(G6PC):c.562G>C ; NM_000151.3(G6PC):c.230+1G>C ; NM_000151.3(G6PC):c.113A>T ; NM_000151.3(G6PC):c.883C>T ; NM_000151.3(G6PC):c.370G>A
GAA	Glycogen storage disease due to acid maltase deficiency, infantile onset	Glycogen storage disease due to acid maltase deficiency, infantile onset is the most severe form of glycogen storage disease due to acid maltase deficiency, characterized by cardiomegaly with respiratory distress, muscle weakness and feeding difficulties. It is often fatal.	Glycogen storage disease II, an autosomal recessive disorder, is the prototypic lysosomal storage disease. In the classic infantile form (Pompe disease), cardiomyopathy and muscular hypotonia are the cardinal features; in the juvenile and adult forms, involvement of skeletal muscles dominates the clinical picture.	c.1847dup ; NM_000152.4(GAA):c.1933G>T ; NM_000152.3(GAA):c.1548G>A ; c.1431del ; c.546+2_546+5del ; NM_000152.4(GAA):c.1912G>T ; NM_000152.4(GAA):c.1115A>T ; NM_000152.4(GAA):c.546G>C ; NM_000152.4(GAA):c.1935C>A ; NM_000152.3(GAA):c.307T>G ; c.698del ; NM_000152.3(GAA):c.525delT ; NM_000152.4(GAA):c.1585_1586delTCinsGT ; NM_000152.3:c.1827_1828insA ; NM_000152.3(GAA):c.655G>A ; NM_000152.3(GAA):c.2238G>A ; c.1327-2A>G ; NM_000152.3(GAA):c.2560C>T ; c.1650dup ; NM_000152.4(GAA):c.1465G>A ; NM_000152.4(GAA):c.1561G>A ; NM_000152.4(GAA):c.2512C>T ; NM_000152.3(GAA):c.1552-3C>G ; NM_000152.4(GAA):c.2066_2070dup ; NM_000152.4(GAA):c.1799G>A ; NM_000152.4(GAA):c.2238G>C ; NM_000152.4(GAA):c.2012T>G ; NM_000152.4(GAA):c.768dup ; c.2041-1G>A ; NM_000152.3(GAA):c.2237G>A ; NM_000152.5:c.1064T>C ; NM_000152.4(GAA):c.1316T>A ; NM_000152.4(GAA):c.2544del ; NM_000152.4(GAA):c.1927G>A ; NM_000152.4(GAA):c.877G>A ; NM_000152.3(GAA):c.2015G>A ; NM_000152.3(GAA):c.118C>T ; NM_000152.4(GAA):c.1634C>T ; NM_000152.4(GAA):c.546G>A ; NM_000152.3(GAA):c.925G>A ; NM_000152.4(GAA):c.2105G>T ; c.1847dup ; NM_000152.4(GAA):c.1933G>T ; NM_000152.3(GAA):c.1548G>A ; c.1431del ; c.546+2_546+5del ; NM_000152.4(GAA):c.1912G>T ; NM_000152.4(GAA):c.1115A>T ; NM_000152.4(GAA):c.546G>C ; NM_000152.4(GAA):c.1935C>A ; NM_000152.3(GAA):c.307T>G ; c.698del ; NM_000152.3(GAA):c.525delT ; NM_000152.4(GAA):c.1585_1586delTCinsGT ; NM_000152.3:c.1827_1828insA ; NM_000152.3(GAA):c.655G>A ; NM_000152.3(GAA):c.2238G>A ; c.1327-2A>G ; NM_000152.3(GAA):c.2560C>T ; c.1650dup ; NM_000152.4(GAA):c.1465G>A ; NM_000152.4(GAA):c.1561G>A ; NM_000152.4(GAA):c.2512C>T ; NM_000152.3(GAA):c.1552-3C>G ; NM_000152.4(GAA):c.2066_2070dup ; NM_000152.4(GAA):c.1799G>A ; NM_000152.4(GAA):c.2238G>C ; NM_000152.4(GAA):c.2012T>G ; NM_000152.4(GAA):c.768dup ; c.2041-1G>A ; NM_000152.3(GAA):c.2237G>A ; NM_000152.5:c.1064T>C ; NM_000152.4(GAA):c.1316T>A ; NM_000152.4(GAA):c.2544del ; NM_000152.4(GAA):c.1927G>A ; NM_000152.4(GAA):c.877G>A ; NM_000152.3(GAA):c.2015G>A ; NM_000152.3(GAA):c.118C>T ; NM_000152.4(GAA):c.1634C>T ; NM_000152.4(GAA):c.546G>A ; NM_000152.3(GAA):c.925G>A ; NM_000152.4(GAA):c.2105G>T

GAA	Glycogen storage disease due to acid maltase deficiency, late-onset	Glycogen storage disease due to acid maltase deficiency, late onset (AMDL), a form of Glycogen storage disease due to acid maltase deficiency (AMD), a degenerative metabolic myopathy particularly affecting respiratory and skeletal muscles, is characterized by an accumulation of glycogen in lysosomes.	Glycogen storage disease II, an autosomal recessive disorder, is the prototypic lysosomal storage disease. In the classic infantile form (Pompe disease), cardiomyopathy and muscular hypotonia are the cardinal features; in the juvenile and adult forms, involvement of skeletal muscles dominates the clinical picture.	c.1847dup ; NM_000152.4(GAA):c.1933G>T ; NM_000152.3(GAA):c.1548G>A ; c.1431del ; c.546+2_546+5del ; NM_000152.4(GAA):c.1912G>T ; NM_000152.4(GAA):c.1115A>T ; NM_000152.4(GAA):c.546G>C ; NM_000152.4(GAA):c.1935C>A ; NM_000152.3(GAA):c.307T>G ; c.698del ; NM_000152.3(GAA):c.525delT ; NM_000152.4(GAA):c.1585_1586delTCinsGT ; NM_000152.3:c.1827_1828insA ; NM_000152.3(GAA):c.655G>A ; NM_000152.3(GAA):c.2238G>A ; c.1327-2A>G ; NM_000152.3(GAA):c.2560C>T ; c.1650dup ; NM_000152.4(GAA):c.1465G>A ; NM_000152.4(GAA):c.1561G>A ; NM_000152.4(GAA):c.2512C>T ; NM_000152.3(GAA):c.1552-3C>G ; NM_000152.4(GAA):c.2066_2070dup ; NM_000152.4(GAA):c.1799G>A ; NM_000152.4(GAA):c.2238G>C ; NM_000152.4(GAA):c.2012T>G ; NM_000152.4(GAA):c.768dup ; c.2041-1G>A ; NM_000152.3(GAA):c.2237G>A ; NM_000152.5:c.1064T>C ; NM_000152.4(GAA):c.1316T>A ; NM_000152.4(GAA):c.2544del ; NM_000152.4(GAA):c.1927G>A ; NM_000152.4(GAA):c.877G>A ; NM_000152.3(GAA):c.2015G>A ; NM_000152.3(GAA):c.118C>T ; NM_000152.4(GAA):c.1634C>T ; NM_000152.4(GAA):c.546G>A ; NM_000152.3(GAA):c.925G>A ; NM_000152.4(GAA):c.2105G>T ; c.1847dup ; NM_000152.4(GAA):c.1933G>T ; NM_000152.3(GAA):c.1548G>A ; c.1431del ; c.546+2_546+5del ; NM_000152.4(GAA):c.1912G>T ; NM_000152.4(GAA):c.1115A>T ; NM_000152.4(GAA):c.546G>C ; NM_000152.4(GAA):c.1935C>A ; NM_000152.3(GAA):c.307T>G ; c.698del ; NM_000152.3(GAA):c.525delT ; NM_000152.4(GAA):c.1585_1586delTCinsGT ; NM_000152.3:c.1827_1828insA ; NM_000152.3(GAA):c.655G>A ; NM_000152.3(GAA):c.2238G>A ; c.1327-2A>G ; NM_000152.3(GAA):c.2560C>T ; c.1650dup ; NM_000152.4(GAA):c.1465G>A ; NM_000152.4(GAA):c.1561G>A ; NM_000152.4(GAA):c.2512C>T ; NM_000152.3(GAA):c.1552-3C>G ; NM_000152.4(GAA):c.2066_2070dup ; NM_000152.4(GAA):c.1799G>A ; NM_000152.4(GAA):c.2238G>C ; NM_000152.4(GAA):c.2012T>G ; NM_000152.4(GAA):c.768dup ; c.2041-1G>A ; NM_000152.3(GAA):c.2237G>A ; NM_000152.5:c.1064T>C ; NM_000152.4(GAA):c.1316T>A ; NM_000152.4(GAA):c.2544del ; NM_000152.4(GAA):c.1927G>A ; NM_000152.4(GAA):c.877G>A ; NM_000152.3(GAA):c.2015G>A ; NM_000152.3(GAA):c.118C>T ; NM_000152.4(GAA):c.1634C>T ; NM_000152.4(GAA):c.546G>A ; NM_000152.3(GAA):c.925G>A ; NM_000152.4(GAA):c.2105G>T
GALC	Adult Krabbe disease	A rare lysosomal disorder that affects the white matter of the central and peripheral nervous systems characterized by neurodegeneration with severity depending on the age of onset (infantile, late-infantile, juvenile, adolescent and adulthood).	The infantile form has an onset at 2-6 months of age and is divided into 3 stages. In the first stage, symptoms include irritability, stiffness, poor head control, feeding difficulties, intermittent thumb clasp, episodes of increased temperature, and developmental delay. In the second stage, hypertonic episodes occur with opisthotonus, myoclonic seizures, developmental regression, fisting and vision deficits. In the third stage, hypotonia, blindness and deafness occur. Patients progress into a vegetative state and usually die before the age of 2-3 years, generally due to respiratory infections. In the late infantile/juvenile (1-16 years) and adult (>16 years) forms, the presenting symptoms vary greatly and progression is variable (generally slower in older patients). Patients with late infantile /juvenile onset most resemble infantile patients, while the first signs in adult forms are often weakness, gait disturbances (spastic paraparesis or ataxia), burning paresthesias, hemiplegia, and/or vision loss, with or without peripheral neuropathy. Cognitive regression is variable and often absent in adult forms. In the later-onset forms the disease progresses at a slower rate than infantile patients with some adults living until the sixth decade with mild symptoms.	NM_000153.3(GALC):c.1161+2T>G ; NM_000153.3(GALC):c.1153G>T ; NM_000153.4(GALC):c.1814dup ; NM_000153.4:c.1796T>G ; c.1695del ; c.1488_1489del ; NM_000153.3(GALC):c.388G>A ; c.655C>T ; NM_000153.3(GALC):c.1591C>T ; NM_000153.3(GALC):c.1592G>A ; NM_000153.3(GALC):c.628A>T ; NM_000153.3:c.1723_1724insT ; NM_000153.3(GALC):c.205C>T ; c.1964del ; c.582+1G>A ; c.2056T>C ; c.1489+2_1489+3del ; NM_000153.3(GALC):c.1488_1489+2delTGGT ; NM_000153.3(GALC):c.658C>T ; NM_000153.3(GALC):c.1700A>C ; NM_000153.3(GALC):c.953C>G ; NM_000153.3(GALC):c.1586C>T ; NM_000153.3(GALC):c.1472delA ; NC_000014.9:g.87984523C>T ; NC_000014.9:g.87965534T>C ; NM_000153.3(GALC):c.430delA ; NM_000153.3(GALC):c.1161+2T>G ; NM_000153.3(GALC):c.1153G>T ; NM_000153.4(GALC):c.1814dup ; NM_000153.4:c.1796T>G ; c.1695del ; c.1488_1489del ; NM_000153.3(GALC):c.388G>A ; c.655C>T ; NM_000153.3(GALC):c.1591C>T ; NM_000153.3(GALC):c.1592G>A ; NM_000153.3(GALC):c.628A>T ; NM_000153.3:c.1723_1724insT ; NM_000153.3(GALC):c.205C>T ; c.1964del ; c.582+1G>A ; c.2056T>C ; c.1489+2_1489+3del ; NM_000153.3(GALC):c.1488_1489+2delTGGT ; NM_000153.3(GALC):c.658C>T ; NM_000153.3(GALC):c.1700A>C ; NM_000153.3(GALC):c.953C>G ; NM_000153.3(GALC):c.1586C>T ; NM_000153.3(GALC):c.1472delA ; NC_000014.9:g.87984523C>T ; NC_000014.9:g.87965534T>C ; NM_000153.3(GALC):c.430delA

GALC	Infantile Krabbe disease	A rare lysosomal disorder that affects the white matter of the central and peripheral nervous systems characterized by neurodegeneration with severity depending on the age of onset (infantile, late-infantile, juvenile, adolescent and adulthood).	The infantile form has an onset at 2-6 months of age and is divided into 3 stages. In the first stage, symptoms include irritability, stiffness, poor head control, feeding difficulties, intermittent thumb clasp, episodes of increased temperature, and developmental delay. In the second stage, hypertonic episodes occur with opisthotonus, myoclonic seizures, developmental regression, fisting and vision deficits. In the third stage, hypotonia, blindness and deafness occur. Patients progress into a vegetative state and usually die before the age of 2-3 years, generally due to respiratory infections. In the late infantile/juvenile (1-16 years) and adult (>16 years) forms, the presenting symptoms vary greatly and progression is variable (generally slower in older patients). Patients with late infantile /juvenile onset most resemble infantile patients, while the first signs in adult forms are often weakness, gait disturbances (spastic paraparesis or ataxia), burning paresthesias, hemiplegia, and/or vision loss, with or without peripheral neuropathy. Cognitive regression is variable and often absent in adult forms. In the later-onset forms the disease progresses at a slower rate than infantile patients with some adults living until the sixth decade with mild symptoms.	NM_000153.3(GALC):c.1161+2T>G ; NM_000153.3(GALC):c.1153G>T ; NM_000153.4(GALC):c.1814dup ; NM_000153.4:c.1796T>G ; c.1695del ; c.1488_1489del ; NM_000153.3(GALC):c.388G>A ; c.655C>T ; NM_000153.3(GALC):c.1591C>T ; NM_000153.3(GALC):c.1592G>A ; NM_000153.3(GALC):c.628A>T ; NM_000153.3:c.1723_1724insT ; NM_000153.3(GALC):c.205C>T ; c.1964del ; c.582+1G>A ; c.2056T>C ; c.1489+2_1489+3del ; NM_000153.3(GALC):c.1488_1489+2delTGGT ; NM_000153.3(GALC):c.658C>T ; NM_000153.3(GALC):c.1700A>C ; NM_000153.3(GALC):c.953C>G ; NM_000153.3(GALC):c.1586C>T ; NM_000153.3(GALC):c.1472delA ; NC_000014.9:g.87984523C>T ; NC_000014.9:g.87965534T>C ; NM_000153.3(GALC):c.430delA ; NM_000153.3(GALC):c.1161+2T>G ; NM_000153.3(GALC):c.1153G>T ; NM_000153.4(GALC):c.1814dup ; NM_000153.4:c.1796T>G ; c.1695del ; c.1488_1489del ; NM_000153.3(GALC):c.388G>A ; c.655C>T ; NM_000153.3(GALC):c.1591C>T ; NM_000153.3(GALC):c.1592G>A ; NM_000153.3(GALC):c.628A>T ; NM_000153.3:c.1723_1724insT ; NM_000153.3(GALC):c.205C>T ; c.1964del ; c.582+1G>A ; c.2056T>C ; c.1489+2_1489+3del ; NM_000153.3(GALC):c.1488_1489+2delTGGT ; NM_000153.3(GALC):c.658C>T ; NM_000153.3(GALC):c.1700A>C ; NM_000153.3(GALC):c.953C>G ; NM_000153.3(GALC):c.1586C>T ; NM_000153.3(GALC):c.1472delA ; NC_000014.9:g.87984523C>T ; NC_000014.9:g.87965534T>C ; NM_000153.3(GALC):c.430delA

GALC	Late-infantile/juvenile Krabbe disease	A rare lysosomal disorder that affects the white matter of the central and peripheral nervous systems characterized by neurodegeneration with severity depending on the age of onset (infantile, late-infantile, juvenile, adolescent and adulthood).	The infantile form has an onset at 2-6 months of age and is divided into 3 stages. In the first stage, symptoms include irritability, stiffness, poor head control, feeding difficulties, intermittent thumb clasp, episodes of increased temperature, and developmental delay. In the second stage, hypertonic episodes occur with opisthotonus, myoclonic seizures, developmental regression, fisting and vision deficits. In the third stage, hypotonia, blindness and deafness occur. Patients progress into a vegetative state and usually die before the age of 2-3 years, generally due to respiratory infections. In the late infantile/juvenile (1-16 years) and adult (>16 years) forms, the presenting symptoms vary greatly and progression is variable (generally slower in older patients). Patients with late infantile /juvenile onset most resemble infantile patients, while the first signs in adult forms are often weakness, gait disturbances (spastic paraparesis or ataxia), burning paresthesias, hemiplegia, and/or vision loss, with or without peripheral neuropathy. Cognitive regression is variable and often absent in adult forms. In the later-onset forms the disease progresses at a slower rate than infantile patients with some adults living until the sixth decade with mild symptoms.	NM_000153.3(GALC):c.1161+2T>G ; NM_000153.3(GALC):c.1153G>T ; NM_000153.4(GALC):c.1814dup ; NM_000153.4:c.1796T>G ; c.1695del ; c.1488_1489del ; NM_000153.3(GALC):c.388G>A ; c.655C>T ; NM_000153.3(GALC):c.1591C>T ; NM_000153.3(GALC):c.1592G>A ; NM_000153.3(GALC):c.628A>T ; NM_000153.3:c.1723_1724insT ; NM_000153.3(GALC):c.205C>T ; c.1964del ; c.582+1G>A ; c.2056T>C ; c.1489+2_1489+3del ; NM_000153.3(GALC):c.1488_1489+2delTGGT ; NM_000153.3(GALC):c.658C>T ; NM_000153.3(GALC):c.1700A>C ; NM_000153.3(GALC):c.953C>G ; NM_000153.3(GALC):c.1586C>T ; NM_000153.3(GALC):c.1472delA ; NC_000014.9:g.87984523C>T ; NC_000014.9:g.87965534T>C ; NM_000153.3(GALC):c.430delA ; NM_000153.3(GALC):c.1161+2T>G ; NM_000153.3(GALC):c.1153G>T ; NM_000153.4(GALC):c.1814dup ; NM_000153.4:c.1796T>G ; c.1695del ; c.1488_1489del ; NM_000153.3(GALC):c.388G>A ; c.655C>T ; NM_000153.3(GALC):c.1591C>T ; NM_000153.3(GALC):c.1592G>A ; NM_000153.3(GALC):c.628A>T ; NM_000153.3:c.1723_1724insT ; NM_000153.3(GALC):c.205C>T ; c.1964del ; c.582+1G>A ; c.2056T>C ; c.1489+2_1489+3del ; NM_000153.3(GALC):c.1488_1489+2delTGGT ; NM_000153.3(GALC):c.658C>T ; NM_000153.3(GALC):c.1700A>C ; NM_000153.3(GALC):c.953C>G ; NM_000153.3(GALC):c.1586C>T ; NM_000153.3(GALC):c.1472delA ; NC_000014.9:g.87984523C>T ; NC_000014.9:g.87965534T>C ; NM_000153.3(GALC):c.430delA

GALT	Classic galactosemia	A life-threatening metabolic disease with onset in the neonatal period. Infants usually develop feeding difficulties, lethargy, and severe liver disease.	When ingesting breast milk or lactose-containing formula, infants develop feeding problems, failure to thrive, and signs of liver damage (jaundice, bleeding tendency, hypoglycemia). In the absence of appropriate treatment (galactose restriction), sepsis (E-coli) and neonatal death may occur. Despite adequate treatment, long-term complications appear including cognitive impairments, motor deficits, ovarian dysfunction with reduced fertility in women and diminished bone density. Male fertility has not yet been thoroughly studied.	NM_000155.3(GALT):c.329-2A>C ; NM_000155.3(GALT):c.113A>C ; NM_000155.3(GALT):c.386T>C ; NM_000155.3(GALT):c.221T>C ; NM_000155.3(GALT):c.290A>G ; NM_000155.3(GALT):c.253-2A>G ; c.118G>T ; NM_000155.3(GALT):c.688-2A>C ; NM_000155.3(GALT):c.957C>A ; NM_000155.3(GALT):c.292G>A ; NM_000155.3(GALT):c.904+1G>T ; NM_000155.3(GALT):c.289_291delAAC ; NM_000155.3(GALT):c.512T>C ; NM_000155.3(GALT):c.442C>T ; NM_000155.3(GALT):c.598delC ; c.158G>A ; NM_000155.3(GALT):c.199C>T ; NM_000155.3(GALT):c.568T>C ; c.790del ; NM_000155.3(GALT):c.443G>A ; NM_000155.3(GALT):c.505C>A ; c.939G>A ; NM_000155.3(GALT):c.563A>G ; NM_000155.3(GALT):c.775C>T ; NM_000155.3(GALT):c.998G>A ; NM_000155.3(GALT):c.584T>C ; NM_000155.3(GALT):c.425T>A ; NM_000155.3(GALT):c.18delC ; NM_000155.3(GALT):c.997C>G ; NM_000155.3(GALT):c.820+13A>G ; NM_000155.3(GALT):c.997C>T ; NM_000155.3(GALT):c.203A>C ; NM_000155.3(GALT):c.1138T>C ; NM_000155.3(GALT):c.132delG ; NM_000155.3(GALT):c.692G>A ; NM_000155.3(GALT):c.947G>A ; NM_000155.3(GALT):c.580T>C ; NM_000155.3(GALT):c.220_221delCT ; NM_000155.3(GALT):c.905-2A>G ; NM_000155.3(GALT):c.265T>G ; NM_000155.3(GALT):c.71_72insA ; NM_001258332.1(GALT):c.274C>T ; NM_000155.3(GALT):c.413C>T ; NM_000155.3(GALT):c.1048delA ; NM_000155.3(GALT):c.855G>T ; NM_000155.3(GALT):c.508-1G>C ; NM_000155.3(GALT):c.985T>C ; NM_000155.3(GALT):c.626A>G ; NM_000155.3(GALT):c.41delCinsTT ; NM_000155.3(GALT):c.602G>A ; NM_000155.3(GALT):c.790_792invCTA ; NM_000155.3(GALT):c.619C>T ; NM_000155.3(GALT):c.130G>A ; NM_000155.3(GALT):c.634C>T ; NM_000155.3(GALT):c.844C>G ; NM_001258332.1(GALT):c.73delT ; NM_000155.3(GALT):c.565_578delGTATGGGCCAGCAG ; NM_000155.3(GALT):c.1052delC ; NM_000155.3(GALT):c.367C>T ; NM_000155.3(GALT):c.610C>T ; NM_000155.3(GALT):c.719_728delTAGTACTGGT ; NM_000155.3(GALT):c.404C>T ; NM_000155.3(GALT):c.428C>T ; NM_000155.3(GALT):c.329-2A>C ; NM_000155.3(GALT):c.113A>C ; NM_000155.3(GALT):c.386T>C ; NM_000155.3(GALT):c.221T>C ; NM_000155.3(GALT):c.290A>G ; NM_000155.3(GALT):c.253-2A>G ; c.118G>T ; NM_000155.3(GALT):c.688-2A>C ; NM_000155.3(GALT):c.957C>A ; NM_000155.3(GALT):c.292G>A ; NM_000155.3(GALT):c.904+1G>T ; NM_000155.3(GALT):c.289_291delAAC ; NM_000155.3(GALT):c.512T>C ; NM_000155.3(GALT):c.442C>T ; NM_000155.3(GALT):c.598delC ; c.158G>A ; NM_000155.3(GALT):c.199C>T ; NM_000155.3(GALT):c.568T>C ; c.790del ; NM_000155.3(GALT):c.443G>A ; NM_000155.3(GALT):c.505C>A ; c.939G>A ; NM_000155.3(GALT):c.563A>G ; NM_000155.3(GALT):c.775C>T ; NM_000155.3(GALT):c.998G>A ; NM_000155.3(GALT):c.584T>C ; NM_000155.3(GALT):c.425T>A ; NM_000155.3(GALT):c.18delC ; NM_000155.3(GALT):c.997C>G ; NM_000155.3(GALT):c.820+13A>G ; NM_000155.3(GALT):c.997C>T ; NM_000155.3(GALT):c.203A>C ; NM_000155.3(GALT):c.1138T>C ; NM_000155.3(GALT):c.132delG ; NM_000155.3(GALT):c.692G>A ; NM_000155.3(GALT):c.947G>A ; NM_000155.3(GALT):c.580T>C ; NM_000155.3(GALT):c.220_221delCT ; NM_000155.3(GALT):c.905-2A>G ; NM_000155.3(GALT):c.265T>G ; NM_000155.3(GALT):c.71_72insA ; NM_001258332.1(GALT):c.274C>T ; NM_000155.3(GALT):c.413C>T ; NM_000155.3(GALT):c.1048delA ; NM_000155.3(GALT):c.855G>T ; NM_000155.3(GALT):c.508-1G>C ; NM_000155.3(GALT):c.985T>C ; NM_000155.3(GALT):c.626A>G ; NM_000155.3(GALT):c.41delCinsTT ; NM_000155.3(GALT):c.602G>A ; NM_000155.3(GALT):c.790_792invCTA ; NM_000155.3(GALT):c.619C>T ; NM_000155.3(GALT):c.130G>A ; NM_000155.3(GALT):c.634C>T ; NM_000155.3(GALT):c.844C>G ; NM_001258332.1(GALT):c.73delT ; NM_000155.3(GALT):c.565_578delGTATGGGCCAGCAG ; NM_000155.3(GALT):c.1052delC ; NM_000155.3(GALT):c.367C>T ; NM_000155.3(GALT):c.610C>T ; NM_000155.3(GALT):c.719_728delTAGTACTGGT ; NM_000155.3(GALT):c.404C>T ; NM_000155.3(GALT):c.428C>T
GAMT	Guanidinoacetate methyltransferase deficiency	Guanidinoacetate methyltransferase (GAMT) deficiency is a creatine deficiency syndrome characterized by global developmental delay/intellectual disability (DD/ID), prominent speech delay, autistic/hyperactive behavioral disorders, seizures, and various types of pyramidal and/or extra-pyramidal manifestations.	Onset of manifestations of GAMT deficiency occurs between 3 months and 3 years of age. Affected individuals have mild to severe intellectual disability with a distinctive deficit in expressive language, regardless of the degree of the intellectual deficit. Seizures, of different types, are observed in most individuals and are often intractable. Behavioral disorders such as hyperactivity and autistic features are also frequent. Patients may also have movement disorders which mainly affect the extra-pyramidal system and manifest as chorea, athetosis and ataxia.	NM_000156.5(GAMT):c.506G>A ; NM_000156.5(GAMT):c.506G>A

GBA	Fetal Gaucher disease	Fetal Gaucher disease is the perinatal lethal form of Gaucher disease (GD; see this term).	This form is particularly severe. The disease manifests in the fetus with a decrease or absence of fetal movements, fetal and placental anasarca, hepatosplenomegaly, ichthyosis, arthrogryposis, facial dysmorphism and fetal thrombocytopenia. Death usually occursÂ in uteroÂ or shortly after birth (<3 months).	NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T ; NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T
GBA	Gaucher disease type 1	Gaucher disease type 1 is the chronic non-neurological form of Gaucher disease (GD; see this term) characterized by organomegaly, bone involvement and cytopenia.	Although the disease can be diagnosed at any age, half of patients are under the age of 20 at diagnosis. The clinical presentation is heterogeneous with occasional asymptomatic forms. It is characterized by the association of frequent asthenia, growth retardation or delayed puberty, splenomegaly (90% of cases) that may be complicated by splenic infarctions (sometimes superinfected), hepatomegaly (80% of cases) and in rare cases can progress towards fibrosis followed by cirrhosis. Bone anomalies are present in 80% of cases. They manifest as deformations, osteopenia that sometimes causes pathological fractures or vertebral compression, bone infarctions or even aseptic osteonecrosis. Involvement of other organs (rarely symptomatic pulmonary, renal and cardiac involvement) is less common. Pancytopenia is frequent and is associated with various degrees of thrombocytopenia (sometimes severe), anemia and, less frequently, leukoneutropenia. Polyclonal hypergammaglobulinemia is often present and is sometimes complicated by monoclonal gammapathy.	NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T ; NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T

GBA	Gaucher disease type 2	Gaucher disease type 2 is the acute neurological form of Gaucher disease (GD; see this term). It is characterized by early-onset and severe neurological involvement of the brainstem, associated with an organomegaly and generally leading to death before the age of 2.	The disease usually presents in infants aged 3 to 6 months with systemic manifestations of hepatosplenomegaly and an early onset and severe neurological syndrome. The first signs are oculomotor paralysis or bilateral fixed strabismus associated with bulbar signs, in particular severe swallowing difficulties, progressive spasticity and dystonic movements. Seizures occur later and manifest as myoclonic epilepsy that is refractory to treatment with antiepileptics.	NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T ; NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T

GBA	Gaucher disease type 3	Gaucher disease type 3 is the subacute neurological form of Gaucher disease (GD; see this term) characterized by progressive encephalopathy and associated with the systemic manifestations (organomegaly, bone involvement, cytopenia) of GD type 1 (see this term).	The clinical presentation is very heterogeneous. Neurological disease appears in childhood or adolescence, a much later onset than in GD type 2 (see this term). Encephalopathy can be the presenting sign of the disease or may occur later in the disease course. Some patients have moderate systemic involvement associated with ophthalmoplegia as the only neurological symptom. For the more severe forms, the neurological signs encountered are variable: supranuclear horizontal ophthalmoplegia, progressive myoclonic epilepsy, cerebellar ataxia, spasticity and dementia. GD type 3 is also associated with the clinical and biological signs of "systemic" disease, such as frequent asthenia, growth retardation or delayed puberty, splenomegaly and hepatomegaly. Bone anomalies may also be present and manifest as deformations, osteopenia, which sometimes leads to pathological fractures or vertebral compression, bone infarctions or even aseptic osteonecrosis. Involvement of other organs (rarely symptomatic pulmonary, renal and cardiac) is less common. Pancytopenia is frequent and involves varying degrees of thrombocytopenia (sometimes severe), anemia and, less frequently, leukoneutropenia. Polyclonal hypergammaglobulinemia is often present and is sometimes complicated by monoclonal gammapathy.	NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T ; NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T

GBA	Gaucher disease-ophthalmoplegia-cardiovascular calcification syndrome	Gaucher disease - ophthalmoplegia - cardiovascular calcification is a variant of Gaucher disease, also known as a Gaucher-like disease that is characterized by cardiac involvement.	The principle manifestation is progressive calcification of the aorta, and of the aortic and/or mitral valves. Other common features include mild splenomegaly, corneal opacities, and supranuclear ophthalmoplegia.	NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T ; NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T
GBA	Hereditary late-onset Parkinson disease	Hereditary late-onset Parkinson disease (LOPD) is a form of Parkinson disease (PD), characterized by an age of onset of more than 50 years, tremor at rest, gait complaints and falls, bradykinesia, rigidity and painful cramps. Patients usually present a low risk of developing non motor symptoms, dystonia, dyskinesia and levodopa-induced dyskinesia (LID).	Onset of LOPD is > 50 years with predominant symptoms including tremor at rest (70% of cases), gait complaints and falls (20%), bradykinesia (20%), rigidity and painful cramps (8%). Compared to young onset PD (YOPD; see this term), a higher risk of developing gait freezing and falls but a lower risk of developing dystonia, dyskinesia and LID have been reported. Patients with hereditary LOPD are also more affected by severe diplopia, cognitive impairment, and gastrointestinal and urinary disorders. LOPD patients report a lower prevalence of non-motor symptoms such as depression, hallucinations, behavioral disturbances (i.e. agitation or impulse control disorder), dementia and apathy.	NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T ; NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T

GBA	NON RARE IN EUROPE: Dementia with Lewy body	Dementia with Lewy bodies (DLB) is a neurodegenerative disorder clinically characterized by dementia and parkinsonism, often with fluctuating cognitive function, visual hallucinations, falls, syncopal episodes, and sensitivity to neuroleptic medication.		NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T ; NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T
GBA	NON RARE IN EUROPE: Parkinson disease	Parkinson disease was first described by James Parkinson in 1817. It is the second most common neurodegenerative disorder after Alzheimer disease (AD), affecting approximately 1% of the population over age 50.	The diagnosis of classic idiopathic PD is primarily clinical, with manifestations including resting tremor, muscular rigidity, bradykinesia, and postural instability. Additional features are characteristic postural abnormalities, dysautonomia, dystonic cramps, and dementia. The disease is progressive and usually has an insidious onset in mid to late adulthood. Pathologic features of classic PD include by a loss of dopaminergic neurons in the substantia nigra (SN) and the presence of Lewy bodies, intracellular inclusions, in surviving neurons in various areas of the brain, particularly the SN.	NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T ; NM_001005741.2(GBA):c.431T>G ; NM_000157.4(GBA):c.160G>T ; NM_001005741.2(GBA):c.1043C>T ; c.1240G>C ; NM_001005741.2(GBA):c.354G>C ; NM_001005741.2(GBA):c.1504C>T ; NM_000157.4:c.1604G>A ; NM_001005741.2(GBA):c.1343A>T ; NM_001005741.3:c.84dupG ; NM_001005741.2(GBA):c.1309G>T ; c.1274dup ; NM_000157.3(GBA):c.1342G>C ; NM_001005741.2(GBA):c.508C>T ; NM_001005741.2(GBA):c.1090G>A ; NM_001005741.2(GBA):c.481C>T ; NM_000157.3(GBA):c.509G>T ; c.407C>A ; NM_000157.4:c.1448T>C ; NM_001005741.2(GBA):c.254G>A ; NM_000157.3(GBA):c.476G>A ; c.1098dup ; NM_001005741.2(GBA):c.1265_1319del55 ; NM_000157.4:c.1448T>G ; NM_001005741.3:c.1297G>T ; NM_001005741.2(GBA):c.1174C>G ; NM_001005741.2(GBA):c.1053G>T ; NM_001005741.2(GBA):c.1348T>A ; NM_001005741.2(GBA):c.487delG ; NM_000157.3(GBA):c.1246G>A ; NM_001005741.2(GBA):c.1240G>T ; NM_001005741.2(GBA):c.1192C>T ; NM_001005741.2(GBA):c.259C>T ; NM_001005741.2(GBA):c.1208G>C ; NM_001005741.3:c.115+1G>A ; NM_001005741.2(GBA):c.586A>C ; c.914del ; NM_001005741.2(GBA):c.1228C>G ; NM_001005741.2(GBA):c.1049A>G ; NM_001005741.2(GBA):c.1319C>T ; NM_001005741.2(GBA):c.1361C>G ; NM_001005741.2(GBA):c.1141T>G ; NM_001005741.2(GBA):c.1171G>C ; NM_001005741.3(GBA):c.497A>T ; NM_000157.3(GBA):c.475C>T ; NM_001005741.2(GBA):c.1085C>T
GBE1	Adult polyglucosan body disease	A glycogen storage disease of adults characterized by progressive upper and lower motor neuron dysfunction, progressive neurogenic bladder and cognitive difficulties that can lead to dementia.	APBD presents after the age of 40, with urinary incontinence (indicative of neurogenic bladder) often being the first manifestation. Progressive spasticity and weakness are also present due to upper and lower motor neuron involvement and patients have difficulty walking. Severity of gait difficulties varies between patients with some requiring a wheelchair at an advanced disease stage. Sensory loss in the distal lower extremities occurs in most individuals and can lead to foot injuries. Cognitive difficulties (such as problems with executive functioning) can be mild but in some cases can lead to dementia.	NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T ; NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T

GBE1	Glycogen storage disease due to glycogen branching enzyme deficiency, adult neuromuscular form	Glycogen branching enzyme (GBE) deficiency (Andersen's disease or amylopectinosis), or glycogen storage disease type 4 (GSD4), is a rare and severe form of glycogen storage disease which accounts for approximately 3% of all the glycogen storage diseases (see these terms).	Clinical presentation is extremely heterogeneous and involves the liver or the neuromuscular system. In the classical form, children are normal at birth, but develop hepatomegaly, hypotonia, and developmental delay during their first months. The disease then rapidly progresses to cirrhosis with portal hypertension and ascites, ultimately causing death in early childhood. A non-progressing hepatic form has been reported in a few cases. In the neuromuscular presentation, the age of onset ranges from fetal to adult age. The most severe form starts before birth with decrease or absence of fetal movements, arthrogryposis, hypoplastic lungs, and perinatal death. Patients with congenital forms have severe hypotonia, cardiomyopathy, depressed respiration and neuronal involvement. Milder forms have been reported with later-onset, marked by muscular weakness or cardiomyopathy and heart failure. Neurological adult forms with central and peripheral nervous system dysfunction have also been described, such as Adult Polyglucosan Body Disease (APBD; see this term), which is characterized by widespread upper and lower motor neuron lesions.	NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T ; NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T

GBE1	Glycogen storage disease due to glycogen branching enzyme deficiency, childhood combined hepatic and myopathic form	Glycogen branching enzyme (GBE) deficiency (Andersen's disease or amylopectinosis), or glycogen storage disease type 4 (GSD4), is a rare and severe form of glycogen storage disease which accounts for approximately 3% of all the glycogen storage diseases (see these terms).	Clinical presentation is extremely heterogeneous and involves the liver or the neuromuscular system. In the classical form, children are normal at birth, but develop hepatomegaly, hypotonia, and developmental delay during their first months. The disease then rapidly progresses to cirrhosis with portal hypertension and ascites, ultimately causing death in early childhood. A non-progressing hepatic form has been reported in a few cases. In the neuromuscular presentation, the age of onset ranges from fetal to adult age. The most severe form starts before birth with decrease or absence of fetal movements, arthrogryposis, hypoplastic lungs, and perinatal death. Patients with congenital forms have severe hypotonia, cardiomyopathy, depressed respiration and neuronal involvement. Milder forms have been reported with later-onset, marked by muscular weakness or cardiomyopathy and heart failure. Neurological adult forms with central and peripheral nervous system dysfunction have also been described, such as Adult Polyglucosan Body Disease (APBD; see this term), which is characterized by widespread upper and lower motor neuron lesions.	NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T ; NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T

GBE1	Glycogen storage disease due to glycogen branching enzyme deficiency, childhood neuromuscular form	Glycogen branching enzyme (GBE) deficiency (Andersen's disease or amylopectinosis), or glycogen storage disease type 4 (GSD4), is a rare and severe form of glycogen storage disease which accounts for approximately 3% of all the glycogen storage diseases (see these terms).	Clinical presentation is extremely heterogeneous and involves the liver or the neuromuscular system. In the classical form, children are normal at birth, but develop hepatomegaly, hypotonia, and developmental delay during their first months. The disease then rapidly progresses to cirrhosis with portal hypertension and ascites, ultimately causing death in early childhood. A non-progressing hepatic form has been reported in a few cases. In the neuromuscular presentation, the age of onset ranges from fetal to adult age. The most severe form starts before birth with decrease or absence of fetal movements, arthrogryposis, hypoplastic lungs, and perinatal death. Patients with congenital forms have severe hypotonia, cardiomyopathy, depressed respiration and neuronal involvement. Milder forms have been reported with later-onset, marked by muscular weakness or cardiomyopathy and heart failure. Neurological adult forms with central and peripheral nervous system dysfunction have also been described, such as Adult Polyglucosan Body Disease (APBD; see this term), which is characterized by widespread upper and lower motor neuron lesions.	NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T ; NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T

GBE1	Glycogen storage disease due to glycogen branching enzyme deficiency, congenital neuromuscular form	Glycogen branching enzyme (GBE) deficiency (Andersen's disease or amylopectinosis), or glycogen storage disease type 4 (GSD4), is a rare and severe form of glycogen storage disease which accounts for approximately 3% of all the glycogen storage diseases (see these terms).	Clinical presentation is extremely heterogeneous and involves the liver or the neuromuscular system. In the classical form, children are normal at birth, but develop hepatomegaly, hypotonia, and developmental delay during their first months. The disease then rapidly progresses to cirrhosis with portal hypertension and ascites, ultimately causing death in early childhood. A non-progressing hepatic form has been reported in a few cases. In the neuromuscular presentation, the age of onset ranges from fetal to adult age. The most severe form starts before birth with decrease or absence of fetal movements, arthrogryposis, hypoplastic lungs, and perinatal death. Patients with congenital forms have severe hypotonia, cardiomyopathy, depressed respiration and neuronal involvement. Milder forms have been reported with later-onset, marked by muscular weakness or cardiomyopathy and heart failure. Neurological adult forms with central and peripheral nervous system dysfunction have also been described, such as Adult Polyglucosan Body Disease (APBD; see this term), which is characterized by widespread upper and lower motor neuron lesions.	NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T ; NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T

GBE1	Glycogen storage disease due to glycogen branching enzyme deficiency, fatal perinatal neuromuscular form	Glycogen branching enzyme (GBE) deficiency (Andersen's disease or amylopectinosis), or glycogen storage disease type 4 (GSD4), is a rare and severe form of glycogen storage disease which accounts for approximately 3% of all the glycogen storage diseases (see these terms).	Clinical presentation is extremely heterogeneous and involves the liver or the neuromuscular system. In the classical form, children are normal at birth, but develop hepatomegaly, hypotonia, and developmental delay during their first months. The disease then rapidly progresses to cirrhosis with portal hypertension and ascites, ultimately causing death in early childhood. A non-progressing hepatic form has been reported in a few cases. In the neuromuscular presentation, the age of onset ranges from fetal to adult age. The most severe form starts before birth with decrease or absence of fetal movements, arthrogryposis, hypoplastic lungs, and perinatal death. Patients with congenital forms have severe hypotonia, cardiomyopathy, depressed respiration and neuronal involvement. Milder forms have been reported with later-onset, marked by muscular weakness or cardiomyopathy and heart failure. Neurological adult forms with central and peripheral nervous system dysfunction have also been described, such as Adult Polyglucosan Body Disease (APBD; see this term), which is characterized by widespread upper and lower motor neuron lesions.	NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T ; NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T

GBE1	Glycogen storage disease due to glycogen branching enzyme deficiency, non progressive hepatic form	Glycogen branching enzyme (GBE) deficiency (Andersen's disease or amylopectinosis), or glycogen storage disease type 4 (GSD4), is a rare and severe form of glycogen storage disease which accounts for approximately 3% of all the glycogen storage diseases (see these terms).	Clinical presentation is extremely heterogeneous and involves the liver or the neuromuscular system. In the classical form, children are normal at birth, but develop hepatomegaly, hypotonia, and developmental delay during their first months. The disease then rapidly progresses to cirrhosis with portal hypertension and ascites, ultimately causing death in early childhood. A non-progressing hepatic form has been reported in a few cases. In the neuromuscular presentation, the age of onset ranges from fetal to adult age. The most severe form starts before birth with decrease or absence of fetal movements, arthrogryposis, hypoplastic lungs, and perinatal death. Patients with congenital forms have severe hypotonia, cardiomyopathy, depressed respiration and neuronal involvement. Milder forms have been reported with later-onset, marked by muscular weakness or cardiomyopathy and heart failure. Neurological adult forms with central and peripheral nervous system dysfunction have also been described, such as Adult Polyglucosan Body Disease (APBD; see this term), which is characterized by widespread upper and lower motor neuron lesions.	NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T ; NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T

GBE1	Glycogen storage disease due to glycogen branching enzyme deficiency, progressive hepatic form	Glycogen branching enzyme (GBE) deficiency (Andersen's disease or amylopectinosis), or glycogen storage disease type 4 (GSD4), is a rare and severe form of glycogen storage disease which accounts for approximately 3% of all the glycogen storage diseases (see these terms).	Clinical presentation is extremely heterogeneous and involves the liver or the neuromuscular system. In the classical form, children are normal at birth, but develop hepatomegaly, hypotonia, and developmental delay during their first months. The disease then rapidly progresses to cirrhosis with portal hypertension and ascites, ultimately causing death in early childhood. A non-progressing hepatic form has been reported in a few cases. In the neuromuscular presentation, the age of onset ranges from fetal to adult age. The most severe form starts before birth with decrease or absence of fetal movements, arthrogryposis, hypoplastic lungs, and perinatal death. Patients with congenital forms have severe hypotonia, cardiomyopathy, depressed respiration and neuronal involvement. Milder forms have been reported with later-onset, marked by muscular weakness or cardiomyopathy and heart failure. Neurological adult forms with central and peripheral nervous system dysfunction have also been described, such as Adult Polyglucosan Body Disease (APBD; see this term), which is characterized by widespread upper and lower motor neuron lesions.	NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T ; NM_000158.3(GBE1):c.1571G>A ; c.2052+1G>A ; NM_000158.3(GBE1):c.1543C>T ; NM_000158.4:c.986A>C ; NM_000158.3(GBE1):c.771T>A ; c.466_470del ; NM_000158.3(GBE1):c.1604A>G ; NM_000158.3(GBE1):c.1774G>T ; NM_000158.3(GBE1):c.1570C>T

GCDH	Glutaryl-CoA dehydrogenase deficiency	Glutaryl-CoA dehydrogenase (GCDH) deficiency (GDD) is an autosomal recessive neurometabolic disorder clinically characterized by encephalopathic crises resulting in striatal injury and a severe dystonic dyskinetic movement disorder.	Neonates are mainly asymptomatic, although 75 % present with macrocephaly and possibly show hypotonia and irritability. If undiagnosed, the initial acute encephalopathic crisis occurs between 3-36 months, typically precipitated by an intercurrent febrile illness, vaccination or a surgical intervention, and characterized by hypotonia, loss of motor skills and convulsions resulting in bilateral striatal injury with severe secondary dystonia and occasionally subdural and retinal hemorrhage. GDD can exceptionally present with hypoglycemia or acidosis. With age (>6 years) and with appropriate treatment, the risk of encephalopathic crises subsides. In some patients, hypotonia and dystonia develop gradually with no encephalopathic crisis, which is known as late-onset or insidious-onset GDD.	NM_000159.3(GCDH):c.1204C>T ; NM_000159.3(GCDH):c.572T>C ; NM_000159.3(GCDH):c.1060G>A ; NM_000159.3(GCDH):c.883T>C ; NM_000159.3(GCDH):c.1198G>A ; NM_000159.3(GCDH):c.1093G>A ; c.74C>A ; NM_000159.3(GCDH):c.764C>T ; NM_000159.3(GCDH):c.680G>C ; NM_000159.3(GCDH):c.271+1G>A ; NM_000159.4(GCDH):c.914C>T ; NM_000159.3(GCDH):c.1262C>T ; NM_000159.3(GCDH):c.1247C>T ; c.1002_1003del ; NM_000159.3(GCDH):c.542A>G ; NM_000159.3(GCDH):c.769C>T ; c.1199dup ; NM_000159.3(GCDH):c.743C>T ; NM_000159.3(GCDH):c.383G>A ; NM_000159.3(GCDH):c.636-1G>A ; NM_000159.3(GCDH):c.1244-2A>C ; NM_000159.3(GCDH):c.751C>T ; NM_000159.3(GCDH):c.1204C>T ; NM_000159.3(GCDH):c.572T>C ; NM_000159.3(GCDH):c.1060G>A ; NM_000159.3(GCDH):c.883T>C ; NM_000159.3(GCDH):c.1198G>A ; NM_000159.3(GCDH):c.1093G>A ; c.74C>A ; NM_000159.3(GCDH):c.764C>T ; NM_000159.3(GCDH):c.680G>C ; NM_000159.3(GCDH):c.271+1G>A ; NM_000159.4(GCDH):c.914C>T ; NM_000159.3(GCDH):c.1262C>T ; NM_000159.3(GCDH):c.1247C>T ; c.1002_1003del ; NM_000159.3(GCDH):c.542A>G ; NM_000159.3(GCDH):c.769C>T ; c.1199dup ; NM_000159.3(GCDH):c.743C>T ; NM_000159.3(GCDH):c.383G>A ; NM_000159.3(GCDH):c.636-1G>A ; NM_000159.3(GCDH):c.1244-2A>C ; NM_000159.3(GCDH):c.751C>T
GFM1	Hepatoencephalopathy due to combined oxidative phosphorylation defect type 1	Combined oxidative phosphorylation deficiency is an autosomal recessive multisystem disorder with variable manifestations resulting from a defect in the mitochondrial oxidative phosphorylation (OXPHOS) system. Onset occurs at or soon after birth, and features can include growth retardation, microcephaly, hypertonicity, axial hypotonia, encephalopathy, cardiomyopathy, and liver dysfunction. Death usually occurs in the first weeks or years of life.	Hepatoencephalopathy due to combined oxidative phosphorylation deficiency type 1 is a rare, inherited mitochondrial disorder due to a defect in mitochondrial protein synthesis characterized by intrauterine growth retardation, metabolic decompensation with recurrent vomiting, persistent severe lactic acidosis, encephalopathy, seizures, failure to thrive, severe global developmental delay, poor eye contact, severe muscular hypotonia or axial hypotonia with limb hypertonia, hepatomegaly and/or liver dysfunction and/or liver failure, leading to fatal outcome in severe cases. Neuroimaging abnormalities may include corpus callosum thinning, leukodystrophy, delayed myelination and basal ganglia involvement.	c.1589_1590del ; c.1354_1357del ; NM_024996.5(GFM1):c.521A>G ; NM_024996.5(GFM1):c.748C>T ; NM_024996.5(GFM1):c.139C>T ; c.1589_1590del ; c.1354_1357del ; NM_024996.5(GFM1):c.521A>G ; NM_024996.5(GFM1):c.748C>T ; NM_024996.5(GFM1):c.139C>T

GJB2	Autosomal dominant non-syndromic sensorineural deafness type DFNA	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	NM_004004.5(GJB2):c.132G>A ; NM_004004.5(GJB2):c.416G>A ; NM_000151.4:c.229T>C ; c.516G>A ; NM_004004.5(GJB2):c.238C>T ; NM_004004.5(GJB2):c.269T>C ; NM_004004.5(GJB2):c.269dupT ; NM_004004.6:c.35delG ; c.402del ; c.310_323del ; NM_004004.5(GJB2):c.250G>C ; c.270dup ; NM_004004.6(GJB2):c.427C>T ; NM_004004.5(GJB2):c.313_326delAAGTTCATCAAGGG ; NM_004004.5(GJB2):c.334_335delAA ; NM_004004.5(GJB2):c.551G>C ; NM_004004.5(GJB2):c.235delC ; NM_004004.5(GJB2):c.365A>T ; NM_004004.5(GJB2):c.139G>T ; NM_004004.5(GJB2):c.299_300delAT ; NM_004004.5(GJB2):c.169C>T ; NM_004004.5(GJB2):c.550C>T ; NM_004004.5(GJB2):c.230G>A ; NM_004004.6(GJB2):c.299A>T ; NM_004004.5(GJB2):c.239A>C ; NM_004004.5(GJB2):c.617A>G ; NM_004004.5(GJB2):c.231G>A ; NM_004004.5(GJB2):c.358_360delGAG ; NM_004004.5(GJB2):c.250G>T ; NM_004004.6(GJB2):c.465T>A ; NM_004004.5(GJB2):c.176_191del16 ; NM_004004.6(GJB2):c.439G>A ; NM_004004.5(GJB2):c.132G>A ; NM_004004.5(GJB2):c.416G>A ; NM_000151.4:c.229T>C ; c.516G>A ; NM_004004.5(GJB2):c.238C>T ; NM_004004.5(GJB2):c.269T>C ; NM_004004.5(GJB2):c.269dupT ; NM_004004.6:c.35delG ; c.402del ; c.310_323del ; NM_004004.5(GJB2):c.250G>C ; c.270dup ; NM_004004.6(GJB2):c.427C>T ; NM_004004.5(GJB2):c.313_326delAAGTTCATCAAGGG ; NM_004004.5(GJB2):c.334_335delAA ; NM_004004.5(GJB2):c.551G>C ; NM_004004.5(GJB2):c.235delC ; NM_004004.5(GJB2):c.365A>T ; NM_004004.5(GJB2):c.139G>T ; NM_004004.5(GJB2):c.299_300delAT ; NM_004004.5(GJB2):c.169C>T ; NM_004004.5(GJB2):c.550C>T ; NM_004004.5(GJB2):c.230G>A ; NM_004004.6(GJB2):c.299A>T ; NM_004004.5(GJB2):c.239A>C ; NM_004004.5(GJB2):c.617A>G ; NM_004004.5(GJB2):c.231G>A ; NM_004004.5(GJB2):c.358_360delGAG ; NM_004004.5(GJB2):c.250G>T ; NM_004004.6(GJB2):c.465T>A ; NM_004004.5(GJB2):c.176_191del16 ; NM_004004.6(GJB2):c.439G>A

GJB2	Autosomal recessive non-syndromic sensorineural deafness type DFNB	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	NM_004004.5(GJB2):c.132G>A ; NM_004004.5(GJB2):c.416G>A ; NM_000151.4:c.229T>C ; c.516G>A ; NM_004004.5(GJB2):c.238C>T ; NM_004004.5(GJB2):c.269T>C ; NM_004004.5(GJB2):c.269dupT ; NM_004004.6:c.35delG ; c.402del ; c.310_323del ; NM_004004.5(GJB2):c.250G>C ; c.270dup ; NM_004004.6(GJB2):c.427C>T ; NM_004004.5(GJB2):c.313_326delAAGTTCATCAAGGG ; NM_004004.5(GJB2):c.334_335delAA ; NM_004004.5(GJB2):c.551G>C ; NM_004004.5(GJB2):c.235delC ; NM_004004.5(GJB2):c.365A>T ; NM_004004.5(GJB2):c.139G>T ; NM_004004.5(GJB2):c.299_300delAT ; NM_004004.5(GJB2):c.169C>T ; NM_004004.5(GJB2):c.550C>T ; NM_004004.5(GJB2):c.230G>A ; NM_004004.6(GJB2):c.299A>T ; NM_004004.5(GJB2):c.239A>C ; NM_004004.5(GJB2):c.617A>G ; NM_004004.5(GJB2):c.231G>A ; NM_004004.5(GJB2):c.358_360delGAG ; NM_004004.5(GJB2):c.250G>T ; NM_004004.6(GJB2):c.465T>A ; NM_004004.5(GJB2):c.176_191del16 ; NM_004004.6(GJB2):c.439G>A ; NM_004004.5(GJB2):c.132G>A ; NM_004004.5(GJB2):c.416G>A ; NM_000151.4:c.229T>C ; c.516G>A ; NM_004004.5(GJB2):c.238C>T ; NM_004004.5(GJB2):c.269T>C ; NM_004004.5(GJB2):c.269dupT ; NM_004004.6:c.35delG ; c.402del ; c.310_323del ; NM_004004.5(GJB2):c.250G>C ; c.270dup ; NM_004004.6(GJB2):c.427C>T ; NM_004004.5(GJB2):c.313_326delAAGTTCATCAAGGG ; NM_004004.5(GJB2):c.334_335delAA ; NM_004004.5(GJB2):c.551G>C ; NM_004004.5(GJB2):c.235delC ; NM_004004.5(GJB2):c.365A>T ; NM_004004.5(GJB2):c.139G>T ; NM_004004.5(GJB2):c.299_300delAT ; NM_004004.5(GJB2):c.169C>T ; NM_004004.5(GJB2):c.550C>T ; NM_004004.5(GJB2):c.230G>A ; NM_004004.6(GJB2):c.299A>T ; NM_004004.5(GJB2):c.239A>C ; NM_004004.5(GJB2):c.617A>G ; NM_004004.5(GJB2):c.231G>A ; NM_004004.5(GJB2):c.358_360delGAG ; NM_004004.5(GJB2):c.250G>T ; NM_004004.6(GJB2):c.465T>A ; NM_004004.5(GJB2):c.176_191del16 ; NM_004004.6(GJB2):c.439G>A

GJB2	Keratoderma hereditarium mutilans	Keratoderma hereditarium mutilans is a rare, diffuse, mutilating, hereditary palmoplantar keratoderma disorder characterized by severe, honeycomb-pattern palmoplantar keratosis and pseudoainhum of the digits leading to autoamputation, associated with mild to moderate congenital sensorineural hearing loss. Additional features include stellate keratosis on the extensor surfaces of the fingers, feet, elbows and knees. Alopecia, onychogryphosis, nail dystrophy or clubbing, spastic paraplegia and myopathy may also be associated.		NM_004004.5(GJB2):c.132G>A ; NM_004004.5(GJB2):c.416G>A ; NM_000151.4:c.229T>C ; c.516G>A ; NM_004004.5(GJB2):c.238C>T ; NM_004004.5(GJB2):c.269T>C ; NM_004004.5(GJB2):c.269dupT ; NM_004004.6:c.35delG ; c.402del ; c.310_323del ; NM_004004.5(GJB2):c.250G>C ; c.270dup ; NM_004004.6(GJB2):c.427C>T ; NM_004004.5(GJB2):c.313_326delAAGTTCATCAAGGG ; NM_004004.5(GJB2):c.334_335delAA ; NM_004004.5(GJB2):c.551G>C ; NM_004004.5(GJB2):c.235delC ; NM_004004.5(GJB2):c.365A>T ; NM_004004.5(GJB2):c.139G>T ; NM_004004.5(GJB2):c.299_300delAT ; NM_004004.5(GJB2):c.169C>T ; NM_004004.5(GJB2):c.550C>T ; NM_004004.5(GJB2):c.230G>A ; NM_004004.6(GJB2):c.299A>T ; NM_004004.5(GJB2):c.239A>C ; NM_004004.5(GJB2):c.617A>G ; NM_004004.5(GJB2):c.231G>A ; NM_004004.5(GJB2):c.358_360delGAG ; NM_004004.5(GJB2):c.250G>T ; NM_004004.6(GJB2):c.465T>A ; NM_004004.5(GJB2):c.176_191del16 ; NM_004004.6(GJB2):c.439G>A ; NM_004004.5(GJB2):c.132G>A ; NM_004004.5(GJB2):c.416G>A ; NM_000151.4:c.229T>C ; c.516G>A ; NM_004004.5(GJB2):c.238C>T ; NM_004004.5(GJB2):c.269T>C ; NM_004004.5(GJB2):c.269dupT ; NM_004004.6:c.35delG ; c.402del ; c.310_323del ; NM_004004.5(GJB2):c.250G>C ; c.270dup ; NM_004004.6(GJB2):c.427C>T ; NM_004004.5(GJB2):c.313_326delAAGTTCATCAAGGG ; NM_004004.5(GJB2):c.334_335delAA ; NM_004004.5(GJB2):c.551G>C ; NM_004004.5(GJB2):c.235delC ; NM_004004.5(GJB2):c.365A>T ; NM_004004.5(GJB2):c.139G>T ; NM_004004.5(GJB2):c.299_300delAT ; NM_004004.5(GJB2):c.169C>T ; NM_004004.5(GJB2):c.550C>T ; NM_004004.5(GJB2):c.230G>A ; NM_004004.6(GJB2):c.299A>T ; NM_004004.5(GJB2):c.239A>C ; NM_004004.5(GJB2):c.617A>G ; NM_004004.5(GJB2):c.231G>A ; NM_004004.5(GJB2):c.358_360delGAG ; NM_004004.5(GJB2):c.250G>T ; NM_004004.6(GJB2):c.465T>A ; NM_004004.5(GJB2):c.176_191del16 ; NM_004004.6(GJB2):c.439G>A

GJB2	KID syndrome	A rare congenital ectodermal disorder characterized by vascularizing keratitis, hyperkeratotic skin lesions and hearing loss.	Patients usually present at birth with generalized erythema and ichthyosiform scaling. The skin manifestations are progressive with erythrokeratoderma characterized by well-demarcated erythematous and keratotic plaques with a verrucous appearance predominantly located on the face, scalp, ears, elbows and knees. Other skin changes include deep furrows around the mouth, palmoplantar hyperkeratosis (PPHK) with leather grain-like keratoderma, follicular HK on the trunk, and spiky HK (hystrix-like ichthyosis) in some cases. The skin lesions are prone to infection and rare fatal cases of severe recurrent infections with septicemia have been reported. Nail dystrophy, alopecia, and sparse or absent eyebrows and eyelashes are also frequent. KID/HID patients have an increased susceptibility for squamous cell and tongue carcinomas. Hearing loss is congenital, usually sensorineural and is often profound. Ocular findings may be absent in some patients but when present onset usually occurs during childhood or adolescence with photophobia, punctate keratitis and progressive corneal vascularization leading to vision loss. The combined vision and hearing loss may lead to severe developmental delay. Cerebellar and neuromuscular defects have been reported in a few cases.	NM_004004.5(GJB2):c.132G>A ; NM_004004.5(GJB2):c.416G>A ; NM_000151.4:c.229T>C ; c.516G>A ; NM_004004.5(GJB2):c.238C>T ; NM_004004.5(GJB2):c.269T>C ; NM_004004.5(GJB2):c.269dupT ; NM_004004.6:c.35delG ; c.402del ; c.310_323del ; NM_004004.5(GJB2):c.250G>C ; c.270dup ; NM_004004.6(GJB2):c.427C>T ; NM_004004.5(GJB2):c.313_326delAAGTTCATCAAGGG ; NM_004004.5(GJB2):c.334_335delAA ; NM_004004.5(GJB2):c.551G>C ; NM_004004.5(GJB2):c.235delC ; NM_004004.5(GJB2):c.365A>T ; NM_004004.5(GJB2):c.139G>T ; NM_004004.5(GJB2):c.299_300delAT ; NM_004004.5(GJB2):c.169C>T ; NM_004004.5(GJB2):c.550C>T ; NM_004004.5(GJB2):c.230G>A ; NM_004004.6(GJB2):c.299A>T ; NM_004004.5(GJB2):c.239A>C ; NM_004004.5(GJB2):c.617A>G ; NM_004004.5(GJB2):c.231G>A ; NM_004004.5(GJB2):c.358_360delGAG ; NM_004004.5(GJB2):c.250G>T ; NM_004004.6(GJB2):c.465T>A ; NM_004004.5(GJB2):c.176_191del16 ; NM_004004.6(GJB2):c.439G>A ; NM_004004.5(GJB2):c.132G>A ; NM_004004.5(GJB2):c.416G>A ; NM_000151.4:c.229T>C ; c.516G>A ; NM_004004.5(GJB2):c.238C>T ; NM_004004.5(GJB2):c.269T>C ; NM_004004.5(GJB2):c.269dupT ; NM_004004.6:c.35delG ; c.402del ; c.310_323del ; NM_004004.5(GJB2):c.250G>C ; c.270dup ; NM_004004.6(GJB2):c.427C>T ; NM_004004.5(GJB2):c.313_326delAAGTTCATCAAGGG ; NM_004004.5(GJB2):c.334_335delAA ; NM_004004.5(GJB2):c.551G>C ; NM_004004.5(GJB2):c.235delC ; NM_004004.5(GJB2):c.365A>T ; NM_004004.5(GJB2):c.139G>T ; NM_004004.5(GJB2):c.299_300delAT ; NM_004004.5(GJB2):c.169C>T ; NM_004004.5(GJB2):c.550C>T ; NM_004004.5(GJB2):c.230G>A ; NM_004004.6(GJB2):c.299A>T ; NM_004004.5(GJB2):c.239A>C ; NM_004004.5(GJB2):c.617A>G ; NM_004004.5(GJB2):c.231G>A ; NM_004004.5(GJB2):c.358_360delGAG ; NM_004004.5(GJB2):c.250G>T ; NM_004004.6(GJB2):c.465T>A ; NM_004004.5(GJB2):c.176_191del16 ; NM_004004.6(GJB2):c.439G>A
GJB2	Knuckle pads-leukonychia-sensorineural deafness-palmoplantar hyperkeratosis syndrome	Bart-Pumphrey syndrome (BAPS) is an autosomal dominant disorder characterized by sensorineural hearing loss, palmoplantar keratoderma, knuckle pads, and leukonychia, which show considerable phenotypic variability.	A rare, syndromic genetic deafness disease characterized by symmetric or asymmetirc knuckle pads (typically located on the distal and interphalangeal joints), leukonychia, diffuse palmoplantar keratoderma, and congenital, mild to moderate sensorineural deafness.	NM_004004.5(GJB2):c.132G>A ; NM_004004.5(GJB2):c.416G>A ; NM_000151.4:c.229T>C ; c.516G>A ; NM_004004.5(GJB2):c.238C>T ; NM_004004.5(GJB2):c.269T>C ; NM_004004.5(GJB2):c.269dupT ; NM_004004.6:c.35delG ; c.402del ; c.310_323del ; NM_004004.5(GJB2):c.250G>C ; c.270dup ; NM_004004.6(GJB2):c.427C>T ; NM_004004.5(GJB2):c.313_326delAAGTTCATCAAGGG ; NM_004004.5(GJB2):c.334_335delAA ; NM_004004.5(GJB2):c.551G>C ; NM_004004.5(GJB2):c.235delC ; NM_004004.5(GJB2):c.365A>T ; NM_004004.5(GJB2):c.139G>T ; NM_004004.5(GJB2):c.299_300delAT ; NM_004004.5(GJB2):c.169C>T ; NM_004004.5(GJB2):c.550C>T ; NM_004004.5(GJB2):c.230G>A ; NM_004004.6(GJB2):c.299A>T ; NM_004004.5(GJB2):c.239A>C ; NM_004004.5(GJB2):c.617A>G ; NM_004004.5(GJB2):c.231G>A ; NM_004004.5(GJB2):c.358_360delGAG ; NM_004004.5(GJB2):c.250G>T ; NM_004004.6(GJB2):c.465T>A ; NM_004004.5(GJB2):c.176_191del16 ; NM_004004.6(GJB2):c.439G>A

GJB2	Palmoplantar keratoderma-deafness syndrome	Palmoplantar keratoderma-deafness syndrome is a keratinization disorder characterized by focal or diffuse palmoplantar keratoderma. A patchy distribution is observed with accentuation on the thenars, hypothenars and the arches of the feet. The disease becomes apparent in infancy and is associated with sensorineural hearing loss that shows a variable age of onset. Due to genetic and clinical similarities, it has been proposed that palmoplantar keratoderma-deafness syndrome, knuckle pads-leukonychia-sensorineural deafness-palmoplantar hyperkeratosis syndrome and keratoderma hereditarium mutilans may represent variants of one broad disorder of syndromic deafness with heterogeneous phenotype. The disease is transmitted in an autosomal dominant manner with incomplete penetrance.		NM_004004.5(GJB2):c.132G>A ; NM_004004.5(GJB2):c.416G>A ; NM_000151.4:c.229T>C ; c.516G>A ; NM_004004.5(GJB2):c.238C>T ; NM_004004.5(GJB2):c.269T>C ; NM_004004.5(GJB2):c.269dupT ; NM_004004.6:c.35delG ; c.402del ; c.310_323del ; NM_004004.5(GJB2):c.250G>C ; c.270dup ; NM_004004.6(GJB2):c.427C>T ; NM_004004.5(GJB2):c.313_326delAAGTTCATCAAGGG ; NM_004004.5(GJB2):c.334_335delAA ; NM_004004.5(GJB2):c.551G>C ; NM_004004.5(GJB2):c.235delC ; NM_004004.5(GJB2):c.365A>T ; NM_004004.5(GJB2):c.139G>T ; NM_004004.5(GJB2):c.299_300delAT ; NM_004004.5(GJB2):c.169C>T ; NM_004004.5(GJB2):c.550C>T ; NM_004004.5(GJB2):c.230G>A ; NM_004004.6(GJB2):c.299A>T ; NM_004004.5(GJB2):c.239A>C ; NM_004004.5(GJB2):c.617A>G ; NM_004004.5(GJB2):c.231G>A ; NM_004004.5(GJB2):c.358_360delGAG ; NM_004004.5(GJB2):c.250G>T ; NM_004004.6(GJB2):c.465T>A ; NM_004004.5(GJB2):c.176_191del16 ; NM_004004.6(GJB2):c.439G>A ; NM_004004.5(GJB2):c.132G>A ; NM_004004.5(GJB2):c.416G>A ; NM_000151.4:c.229T>C ; c.516G>A ; NM_004004.5(GJB2):c.238C>T ; NM_004004.5(GJB2):c.269T>C ; NM_004004.5(GJB2):c.269dupT ; NM_004004.6:c.35delG ; c.402del ; c.310_323del ; NM_004004.5(GJB2):c.250G>C ; c.270dup ; NM_004004.6(GJB2):c.427C>T ; NM_004004.5(GJB2):c.313_326delAAGTTCATCAAGGG ; NM_004004.5(GJB2):c.334_335delAA ; NM_004004.5(GJB2):c.551G>C ; NM_004004.5(GJB2):c.235delC ; NM_004004.5(GJB2):c.365A>T ; NM_004004.5(GJB2):c.139G>T ; NM_004004.5(GJB2):c.299_300delAT ; NM_004004.5(GJB2):c.169C>T ; NM_004004.5(GJB2):c.550C>T ; NM_004004.5(GJB2):c.230G>A ; NM_004004.6(GJB2):c.299A>T ; NM_004004.5(GJB2):c.239A>C ; NM_004004.5(GJB2):c.617A>G ; NM_004004.5(GJB2):c.231G>A ; NM_004004.5(GJB2):c.358_360delGAG ; NM_004004.5(GJB2):c.250G>T ; NM_004004.6(GJB2):c.465T>A ; NM_004004.5(GJB2):c.176_191del16 ; NM_004004.6(GJB2):c.439G>A
GJB2	Porokeratotic eccrine ostial and dermal duct nevus			NM_004004.5(GJB2):c.132G>A ; NM_004004.5(GJB2):c.416G>A ; NM_000151.4:c.229T>C ; c.516G>A ; NM_004004.5(GJB2):c.238C>T ; NM_004004.5(GJB2):c.269T>C ; NM_004004.5(GJB2):c.269dupT ; NM_004004.6:c.35delG ; c.402del ; c.310_323del ; NM_004004.5(GJB2):c.250G>C ; c.270dup ; NM_004004.6(GJB2):c.427C>T ; NM_004004.5(GJB2):c.313_326delAAGTTCATCAAGGG ; NM_004004.5(GJB2):c.334_335delAA ; NM_004004.5(GJB2):c.551G>C ; NM_004004.5(GJB2):c.235delC ; NM_004004.5(GJB2):c.365A>T ; NM_004004.5(GJB2):c.139G>T ; NM_004004.5(GJB2):c.299_300delAT ; NM_004004.5(GJB2):c.169C>T ; NM_004004.5(GJB2):c.550C>T ; NM_004004.5(GJB2):c.230G>A ; NM_004004.6(GJB2):c.299A>T ; NM_004004.5(GJB2):c.239A>C ; NM_004004.5(GJB2):c.617A>G ; NM_004004.5(GJB2):c.231G>A ; NM_004004.5(GJB2):c.358_360delGAG ; NM_004004.5(GJB2):c.250G>T ; NM_004004.6(GJB2):c.465T>A ; NM_004004.5(GJB2):c.176_191del16 ; NM_004004.6(GJB2):c.439G>A ; NM_004004.5(GJB2):c.132G>A ; NM_004004.5(GJB2):c.416G>A ; NM_000151.4:c.229T>C ; c.516G>A ; NM_004004.5(GJB2):c.238C>T ; NM_004004.5(GJB2):c.269T>C ; NM_004004.5(GJB2):c.269dupT ; NM_004004.6:c.35delG ; c.402del ; c.310_323del ; NM_004004.5(GJB2):c.250G>C ; c.270dup ; NM_004004.6(GJB2):c.427C>T ; NM_004004.5(GJB2):c.313_326delAAGTTCATCAAGGG ; NM_004004.5(GJB2):c.334_335delAA ; NM_004004.5(GJB2):c.551G>C ; NM_004004.5(GJB2):c.235delC ; NM_004004.5(GJB2):c.365A>T ; NM_004004.5(GJB2):c.139G>T ; NM_004004.5(GJB2):c.299_300delAT ; NM_004004.5(GJB2):c.169C>T ; NM_004004.5(GJB2):c.550C>T ; NM_004004.5(GJB2):c.230G>A ; NM_004004.6(GJB2):c.299A>T ; NM_004004.5(GJB2):c.239A>C ; NM_004004.5(GJB2):c.617A>G ; NM_004004.5(GJB2):c.231G>A ; NM_004004.5(GJB2):c.358_360delGAG ; NM_004004.5(GJB2):c.250G>T ; NM_004004.6(GJB2):c.465T>A ; NM_004004.5(GJB2):c.176_191del16 ; NM_004004.6(GJB2):c.439G>A

GJB3	Autosomal dominant non-syndromic sensorineural deafness type DFNA			
GJB3	Autosomal dominant non-syndromic sensorineural deafness type DFNB	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in the PDS gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in the COCH gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in the WFS1 gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	

GJB3	Â Erythrokeratodermia variabilis	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in the PDS gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in the COCH gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in the WFS1 gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	

GJB3	Neuropathy with hearing impairment	Erythrokeratoderma variabilis progressiva (EKVP) is a type of erythrokeratoderma characterized by the association of hyperkeratosis and erythema in persistent, although sometimes variable, circumscribed lesions. Progressive symmetric erythrokeratoderma (PSEK) and erythrokeratoderma variabilis (EKV) are probably no longer two distinctive diseases but rather the two clinical manifestations of a same disease, now known as EKVP.	The disease usually starts in the early months of life or later in infancy. Erythema at birth has been described. Patients present with well-demarcated, erythematous patches and hyperkeratotic plaques that are arranged symmetrically. The lesions favor the extensor surface of the upper and lower extremities, buttocks and face. The plaques tend to progress during childhood, with lesions stabilizing thereafter. Considerable clinical overlap exists between PSEK and EKV, the main distinguishing feature being the presence of migratory erythema in patients with EKV. The migratory aspects of the lesions may also change over time, according to lifetime periods. The palms and soles are usually normal but some patients may have palmoplantar keratoderma. Minimal pruritus may be noted. Improvement has rarely been reported.	
GJB6	Autosomal dominant non-syndromic sensorineural deafness type DFNA	This syndrome is characterized by the association of sensorineural hearing impairment and peripheral neuropathy.	The hearing impairment was mild and often asymmetrical. The neuropathy was demyelinating with predominantly sensory involvement but severity was variable ranging from asymptomatic individuals to patients with skin ulcers and osteomyelitis requiring amputation.	c.383_384del ; c.443del ; c.169C>T ; NM_001110219.2(GJB6):c.14C>T ; NM_006783.4(GJB6):c.261dupA ; c.485dup ; c.383_384del ; c.443del ; c.169C>T ; NM_001110219.2(GJB6):c.14C>T ; NM_006783.4(GJB6):c.261dupA ; c.485dup

GJB6	Autosomal recessive non-syndromic sensorineural deafness type DFNB	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	c.383_384del ; c.443del ; c.169C>T ; NM_001110219.2(GJB6):c.14C>T ; NM_006783.4(GJB6):c.261dupA ; c.485dup ; c.383_384del ; c.443del ; c.169C>T ; NM_001110219.2(GJB6):c.14C>T ; NM_006783.4(GJB6):c.261dupA ; c.485dup

GJB6	Hidrotic ectodermal dysplasia	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	c.383_384del ; c.443del ; c.169C>T ; NM_001110219.2(GJB6):c.14C>T ; NM_006783.4(GJB6):c.261dupA ; c.485dup ; c.383_384del ; c.443del ; c.169C>T ; NM_001110219.2(GJB6):c.14C>T ; NM_006783.4(GJB6):c.261dupA ; c.485dup

GJB6	KID syndrome	Clouston syndrome (or hidrotic ectodermal dysplasia) is characterised by the clinical triad of nail dystrophy, alopecia, and palmoplantar hyperkeratosis.	Nail abnormalities are the most consistent feature and frequently manifest at birth or in early infancy. The nails are thickened, slow growing, brittle, often hyperconvex and discoloured with striation. Additional reported features include micronychia, onycholysis and recurrent paronychial infections leading to nail loss. Hair involvement manifests at birth or later during infancy or childhood, and ranges from total to partial, often progressive, alopecia. Residual scalp hair is slow growing, sparse, fine and brittle. Eyebrows and eyelashes are also frequently sparse and axillary, pubic and body hair can be affected. Palmoplantar hyperkeratosis is not a constant finding. When present, it usually begins in childhood and tends to worsen with age; some patients also develop hyperkeratosis and hyperpigmentation over the joints and bony prominences. The teeth are usually unaffected and sweating is normal.	c.383_384del ; c.443del ; c.169C>T ; NM_001110219.2(GJB6):c.14C>T ; NM_006783.4(GJB6):c.261dupA ; c.485dup ; c.383_384del ; c.443del ; c.169C>T ; NM_001110219.2(GJB6):c.14C>T ; NM_006783.4(GJB6):c.261dupA ; c.485dup

GLB1	GM1 gangliosidosis type 1	A rare congenital ectodermal disorder characterized by vascularizing keratitis, hyperkeratotic skin lesions and hearing loss.	Patients usually present at birth with generalized erythema and ichthyosiform scaling. The skin manifestations are progressive with erythrokeratoderma characterized by well-demarcated erythematous and keratotic plaques with a verrucous appearance predominantly located on the face, scalp, ears, elbows and knees. Other skin changes include deep furrows around the mouth, palmoplantar hyperkeratosis (PPHK) with leather grain-like keratoderma, follicular HK on the trunk, and spiky HK (hystrix-like ichthyosis) in some cases. The skin lesions are prone to infection and rare fatal cases of severe recurrent infections with septicemia have been reported. Nail dystrophy, alopecia, and sparse or absent eyebrows and eyelashes are also frequent. KID/HID patients have an increased susceptibility for squamous cell and tongue carcinomas. Hearing loss is congenital, usually sensorineural and is often profound. Ocular findings may be absent in some patients but when present onset usually occurs during childhood or adolescence with photophobia, punctate keratitis and progressive corneal vascularization leading to vision loss. The combined vision and hearing loss may lead to severe developmental delay. Cerebellar and neuromuscular defects have been reported in a few cases.	NM_000404.3(GLB1):c.276G>A ; NM_000404.3(GLB1):c.947A>G ; c.1068+1G>T ; NM_000404.3(GLB1):c.1325G>A ; c.1549G>T ; c.1355dup ; NM_000404.2(GLB1):c.176G>A ; NM_000404.3(GLB1):c.1369C>T ; NM_000404.3(GLB1):c.1174_1175delCT ; NM_000404.3(GLB1):c.901G>A ; NM_000404.3(GLB1):c.1456_1466dupGGTGCATATAT ; NM_000404.3(GLB1):c.1004C>T ; NM_000404.3(GLB1):c.818G>T ; c.591dup ; NM_000404.2(GLB1):c.1646C>T ; NM_000404.3(GLB1):c.1733A>G ; NM_000404.3(GLB1):c.1572dup ; NM_000404.3(GLB1):c.1321G>A ; NM_000404.3(GLB1):c.622C>T ; NM_000404.3(GLB1):c.152T>C ; NM_000404.3(GLB1):c.457+2T>C ; NM_000404.2(GLB1):c.442C>A ; NM_000404.3(GLB1):c.1445G>A ; NM_000404.3(GLB1):c.175C>T ; NM_000404.2(GLB1):c.202C>T ; NM_000404.3(GLB1):c.171C>G ; NM_000404.3(GLB1):c.1051C>T ; NM_000404.2(GLB1):c.442C>T ; NM_000404.3(GLB1):c.1370G>A ; NM_000404.2(GLB1):c.602G>A ; NM_000404.3(GLB1):c.1313G>A ; NM_000404.3(GLB1):c.276G>A ; NM_000404.3(GLB1):c.947A>G ; c.1068+1G>T ; NM_000404.3(GLB1):c.1325G>A ; c.1549G>T ; c.1355dup ; NM_000404.2(GLB1):c.176G>A ; NM_000404.3(GLB1):c.1369C>T ; NM_000404.3(GLB1):c.1174_1175delCT ; NM_000404.3(GLB1):c.901G>A ; NM_000404.3(GLB1):c.1456_1466dupGGTGCATATAT ; NM_000404.3(GLB1):c.1004C>T ; NM_000404.3(GLB1):c.818G>T ; c.591dup ; NM_000404.2(GLB1):c.1646C>T ; NM_000404.3(GLB1):c.1733A>G ; NM_000404.3(GLB1):c.1572dup ; NM_000404.3(GLB1):c.1321G>A ; NM_000404.3(GLB1):c.622C>T ; NM_000404.3(GLB1):c.152T>C ; NM_000404.3(GLB1):c.457+2T>C ; NM_000404.2(GLB1):c.442C>A ; NM_000404.3(GLB1):c.1445G>A ; NM_000404.3(GLB1):c.175C>T ; NM_000404.2(GLB1):c.202C>T ; NM_000404.3(GLB1):c.171C>G ; NM_000404.3(GLB1):c.1051C>T ; NM_000404.2(GLB1):c.442C>T ; NM_000404.3(GLB1):c.1370G>A ; NM_000404.2(GLB1):c.602G>A ; NM_000404.3(GLB1):c.1313G>A
GLB1	GM1 gangliosidosis type 2	GM1 gangliosidosis type 1 is the severe infantile form of GM1 gangliosidosis (see this term) with variable neurological and systemic manifestations.	The onset of this disorder may beÂ in uteroÂ (non immune hydrops fetalis) or by the age of six months. Clinical signs are variable and include arrest/regression of neurological development, hypotonia, visceromegaly, macular cherry-red spots, dysostosis and coarse facial features. Cardiomyopathy may occur.	NM_000404.3(GLB1):c.276G>A ; NM_000404.3(GLB1):c.947A>G ; c.1068+1G>T ; NM_000404.3(GLB1):c.1325G>A ; c.1549G>T ; c.1355dup ; NM_000404.2(GLB1):c.176G>A ; NM_000404.3(GLB1):c.1369C>T ; NM_000404.3(GLB1):c.1174_1175delCT ; NM_000404.3(GLB1):c.901G>A ; NM_000404.3(GLB1):c.1456_1466dupGGTGCATATAT ; NM_000404.3(GLB1):c.1004C>T ; NM_000404.3(GLB1):c.818G>T ; c.591dup ; NM_000404.2(GLB1):c.1646C>T ; NM_000404.3(GLB1):c.1733A>G ; NM_000404.3(GLB1):c.1572dup ; NM_000404.3(GLB1):c.1321G>A ; NM_000404.3(GLB1):c.622C>T ; NM_000404.3(GLB1):c.152T>C ; NM_000404.3(GLB1):c.457+2T>C ; NM_000404.2(GLB1):c.442C>A ; NM_000404.3(GLB1):c.1445G>A ; NM_000404.3(GLB1):c.175C>T ; NM_000404.2(GLB1):c.202C>T ; NM_000404.3(GLB1):c.171C>G ; NM_000404.3(GLB1):c.1051C>T ; NM_000404.2(GLB1):c.442C>T ; NM_000404.3(GLB1):c.1370G>A ; NM_000404.2(GLB1):c.602G>A ; NM_000404.3(GLB1):c.1313G>A

GLB1	GM1 gangliosidosis type 3	GM1 gangliosidosis type 2 is a clinically variable, infancy or childhood-onset form of GM1 gangliosidosis (see this term) characterized by normal early development and psychomotor regression between seven months and three years of age.	Patients with the childhood form of this disorder develop signs and symptoms of intermediate severity including locomotor disturbances, strabismus, muscle weakness, seizures, lethargy and lung infections. Compared to type 1, visceromegaly and skeletal anomalies are milder or may be absent. Macular cherry-red spots are infrequent. The course of the disorder is characterized by slower progression. Facial coarsening develops over time.	NM_000404.3(GLB1):c.276G>A ; NM_000404.3(GLB1):c.947A>G ; c.1068+1G>T ; NM_000404.3(GLB1):c.1325G>A ; c.1549G>T ; c.1355dup ; NM_000404.2(GLB1):c.176G>A ; NM_000404.3(GLB1):c.1369C>T ; NM_000404.3(GLB1):c.1174_1175delCT ; NM_000404.3(GLB1):c.901G>A ; NM_000404.3(GLB1):c.1456_1466dupGGTGCATATAT ; NM_000404.3(GLB1):c.1004C>T ; NM_000404.3(GLB1):c.818G>T ; c.591dup ; NM_000404.2(GLB1):c.1646C>T ; NM_000404.3(GLB1):c.1733A>G ; NM_000404.3(GLB1):c.1572dup ; NM_000404.3(GLB1):c.1321G>A ; NM_000404.3(GLB1):c.622C>T ; NM_000404.3(GLB1):c.152T>C ; NM_000404.3(GLB1):c.457+2T>C ; NM_000404.2(GLB1):c.442C>A ; NM_000404.3(GLB1):c.1445G>A ; NM_000404.3(GLB1):c.175C>T ; NM_000404.2(GLB1):c.202C>T ; NM_000404.3(GLB1):c.171C>G ; NM_000404.3(GLB1):c.1051C>T ; NM_000404.2(GLB1):c.442C>T ; NM_000404.3(GLB1):c.1370G>A ; NM_000404.2(GLB1):c.602G>A ; NM_000404.3(GLB1):c.1313G>A ; NM_000404.3(GLB1):c.276G>A ; NM_000404.3(GLB1):c.947A>G ; c.1068+1G>T ; NM_000404.3(GLB1):c.1325G>A ; c.1549G>T ; c.1355dup ; NM_000404.2(GLB1):c.176G>A ; NM_000404.3(GLB1):c.1369C>T ; NM_000404.3(GLB1):c.1174_1175delCT ; NM_000404.3(GLB1):c.901G>A ; NM_000404.3(GLB1):c.1456_1466dupGGTGCATATAT ; NM_000404.3(GLB1):c.1004C>T ; NM_000404.3(GLB1):c.818G>T ; c.591dup ; NM_000404.2(GLB1):c.1646C>T ; NM_000404.3(GLB1):c.1733A>G ; NM_000404.3(GLB1):c.1572dup ; NM_000404.3(GLB1):c.1321G>A ; NM_000404.3(GLB1):c.622C>T ; NM_000404.3(GLB1):c.152T>C ; NM_000404.3(GLB1):c.457+2T>C ; NM_000404.2(GLB1):c.442C>A ; NM_000404.3(GLB1):c.1445G>A ; NM_000404.3(GLB1):c.175C>T ; NM_000404.2(GLB1):c.202C>T ; NM_000404.3(GLB1):c.171C>G ; NM_000404.3(GLB1):c.1051C>T ; NM_000404.2(GLB1):c.442C>T ; NM_000404.3(GLB1):c.1370G>A ; NM_000404.2(GLB1):c.602G>A ; NM_000404.3(GLB1):c.1313G>A
GLB1	Mucopolysaccharidosis type 4B	GM1 gangliosidosis type 3 is a mild, chronic, adult form of GM1 gangliosidosis (see this term) characterized by onset generally during childhood or adolescence and by cerebellar dysfunction.	Marked variability of clinical signs and age of onset has been reported. Patients generally show slowly progressive dementia, dysarthria, dystonia, short stature, mild vertebral anomalies and ataxia. Eye movements are normal.	NM_000404.3(GLB1):c.276G>A ; NM_000404.3(GLB1):c.947A>G ; c.1068+1G>T ; NM_000404.3(GLB1):c.1325G>A ; c.1549G>T ; c.1355dup ; NM_000404.2(GLB1):c.176G>A ; NM_000404.3(GLB1):c.1369C>T ; NM_000404.3(GLB1):c.1174_1175delCT ; NM_000404.3(GLB1):c.901G>A ; NM_000404.3(GLB1):c.1456_1466dupGGTGCATATAT ; NM_000404.3(GLB1):c.1004C>T ; NM_000404.3(GLB1):c.818G>T ; c.591dup ; NM_000404.2(GLB1):c.1646C>T ; NM_000404.3(GLB1):c.1733A>G ; NM_000404.3(GLB1):c.1572dup ; NM_000404.3(GLB1):c.1321G>A ; NM_000404.3(GLB1):c.622C>T ; NM_000404.3(GLB1):c.152T>C ; NM_000404.3(GLB1):c.457+2T>C ; NM_000404.2(GLB1):c.442C>A ; NM_000404.3(GLB1):c.1445G>A ; NM_000404.3(GLB1):c.175C>T ; NM_000404.2(GLB1):c.202C>T ; NM_000404.3(GLB1):c.171C>G ; NM_000404.3(GLB1):c.1051C>T ; NM_000404.2(GLB1):c.442C>T ; NM_000404.3(GLB1):c.1370G>A ; NM_000404.2(GLB1):c.602G>A ; NM_000404.3(GLB1):c.1313G>A ; NM_000404.3(GLB1):c.276G>A ; NM_000404.3(GLB1):c.947A>G ; c.1068+1G>T ; NM_000404.3(GLB1):c.1325G>A ; c.1549G>T ; c.1355dup ; NM_000404.2(GLB1):c.176G>A ; NM_000404.3(GLB1):c.1369C>T ; NM_000404.3(GLB1):c.1174_1175delCT ; NM_000404.3(GLB1):c.901G>A ; NM_000404.3(GLB1):c.1456_1466dupGGTGCATATAT ; NM_000404.3(GLB1):c.1004C>T ; NM_000404.3(GLB1):c.818G>T ; c.591dup ; NM_000404.2(GLB1):c.1646C>T ; NM_000404.3(GLB1):c.1733A>G ; NM_000404.3(GLB1):c.1572dup ; NM_000404.3(GLB1):c.1321G>A ; NM_000404.3(GLB1):c.622C>T ; NM_000404.3(GLB1):c.152T>C ; NM_000404.3(GLB1):c.457+2T>C ; NM_000404.2(GLB1):c.442C>A ; NM_000404.3(GLB1):c.1445G>A ; NM_000404.3(GLB1):c.175C>T ; NM_000404.2(GLB1):c.202C>T ; NM_000404.3(GLB1):c.171C>G ; NM_000404.3(GLB1):c.1051C>T ; NM_000404.2(GLB1):c.442C>T ; NM_000404.3(GLB1):c.1370G>A ; NM_000404.2(GLB1):c.602G>A ; NM_000404.3(GLB1):c.1313G>A

GLDC	Atypical glycine encephalopathy	A rare lysosomal storage disease characterized by mild to severe spondylo-epiphyso-metaphyseal dysplasia, manifesting with disproportionate short stature (short neck and trunk), joint laxity, pectus carinatum, genum valgum, abnormal gait, tracheal narrowing, spinal abnormalities (kyphosis and scoliosis), respiratory impairment and valvular heart disease.	Clinically, the two forms of MPS, IVA and IVB, have similar skeletal manifestations; however, MPS IVA has a more severe phenotype. MPS IVA is generally diagnosed during the second year of life. Progressive skeletal and joint deformities lead to impairment in walking and daily activities, and include platyspondyly, kyphosis, scoliosis, pectus carinatum, genu valgum, long bone deformities, and joint hyperlaxity (neck, hands, fingers, hips, knees). A rapidly progressive growth failure, with arrest at around 3-5 years of age in severe cases, results in short stature. Potential nervous complications are secondary to skeletal deformations. From the age of 2 to 5 years, hypoplasia of the odontoid vertebra combined with joint hyperlaxity leads to an instability at the level of the first two cervical vertebrae, with a risk of spinal cord compression. Facial dysmorphism includes prominent forehead, large mandible, and short neck. Respiratory impairment, with heavy restriction of lung capacity, susceptibility to pneumonia, and tracheal obstruction/narrowing, is often indicated by life-threatening sleep apnea, cor pulmonale or anesthetic complications. Extra-skeletal manifestations include hepatomegaly, valvulopathies, hearing loss, corneal clouding and dental hypoplasia. Intelligence is normal. Patients typically have low endurance, debilitating fatigue, and pain. Many patients become wheelchair-dependent in their second decade.	NM_000170.2(GLDC):c.2284G>A ; NM_000170.2(GLDC):c.2216G>A ; c.322G>T ; NM_000170.2(GLDC):c.2405C>T ; NM_000170.2(GLDC):c.1166C>T ; NM_000170.2(GLDC):c.1545G>C ; NM_000170.2(GLDC):c.1691G>T ; NM_000170.2(GLDC):c.2284G>A ; NM_000170.2(GLDC):c.2216G>A ; c.322G>T ; NM_000170.2(GLDC):c.2405C>T ; NM_000170.2(GLDC):c.1166C>T ; NM_000170.2(GLDC):c.1545G>C ; NM_000170.2(GLDC):c.1691G>T

GLDC	Infantile glycine encephalopathy	A rare form of glycine encephalopathy presenting disease onset or clinical manifestations that differ from neonatal or infantile glycine encephalopathy.	Symptoms are mostly non-specific and are not similar to the severe neurological symptoms observed in neonatal and infantile GE (see these terms). Some patients have milder disease with onset from late infancy to adulthood, while others have rapidly progressive severe disease often of late onset. It also includes patients with transient hyperglycinemia, whose symptoms in neonatal period resemble those of neonatal form. Manifestations include cognitive decline, behavioral disorders, ataxia, peripheral neuropathy and optic atrophy.	NM_000170.2(GLDC):c.2284G>A ; NM_000170.2(GLDC):c.2216G>A ; c.322G>T ; NM_000170.2(GLDC):c.2405C>T ; NM_000170.2(GLDC):c.1166C>T ; NM_000170.2(GLDC):c.1545G>C ; NM_000170.2(GLDC):c.1691G>T ; NM_000170.2(GLDC):c.2284G>A ; NM_000170.2(GLDC):c.2216G>A ; c.322G>T ; NM_000170.2(GLDC):c.2405C>T ; NM_000170.2(GLDC):c.1166C>T ; NM_000170.2(GLDC):c.1545G>C ; NM_000170.2(GLDC):c.1691G>T
GLDC	Neonatal glycine encephalopathy	Infantile glycine encephalopathy is a mild to severe form of glycine encephalopathy (GE; see this term), characterized by early hypotonia, developmental delay and seizures.	Patients present with infantile-onset seizures and variable psychomotor delay after initially normal development, and often have a relatively long history of hypotonia. Seizures of any type are found in less than half of patients and some develop choreoathetosis. Developmental delay mostly affects language and behavioral problems are sometimes found including temper tantrums, irritability, aggressiveness and rage. Attention deficit-hyperactivity disorder (AD-HD) is also sometimes found. Patients do not have lethargy or coma in the neonatal period, unlike those with neonatal GE. The course may be mild or severe (50% of patients in each case).	NM_000170.2(GLDC):c.2284G>A ; NM_000170.2(GLDC):c.2216G>A ; c.322G>T ; NM_000170.2(GLDC):c.2405C>T ; NM_000170.2(GLDC):c.1166C>T ; NM_000170.2(GLDC):c.1545G>C ; NM_000170.2(GLDC):c.1691G>T ; NM_000170.2(GLDC):c.2284G>A ; NM_000170.2(GLDC):c.2216G>A ; c.322G>T ; NM_000170.2(GLDC):c.2405C>T ; NM_000170.2(GLDC):c.1166C>T ; NM_000170.2(GLDC):c.1545G>C ; NM_000170.2(GLDC):c.1691G>T

GLE1	Amyotrophic lateral sclerosis	Neonatal glycine encephalopathy is a frequent, usually severe form of glycine encephalopathy (GE; see this term) characterized by coma, apnea, hypotonia, seizure and myoclonic jerks in the neonatal period, and subsequent developmental delay.	Patients develop disease manifestations within the first hours or days of life. Symptoms include progressive lethargy, hypotonia, myoclonic jerks leading to apnea. In the absence of intubation and ventilation, apnea may be fatal. With supportive measures, most patients regain spontaneous respiration and some show improvement in alertness over time. Subsequently, they have profound intellectual deficit and increasingly intractable seizures over the first year of life, which often require multiple anticonvulsants. In the vast majority of cases (85%), the course is severe, but some patients have a milder course and less severe clinical outcome. In severe cases, patients make little developmental progress and have limited interaction with their environment. Early spasticity, scoliosis and club feet have also been reported. In milder cases, developmental progress is considerably greater with patients learning to walk and interact, and seizures are generally easier to treat.	c.1412_1413del ; c.898-2A>G ; NM_001003722.1(GLE1):c.2051T>C ; c.2069_2072del ; c.1412_1413del ; c.898-2A>G ; NM_001003722.1(GLE1):c.2051T>C ; c.2069_2072del
GLE1	Arthrogryposis-anterior horn cell disease syndrome	A neurodegenerative disease characterized by progressive muscular paralysis reflecting degeneration of motor neurons in the primary motor cortex, corticospinal tracts, brainstem and spinal cord.	Approximately two thirds of patients with typical ALS have a spinal form of the disease (limb onset) and present with symptoms related to focal muscle weakness and wasting, in which onset of symptoms may start either distally or proximally in the upper and lower limbs. Gradually, spasticity may develop in the weakened atrophic limbs, affecting manual dexterity and gait. Patients with bulbar onset ALS usually present with dysarthria and dysphagia for solids or liquids. Limb symptoms can develop almost simultaneously with bulbar symptoms, and in the vast majority of cases will occur within 1-2 years. Paralysis is progressive and leads to death due to respiratory failure within 2-3 years for bulbar onset cases and 3-5 years for limb onset ALS cases.	c.1412_1413del ; c.898-2A>G ; NM_001003722.1(GLE1):c.2051T>C ; c.2069_2072del ; c.1412_1413del ; c.898-2A>G ; NM_001003722.1(GLE1):c.2051T>C ; c.2069_2072del

GLE1	Lethal congenital contracture syndrome type 1	A rare arthrogryposis syndrome characterized by the association of arthrogryposis multiplex congenita and a severe form of motor neuron disease with loss of anterior horn cells in the spinal cord. Patients present with fetal akinesia deformation sequence with multiple contractures and facial anomalies, such as low-set ears, hypoplastic jaw, and short neck, as well as hypotonia and respiratory insufficiency. Some patients may survive into childhood and show developmental delay, markedly decreased muscle bulk, dystonic and involuntary movements, ataxia, and poor speech.	Congenital arthrogryposis with anterior horn cell disease (CAAHD) is an autosomal recessive neuromuscular disorder with highly variable severity. Affected individuals are usually noted to have contractures in utero on prenatal ultrasound studies, and present at birth with generalized contractures manifest as arthrogryposis multiplex congenita (AMC). Patients have severe hypotonia with respiratory insufficiency, often resulting in death in infancy or early childhood. Some patients may survive into later childhood with supportive care, but may be unable to walk or sit independently due to a combination of muscle weakness and contractures. Cognition may be normal. The disorder also includes multiple congenital anomalies associated with AMC and hypotonia, including high-arched palate, myopathic facies, and bulbar weakness. Neuropathologic studies demonstrate severe loss of anterior horn cells in the spinal cord, as well as diffuse motor neuron axonopathy.	c.1412_1413del ; c.898-2A>G ; NM_001003722.1(GLE1):c.2051T>C ; c.2069_2072del ; c.1412_1413del ; c.898-2A>G ; NM_001003722.1(GLE1):c.2051T>C ; c.2069_2072del
GNE	GNE myopathy	Autosomal recessive lethal congenital contracture syndrome (LCCS) is the most severe, neonatally lethal, form of arthrogryposis, a disorder characterized by congenital nonprogressive joint contractures. The contractures can involve the upper or lower limbs and/or the vertebral column, leading to various degrees of flexion or extension limitations evident at birth.	Lethal congenital contracture syndrome type 1 is a rare, genetic arthrogryposis syndrome characterized by total fetal akinesia (detectable since the 13th week of gestation) accompanied by hydrops, micrognathia, pulmonary hypoplasia, pterygia and multiple joint contractures (usually flexion contractures in the elbows and extension in the knees), leading invariably to death before the 32nd week of gestation. Lack of anterior horn motoneurons, severe atrophy of the ventral spinal cord and severe skeletal muscle hypoplasia are characteristic neuropathological findings, with no evidence of other organ structural anomalies.	NM_001128227.2(GNE):c.1002T>A ; NM_001128227.2(GNE):c.1820G>A ; NM_005476.5(GNE):c.2086G>A ; NM_005476.7:c.2228T>C ; NM_001128227.2(GNE):c.830G>A ; NM_001128227.2(GNE):c.478C>T ; c.880C>T ; NM_001128227.2(GNE):c.1937C>G ; c.2086G>A ; NM_001128227.2(GNE):c.1002T>A ; NM_001128227.2(GNE):c.1820G>A ; NM_005476.5(GNE):c.2086G>A ; NM_005476.7:c.2228T>C ; NM_001128227.2(GNE):c.830G>A ; NM_001128227.2(GNE):c.478C>T ; c.880C>T ; NM_001128227.2(GNE):c.1937C>G ; c.2086G>A

GNE	Sialuria	GNE myopathy is a rare autosomal recessive distal myopathy characterized by early adult-onset, slowly to moderately progressive distal muscle weakness that preferentially affects the tibialis anterior muscle and that usually spares the quadriceps femoris. Muscle biopsy reveals presence of rimmed vacuoles.	The disease usually starts during the third decade of life (but the onset may range from the early teens to the 5th decade). Typically, distal weakness in the legs with foot drop is the first sign, followed by (usually) slow progression to the proximal muscles (thigh) and the upper limbs (hand muscles). Shoulder girdle muscles are subsequently involved, with relative sparing of the triceps. Neck flexor muscles are also commonly affected. A unique clinical pattern of this myopathy is sparing of quadriceps in spite of major involvement of other thigh muscles. Unusual patterns of onset in proximal lower limb musculature and even in the upper limbs have been observed. Ocular, pharyngeal, and cardiac muscles are usually spared. Respiratory muscles are generally not affected until the very late stages in wheelchair-bound patients. Occasionally, affected individuals may present facial weakness.	NM_001128227.2(GNE):c.1002T>A ; NM_001128227.2(GNE):c.1820G>A ; NM_005476.5(GNE):c.2086G>A ; NM_005476.7:c.2228T>C ; NM_001128227.2(GNE):c.830G>A ; NM_001128227.2(GNE):c.478C>T ; c.880C>T ; NM_001128227.2(GNE):c.1937C>G ; c.2086G>A ; NM_001128227.2(GNE):c.1002T>A ; NM_001128227.2(GNE):c.1820G>A ; NM_005476.5(GNE):c.2086G>A ; NM_005476.7:c.2228T>C ; NM_001128227.2(GNE):c.830G>A ; NM_001128227.2(GNE):c.478C>T ; c.880C>T ; NM_001128227.2(GNE):c.1937C>G ; c.2086G>A
GNPTAB	Mucolipidosis type II	Sialuria is a rare inborn error of metabolism in which excessive free sialic acid is synthesized. Clinical features include hepatosplenomegaly, coarse facial features, and varying degrees of developmental delay.	Sialuria is an extremely rare metabolic disorder described in fewer than 10 patients to date and characterized by variable signs and symptoms, mostly in infancy, including transient failure to thrive, slightly prolonged neonatal jaundice, equivocal or mild hepatomegaly, microcytic anemia, frequent upper respiratory infections, gastroenteritis, dehydration and flat and coarse facies. Learning difficulties and seizures may occur in childhood.	c.25C>T ; NM_024312.4(GNPTAB):c.3560_3561delAG ; NM_024312.4(GNPTAB):c.3410T>A ; NM_024312.4(GNPTAB):c.648_651delAGAA ; NM_024312.4(GNPTAB):c.1759C>T ; c.2383del ; NM_024312.4(GNPTAB):c.2896delA ; NM_024312.4(GNPTAB):c.616_619delACAG ; NM_024312.4(GNPTAB):c.3326dupA ; NM_024312.4(GNPTAB):c.749dupA ; NM_024312.4(GNPTAB):c.732_733delAA ; c.3663del ; NM_024312.4(GNPTAB):c.1906dupA ; NM_024312.4(GNPTAB):c.99delC ; NM_024312.4(GNPTAB):c.3503_3504delTC ; NM_024312.4(GNPTAB):c.3565C>T ; NM_024312.4(GNPTAB):c.3173C>G ; NM_024312.4(GNPTAB):c.1000C>T ; NM_024312.4(GNPTAB):c.1196C>T ; c.25C>T ; NM_024312.4(GNPTAB):c.3560_3561delAG ; NM_024312.4(GNPTAB):c.3410T>A ; NM_024312.4(GNPTAB):c.648_651delAGAA ; NM_024312.4(GNPTAB):c.1759C>T ; c.2383del ; NM_024312.4(GNPTAB):c.2896delA ; NM_024312.4(GNPTAB):c.616_619delACAG ; NM_024312.4(GNPTAB):c.3326dupA ; NM_024312.4(GNPTAB):c.749dupA ; NM_024312.4(GNPTAB):c.732_733delAA ; c.3663del ; NM_024312.4(GNPTAB):c.1906dupA ; NM_024312.4(GNPTAB):c.99delC ; NM_024312.4(GNPTAB):c.3503_3504delTC ; NM_024312.4(GNPTAB):c.3565C>T ; NM_024312.4(GNPTAB):c.3173C>G ; NM_024312.4(GNPTAB):c.1000C>T ; NM_024312.4(GNPTAB):c.1196C>T

GNPTAB	Mucolipidosis type III alpha/beta	Mucolipidosis II (MLII) is a slowly progressive lysosomal disorder characterized by growth retardation, skeletal abnormalities, facial dysmorphism, stiff skin, developmental delay and cardiomegaly.	Infants present at birth with hypotonia, growth retardation and gradually worsening skeletal deformities, including ulnar deviation of hands with broadening and camptomelic fingers, kyphosis, hip dislocation, clubfeet and deformed long bones. A limited range of motion of shoulder joints is noted at birth. Neonatal transient hyperparathyroidism has been documented in severe cases of MLII. Flat face, shallow orbits with proptotic eyes, depressed nasal bridge, prominent mouth and gingival hypertrophy are apparent soon after birth. Coarsening of facial features is progressive. Skin is stiff and thickened, especially around the earlobes. Early motor milestones are delayed and cognitive functioning is below normal. Postnatal growth usually stops in the 2nd year of life and contractures develop in all joints. Most patients never walk. Cardiac involvement most commonly includes the thickening and insufficiency of the mitral or aortic valves. Voice is hoarse and breathing is noisy due to the progressive narrowing of airways, mucosal thickening and stiffening of all connective tissues which, along with cardiac involvement, leads to cardiorespiratory insufficiency.	c.25C>T ; NM_024312.4(GNPTAB):c.3560_3561delAG ; NM_024312.4(GNPTAB):c.3410T>A ; NM_024312.4(GNPTAB):c.648_651delAGAA ; NM_024312.4(GNPTAB):c.1759C>T ; c.2383del ; NM_024312.4(GNPTAB):c.2896delA ; NM_024312.4(GNPTAB):c.616_619delACAG ; NM_024312.4(GNPTAB):c.3326dupA ; NM_024312.4(GNPTAB):c.749dupA ; NM_024312.4(GNPTAB):c.732_733delAA ; c.3663del ; NM_024312.4(GNPTAB):c.1906dupA ; NM_024312.4(GNPTAB):c.99delC ; NM_024312.4(GNPTAB):c.3503_3504delTC ; NM_024312.4(GNPTAB):c.3565C>T ; NM_024312.4(GNPTAB):c.3173C>G ; NM_024312.4(GNPTAB):c.1000C>T ; NM_024312.4(GNPTAB):c.1196C>T ; c.25C>T ; NM_024312.4(GNPTAB):c.3560_3561delAG ; NM_024312.4(GNPTAB):c.3410T>A ; NM_024312.4(GNPTAB):c.648_651delAGAA ; NM_024312.4(GNPTAB):c.1759C>T ; c.2383del ; NM_024312.4(GNPTAB):c.2896delA ; NM_024312.4(GNPTAB):c.616_619delACAG ; NM_024312.4(GNPTAB):c.3326dupA ; NM_024312.4(GNPTAB):c.749dupA ; NM_024312.4(GNPTAB):c.732_733delAA ; c.3663del ; NM_024312.4(GNPTAB):c.1906dupA ; NM_024312.4(GNPTAB):c.99delC ; NM_024312.4(GNPTAB):c.3503_3504delTC ; NM_024312.4(GNPTAB):c.3565C>T ; NM_024312.4(GNPTAB):c.3173C>G ; NM_024312.4(GNPTAB):c.1000C>T ; NM_024312.4(GNPTAB):c.1196C>T

GNS	Sanfilippo syndrome type D	Mucolipidosis III alpha/beta (MLIII alpha/beta) is a lysosomal disorder characterized by progressive slowing of the growth rate from early childhood, stiffness and pain in joints, gradual coarsening of facial features, moderate developmental delay and mild intellectual disability in most patients.	Infants appear normal at birth. Onset is gradual and usually observed at around the age of 3 years with slowing of growth rate and apparent shoulder, hip and knee contractures. Dysmorphic facial features (full cheeks, depressed nasal bridge, prominent mouth and inconsistently mild gingival hypertrophy) are mild but coarsen with age. Otitis media is common in the young. Functional changes in hard and soft connective tissues result in a slowly progressive reduction in the range of motion in the shoulders, hips and knees. Gradual hardening of the cardiac valves, from childhood onwards, ultimately leads to cardiac insufficiency. Gait slows in childhood, becoming increasingly painful due to severe hip disease. Bone pain, even at rest, results from osteoporosis and osteolytic bone lesions. Moderate claw-like flexion deformity of the fingers and carpal tunnel syndrome are common complications. Bronchitis/bronchopneumonia is frequent in childhood and gradual restrictive lung disease becomes life-threatening in older patients. Mild intellectual disability has been reported in most patients. Death is often due to treatment-refractory cardiopulmonary failure.	NM_002076.3(GNS):c.1063C>T ; c.413C>G ; NM_002076.3(GNS):c.1169del ; NM_002076.3(GNS):c.1168C>T ; NM_002076.3(GNS):c.1226_1227insG ; NM_002076.3(GNS):c.1063C>T ; c.413C>G ; NM_002076.3(GNS):c.1169del ; NM_002076.3(GNS):c.1168C>T ; NM_002076.3(GNS):c.1226_1227insG
GRHPR	Primary hyperoxaluria type 2			c.435G>A ; c.622C>T ; NM_012203.1(GRHPR):c.295C>T ; NM_012203.1(GRHPR):c.103delG ; c.435G>A ; c.622C>T ; NM_012203.1(GRHPR):c.295C>T ; NM_012203.1(GRHPR):c.103delG

GUCY2D	Central areolar choroidal dystrophy	A disorder of glyoxylate metabolism characterized by an excess of oxalate resulting in kidney stones, nephrocalcinosis and ultimately renal failure and systemic oxalosis. There are 3 types of PH, types 1-3, all caused by liver-specific enzyme defects.	Hyperoxaluria may lead to kidney stones, nephrocalcinosis and ultimately renal failure and systemic oxalosis. Symptoms can appear at any age and may vary from infantile failure to thrive and cortical nephrocalcinosis with renal failure to hematuria, medullary nephrocalcinosis or sporadic stone disease, even within one family. PH1 is the most severe form; overall, more than 70% of PH1 patients develop end-stage kidney disease over time; this may even occur in patients with sporadic stone disease. Storage of oxalate occurs in severe renal failure and may affect bone, eyes, heart, arteries and peripheral nerves (systemic oxalosis). PH2 has a more benign course; no infantile oxalosis has been described and end-stage kidney disease occurs at relatively late age in about 20% of patients. PH3 is most benign with so far only a few reports of renal impairment and no end-stage kidney disease.	c.456C>A ; NM_000180.3(GUCY2D):c.620delC ; c.2735_2736del ; c.2945del ; NM_000180.3(GUCY2D):c.1694T>C ; c.456C>A ; NM_000180.3(GUCY2D):c.620delC ; c.2735_2736del ; c.2945del ; NM_000180.3(GUCY2D):c.1694T>C
GUCY2D	Cone rod dystrophy	Central areolar choroidal dystrophy (CACD) is a hereditary macular disorder, usually presenting between the ages of 30-60, characterized by a large area of atrophy in the centre of the macula and the loss or absence of photoreceptors, retinal pigment epithelium and choriocapillaris in this area, resulting in a progressive decrease in visual acuity.	Central areolar choroidal dystrophy (CACD) is a hereditary retinal disorder that principally affects the macula, often resulting in a well-defined area of atrophy of the retinal pigment epithelium (RPE) and choriocapillaris in the center of the macula. Dysfunction of macular photoreceptors usually leads to a decrease in visual acuity, generally occurring between the ages of 30 and 60 years.	c.456C>A ; NM_000180.3(GUCY2D):c.620delC ; c.2735_2736del ; c.2945del ; NM_000180.3(GUCY2D):c.1694T>C ; c.456C>A ; NM_000180.3(GUCY2D):c.620delC ; c.2735_2736del ; c.2945del ; NM_000180.3(GUCY2D):c.1694T>C

GUCY2D	Leber congenital amaurosis	A rare genetic isolated inherited retinal disorder characterized by primary cone degeneration with significant secondary rod involvement, with a variable fundus appearance. Typical presentation includes decreased visual acuity, central scotoma, photophobia, color vision alteration, followed by night blindness and loss of peripheral visual field.	Cone rod dystrophy (CRD) is characterized by primary cone involvement or, occasionally, by concomitant loss of both cones and rods, explaining the predominant symptoms of CRDs: decreased visual acuity, color vision defects, photoaversion and decreased sensitivity in the central visual field, later followed by progressive loss in peripheral vision and night blindness. The fundus appearance is varaible ranging from normal in the early stages, with only subtle temporal optic nerve pallor, macular pigment migration and atrophy or a bull's-eye maculopathy, to peripheral retinal pigment epithelium atrophy, intra retinal pigmentation migration, arteriolar attenuation, and optic disc pallor as disease progresses. Cone-rod dystrophy (CRD) should be distinguished from rod-cone dystrophy (RCD), also known as retinitis pigmentosa. Unlike RCD, which typically start with night blindness and progressive visual field constriction while central vision is preserved until late stages, CRD is characterized by a primary decrease in central vision leading to earlier legal blindness. At end stage, however, CRDs do not differ from end stage RCDs. CRDs are most frequently nonsyndromic, however they may also be part of several syndromes, such as AlstrÃ¶m syndrome, Bardet-Biedl syndrome and Spinocerebellar Ataxia Type 7.	c.456C>A ; NM_000180.3(GUCY2D):c.620delC ; c.2735_2736del ; c.2945del ; NM_000180.3(GUCY2D):c.1694T>C ; c.456C>A ; NM_000180.3(GUCY2D):c.620delC ; c.2735_2736del ; c.2945del ; NM_000180.3(GUCY2D):c.1694T>C

GUSB	Mucopolysaccharidosis type 7	Leber congenital amaurosis (LCA) is a retinal dystrophy defined by blindness and responses to electrophysiological stimulation (Ganzfeld electroretinogram (ERG)) below threshold, associated with severe visual impairment within the first year of life.	LCA is characterized by severely reduced visual acuity (less or equal 20/400) or blindness within in the first year of life. Sluggish pupillary responses, roving eye movement, photophobia, high hyperopia, nystagmus, convergent strabismus, or keratoconus may occur depending on the genetic cause. The Franceschetti's oculo-digital sign, comprising eye poking, pressing, and rubbing is pathognomonic. LCA may be associated with mutations in genes linked to syndromes presenting with neurodevelopmental delay, intellectual disability, oculomotor apraxia-type behavior (difficulty moving the eye) and renal dysfunction.	NM_000181.3(GUSB):c.1521G>A ; NM_000181.3(GUSB):c.1084G>A ; c.820_821del ; NM_000181.3(GUSB):c.1730G>T ; NM_000181.4(GUSB):c.1429C>T ; NM_000181.3(GUSB):c.1061C>T ; c.1618G>T ; c.499C>T ; NM_000181.3(GUSB):c.1050G>C ; NM_000181.3(GUSB):c.1856C>T ; NM_000181.3(GUSB):c.1338G>A ; NM_000181.3(GUSB):c.1831C>T ; NM_000181.3(GUSB):c.646C>T ; NM_000181.3:c.1219_1220insC ; NM_000181.3(GUSB):c.1144C>T ; NM_000181.3(GUSB):c.1881G>T ; c.1244+1G>A ; c.1065+1G>T ; NM_000181.3(GUSB):c.442C>T ; NM_000181.3(GUSB):c.1337G>A ; NM_000181.3(GUSB):c.1534G>A ; NM_000181.3(GUSB):c.866G>A ; NM_000181.3(GUSB):c.526C>T ; NM_000181.3(GUSB):c.1521G>A ; NM_000181.3(GUSB):c.1084G>A ; c.820_821del ; NM_000181.3(GUSB):c.1730G>T ; NM_000181.4(GUSB):c.1429C>T ; NM_000181.3(GUSB):c.1061C>T ; c.1618G>T ; c.499C>T ; NM_000181.3(GUSB):c.1050G>C ; NM_000181.3(GUSB):c.1856C>T ; NM_000181.3(GUSB):c.1338G>A ; NM_000181.3(GUSB):c.1831C>T ; NM_000181.3(GUSB):c.646C>T ; NM_000181.3:c.1219_1220insC ; NM_000181.3(GUSB):c.1144C>T ; NM_000181.3(GUSB):c.1881G>T ; c.1244+1G>A ; c.1065+1G>T ; NM_000181.3(GUSB):c.442C>T ; NM_000181.3(GUSB):c.1337G>A ; NM_000181.3(GUSB):c.1534G>A ; NM_000181.3(GUSB):c.866G>A ; NM_000181.3(GUSB):c.526C>T
HADHA	Acute fatty liver of pregnancy	A rare, genetic lysosomal storage disease characterized by accumulation of glycosaminoglycans in connective tissue which results in progressive multisystem involvement with severity ranging from mild to severe. The most consistent features include musculoskeletal involvement (particularly dysostosis multiplex, joint restriction, thorax abnormalities, and short stature), limited vocabulary, intellectual disability, coarse facies with a short neck, pulmonary involvement (predominantly decreased pulmonary function), corneal clouding, and cardiac valve disease.	Signs are extremely variable: there are prenatal forms with non-immune hydrops fetalis, and severe neonatal forms with dysmorphism, hernias, hepatosplenomegaly, club feet, dysostosis, small stature and severe hypotonia and neurological involvement that ultimately lead to profound intellectual deficit in patients who survive. At the other end of the spectrum, there are very mild cases that are discovered during adolescence or adulthood following presentation with thoracic kyphosis.	NC_000002.12:g.26194616del ; NM_000182.4(HADHA):c.1620+2_1620+6del5 ; c.499del ; NM_000182.4(HADHA):c.845T>A ; NM_000182.4(HADHA):c.1793_1794delAT ; c.1422dup ; NM_000182.4(HADHA):c.2146+1G>A ; NM_000182.4(HADHA):c.1918C>T ; NM_000182.4(HADHA):c.1678C>T ; NM_000182.4(HADHA):c.1132C>T ; NM_000182.4(HADHA):c.919-2A>G ; c.2132dupC ; NM_000182.4(HADHA):c.274_278delTCATC ; NM_000182.4(HADHA):c.1528G>C ; NC_000002.12:g.26194616del ; NM_000182.4(HADHA):c.1620+2_1620+6del5 ; c.499del ; NM_000182.4(HADHA):c.845T>A ; NM_000182.4(HADHA):c.1793_1794delAT ; c.1422dup ; NM_000182.4(HADHA):c.2146+1G>A ; NM_000182.4(HADHA):c.1918C>T ; NM_000182.4(HADHA):c.1678C>T ; NM_000182.4(HADHA):c.1132C>T ; NM_000182.4(HADHA):c.919-2A>G ; c.2132dupC ; NM_000182.4(HADHA):c.274_278delTCATC ; NM_000182.4(HADHA):c.1528G>C

HADHA	Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency	Isolated deficiency of long-chain 3-hydroxyl-CoA dehydrogenase (LCHAD) is an autosomal recessive disorder characterized by early-onset cardiomyopathy, hypoglycemia, neuropathy, and pigmentary retinopathy, and sudden death.	A rare, severe complication occurring in the third trimester of pregnancy or in early postpartum period bearing a risk for perinatal and maternal mortality and characterized by jaundice, rise of hepatic injuries and evolving to acute liver failure and encephalopathy.	NC_000002.12:g.26194616del ; NM_000182.4(HADHA):c.1620+2_1620+6del5 ; c.499del ; NM_000182.4(HADHA):c.845T>A ; NM_000182.4(HADHA):c.1793_1794delAT ; c.1422dup ; NM_000182.4(HADHA):c.2146+1G>A ; NM_000182.4(HADHA):c.1918C>T ; NM_000182.4(HADHA):c.1678C>T ; NM_000182.4(HADHA):c.1132C>T ; NM_000182.4(HADHA):c.919-2A>G ; c.2132dupC ; NM_000182.4(HADHA):c.274_278delTCATC ; NM_000182.4(HADHA):c.1528G>C ; NC_000002.12:g.26194616del ; NM_000182.4(HADHA):c.1620+2_1620+6del5 ; c.499del ; NM_000182.4(HADHA):c.845T>A ; NM_000182.4(HADHA):c.1793_1794delAT ; c.1422dup ; NM_000182.4(HADHA):c.2146+1G>A ; NM_000182.4(HADHA):c.1918C>T ; NM_000182.4(HADHA):c.1678C>T ; NM_000182.4(HADHA):c.1132C>T ; NM_000182.4(HADHA):c.919-2A>G ; c.2132dupC ; NM_000182.4(HADHA):c.274_278delTCATC ; NM_000182.4(HADHA):c.1528G>C
HADHA	Mitochondrial trifunctional protein deficiency	A mitochondrial disorder of long chain fatty acid oxidation characterized in most patients by onset in infancy/ early childhood of hypoketotic hypoglycemia, metabolic acidosis, liver disease, hypotonia and, frequently, cardiac involvement with arrhythmias and/or cardiomyopathy.	Most patients display a severe phenotype that presents in infancy, usually from the neonatal period up until 12 months of age. The disease manifests as hypoketotic hypoglycemia, metabolic acidosis, hypotonia, liver involvement with hepatic encephalopathy, cardiomyopathy and arrhythmias. Clinical presentation is frequently preceded by fasting and/or intercurrent illness and often presents with hypoketotic hypoglycemia. Chronic peripheral neuropathy and pigmentary retinopathy develop over time in many surviving patients. Rarer presentations of LCHADD are sudden cardiac arrest or sudden infant death. HELLP syndrome (see this term) often occurs in pregnant women carrying a fetus affected with LCHADD.	NC_000002.12:g.26194616del ; NM_000182.4(HADHA):c.1620+2_1620+6del5 ; c.499del ; NM_000182.4(HADHA):c.845T>A ; NM_000182.4(HADHA):c.1793_1794delAT ; c.1422dup ; NM_000182.4(HADHA):c.2146+1G>A ; NM_000182.4(HADHA):c.1918C>T ; NM_000182.4(HADHA):c.1678C>T ; NM_000182.4(HADHA):c.1132C>T ; NM_000182.4(HADHA):c.919-2A>G ; c.2132dupC ; NM_000182.4(HADHA):c.274_278delTCATC ; NM_000182.4(HADHA):c.1528G>C ; NC_000002.12:g.26194616del ; NM_000182.4(HADHA):c.1620+2_1620+6del5 ; c.499del ; NM_000182.4(HADHA):c.845T>A ; NM_000182.4(HADHA):c.1793_1794delAT ; c.1422dup ; NM_000182.4(HADHA):c.2146+1G>A ; NM_000182.4(HADHA):c.1918C>T ; NM_000182.4(HADHA):c.1678C>T ; NM_000182.4(HADHA):c.1132C>T ; NM_000182.4(HADHA):c.919-2A>G ; c.2132dupC ; NM_000182.4(HADHA):c.274_278delTCATC ; NM_000182.4(HADHA):c.1528G>C

HADHB	Mitochondrial trifunctional protein deficiency	A rare disorder of fatty acid oxidation characterized by a wide clinical spectrum ranging from severe neonatal manifestations including cardiomyopathy, hypoglycemia, metabolic acidosis, skeletal myopathy and neuropathy, liver disease and death to a mild phenotype with peripheral polyneuropathy, episodic rhabdomyolysis and pigmentary retinopathy..	The neonatal onset, severe form manifests as hepatic steatosis, cardiomyopathy, skeletal myopathy and neuropathy and is usually fatal. A moderately severe form, with onset usually from the neonatal period to 18 months of age, presents primarily with hypoketotic hypoglycemia and metabolic acidosis which is often precipitated by prolonged fasting and/or intercurrent illness. Both forms can manifest with neuropathy with or without cardiomyopathy and can be fatal. The mild form merges with the moderately severe infantile form and can present from a few months of age until adolescence as a peripheral polyneuropathy with episodic rhabdomyolysis triggered by prolonged fasting, illness, exercise or exposure to heat or cold. There is respiratory failure associated with the episodes of rhabdomyolysis. A pigmentary retinopathy may also develop over time. Very occasionally, adults presenting for the first time with a previously unrecognized disease are described.	NM_000183.2(HADHB):c.788A>G ; NM_000183.2(HADHB):c.1364T>G ; NM_000183.2(HADHB):c.1331G>A ; NM_000183.2(HADHB):c.788A>G ; NM_000183.2(HADHB):c.1364T>G ; NM_000183.2(HADHB):c.1331G>A

HBA1 / HBA2	Alpha-thalassemia-intellectual disability syndrome linked to chromosome 16	A rare disorder of fatty acid oxidation characterized by a wide clinical spectrum ranging from severe neonatal manifestations including cardiomyopathy, hypoglycemia, metabolic acidosis, skeletal myopathy and neuropathy, liver disease and death to a mild phenotype with peripheral polyneuropathy, episodic rhabdomyolysis and pigmentary retinopathy..	The neonatal onset, severe form manifests as hepatic steatosis, cardiomyopathy, skeletal myopathy and neuropathy and is usually fatal. A moderately severe form, with onset usually from the neonatal period to 18 months of age, presents primarily with hypoketotic hypoglycemia and metabolic acidosis which is often precipitated by prolonged fasting and/or intercurrent illness. Both forms can manifest with neuropathy with or without cardiomyopathy and can be fatal. The mild form merges with the moderately severe infantile form and can present from a few months of age until adolescence as a peripheral polyneuropathy with episodic rhabdomyolysis triggered by prolonged fasting, illness, exercise or exposure to heat or cold. There is respiratory failure associated with the episodes of rhabdomyolysis. A pigmentary retinopathy may also develop over time. Very occasionally, adults presenting for the first time with a previously unrecognized disease are described.	--MED ; --SEA ; --THAI ; - Î±3.7 ; - Î±4.2 ; - Î±20.5 ; --FIL
HBA1 / HBA3	Hb Bart's hydrops fetalis	A rare developmental defect during embryogenesis, a contiguous gene deletion syndrome, is a form of alpha-thalassemia characterized by microcytosis, hypochromia, normal hemoglobin (Hb) level or mild anemia, associated with developmental abnormalities.	ATR-16 is a congenital disease. Patients present with either alpha-thalassemia trait or mild hemoglobin H disease (HbH disease) associated with a mild to profound (in most cases) intellectual disability and, in some cases, with mild, nonspecific dysmorphic features (mild hypertelorism, down slanted palpebral fissures, broad or prominent nasal bridge, small ears, short neck), microcephaly and short stature. Genital abnormalities (hypospadias and cryptorchidism) have been reported in males. Club foot is common.	

HBA1 / HBA4	Hemoglobin H disease	A rare, severe form of alpha-thalassemia that is almost always lethal. It is characterized by fetal onset of generalized edema, pleural and pericardial effusions, and severe hypochromic anemia.	Affected fetuses suffer from severe anemiaÂ in utero, causing severe tissue hypoxia, heart failure and a range of developmental abnormalities associated with hydrops fetalis (marked hepatosplenomegaly, urogenital and limb abnormalities). In survivors, the neonatal period is often stormy, and growth retardation and neurodevelopmental delay are the major adverse long-term outcomes. Maternal complications during pregnancy include preeclampsia, polyhydramnios or oligohydramnios, antepartum hemorrhage, and premature delivery. Although intrauterine transfusions and perinatal intensive care have resulted in increasing fetal survival to the perinatal period, Early early therapeutic termination of at-risk pregnancies is usually recommended due to the severity of the syndrome and the risk of potentially serious maternal complications during pregnancy.	
HBA1 / HBA5	Hemoglobin M disease	An intermediate form of alpha-thalassemia characterized by increased hemolysis and mild to severe anemia with marked microcytosis and hypochromia. Hemoglobin H disease (HbH) disease belongs to the group of nontransfusion-dependent thalassemia.	Clinical features are highly variable and generally develop in the first years of life. Initial signs may be noticed only during routine hematologic analyses. Patients have variable microcytic hypochromic hemolytic anemia, requiring no or occasional blood transfusions during infectious episodes, exposure to oxidizing agents or pregnancy. Splenomegaly is frequently found. Non-deletional forms of alpha-thalassemia typically have more severe anemia, splenomegaly, hepatomegaly, cholelithiasis, growth retardation, decreased bone density; and have earlier and more frequent transfusion requirements. Skeletal changes mainly affecting the face can rarely occur in non-deletional forms. Iron overload develops secondary to increased intestinal iron absorption even in the absence of transfusion.	

HBA1 / HBA6	Alpha-thalassemia-intellectual disability syndrome linked to chromosome 16	A rare hemoglobinopathy characterized by the presence of hemoglobin variants with structural abnormalities in the globin portion of the molecule which lead to auto-oxidation of heme iron, resulting in methemoglobinemia. Patients present with cyanosis for which no treatment is necessary. Mode of inheritance is autosomal dominant.	Methemoglobinemia is a clinical condition in which more than 1% of hemoglobin is oxidized to methemoglobin, a type of hemoglobin that contains the ferric (Fe3+) form of iron. Patients with hemoglobin M are cyanotic but otherwise asymptomatic. If the mutation occurs in the hemoglobin alpha subunit, cyanosis is apparent at birth, whereas if the beta chain is affected, cyanosis appears later or intensifies when beta subunit production increases. If a newborn carries a fetal M hemoglobin (gamma subunit), cyanosis disappears when the complete gamma-beta-switch occurs.	
HBA1 / HBA7	Hb Bart's hydrops fetalis	A rare developmental defect during embryogenesis, a contiguous gene deletion syndrome, is a form of alpha-thalassemia characterized by microcytosis, hypochromia, normal hemoglobin (Hb) level or mild anemia, associated with developmental abnormalities.	ATR-16 is a congenital disease. Patients present with either alpha-thalassemia trait or mild hemoglobin H disease (HbH disease) associated with a mild to profound (in most cases) intellectual disability and, in some cases, with mild, nonspecific dysmorphic features (mild hypertelorism, down slanted palpebral fissures, broad or prominent nasal bridge, small ears, short neck), microcephaly and short stature. Genital abnormalities (hypospadias and cryptorchidism) have been reported in males. Club foot is common.	

HBA1 / HBA8	Hemoglobin H disease	A rare, severe form of alpha-thalassemia that is almost always lethal. It is characterized by fetal onset of generalized edema, pleural and pericardial effusions, and severe hypochromic anemia.	Affected fetuses suffer from severe anemiaÂ in utero, causing severe tissue hypoxia, heart failure and a range of developmental abnormalities associated with hydrops fetalis (marked hepatosplenomegaly, urogenital and limb abnormalities). In survivors, the neonatal period is often stormy, and growth retardation and neurodevelopmental delay are the major adverse long-term outcomes. Maternal complications during pregnancy include preeclampsia, polyhydramnios or oligohydramnios, antepartum hemorrhage, and premature delivery. Although intrauterine transfusions and perinatal intensive care have resulted in increasing fetal survival to the perinatal period, Early early therapeutic termination of at-risk pregnancies is usually recommended due to the severity of the syndrome and the risk of potentially serious maternal complications during pregnancy.	
HBA1 / HBA9	Hemoglobin M disease	An intermediate form of alpha-thalassemia characterized by increased hemolysis and mild to severe anemia with marked microcytosis and hypochromia. Hemoglobin H disease (HbH) disease belongs to the group of nontransfusion-dependent thalassemia.	Clinical features are highly variable and generally develop in the first years of life. Initial signs may be noticed only during routine hematologic analyses. Patients have variable microcytic hypochromic hemolytic anemia, requiring no or occasional blood transfusions during infectious episodes, exposure to oxidizing agents or pregnancy. Splenomegaly is frequently found. Non-deletional forms of alpha-thalassemia typically have more severe anemia, splenomegaly, hepatomegaly, cholelithiasis, growth retardation, decreased bone density; and have earlier and more frequent transfusion requirements. Skeletal changes mainly affecting the face can rarely occur in non-deletional forms. Iron overload develops secondary to increased intestinal iron absorption even in the absence of transfusion.	

HBB	Beta-thalassemia intermedia	A rare hemoglobinopathy characterized by the presence of hemoglobin variants with structural abnormalities in the globin portion of the molecule which lead to auto-oxidation of heme iron, resulting in methemoglobinemia. Patients present with cyanosis for which no treatment is necessary. Mode of inheritance is autosomal dominant.	Methemoglobinemia is a clinical condition in which more than 1% of hemoglobin is oxidized to methemoglobin, a type of hemoglobin that contains the ferric (Fe3+) form of iron. Patients with hemoglobin M are cyanotic but otherwise asymptomatic. If the mutation occurs in the hemoglobin alpha subunit, cyanosis is apparent at birth, whereas if the beta chain is affected, cyanosis appears later or intensifies when beta subunit production increases. If a newborn carries a fetal M hemoglobin (gamma subunit), cyanosis disappears when the complete gamma-beta-switch occurs.	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)
HBB	Beta-thalassemia major	Beta-thalassemia (BT) intermedia is a form of BT (see this term) characterized by mild to moderate anemia which does not or only occasionally requires transfusion.	BT intermedia encompasses a wide clinical spectrum with more severe cases presenting between 2 and 6 years of age with anemia, spleen and sometimes liver enlargement, as well as delayed growth and development. In other cases, patients are completely asymptomatic until adult life with only mild anemia. Hypertrophy of erythroid marrow, with the possibility of extramedullary erythropoiesis, is common and leads to characteristic deformities of the bone and face, osteoporosis with pathologic fractures of long bones and formation of erythropoietic masses primarily affecting the spleen, liver, lymph nodes, chest and spine. Less commonly, erythroid marrow hypertrophy may cause neurological problems (spinal cord compression with paraplegia). Patients may also develop leg ulcers and gallstones. An increased predisposition to thrombosis versus BT major has been reported, especially after splenectomy. Although patients are at risk of iron overload, hypogonadism, hypothyroidism and diabetes are not common. Cardiac involvement may also occur as a result of a high-output state and pulmonary hypertension, while systolic left ventricle function is usually preserved.	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)

HBB	Delta-beta-thalassemia	Beta-thalassemia (BT) major is a severe early-onset form of BT (see this term) characterized by severe anemia requiring regular red blood cell transfusions.	Onset is during infancy with severe anemia, failure to thrive and progressive pallor. Feeding problems, diarrhea, irritability, recurrent bouts of fever, and progressive enlargement of the abdomen caused by splenomegaly and hepatomegaly may occur. Untreated or poorly transfused patients show growth retardation, pallor, jaundice, poor musculature, genu valgum, leg ulcers, formation of masses due to extramedullary hematopoiesis, and skeletal changes including deformities in the long bones of the legs and typical craniofacial changes such as bossing of the skull, prominent malar eminence, depression of the bridge of the nose, tendency to a mongoloid slant of the eye, and maxillae hypertrophy, which tends to expose upper teeth. In regularly transfused patients, growth and development tend to be normal but complications related to iron overload may develop, including growth retardation and failure or delay of sexual maturation. Later-onset iron overload complications include dilated myocardiopathy, arrhythmias, liver fibrosis and cirrhosis, diabetes mellitus, and insufficiency of the parathyroid, thyroid, pituitary, and, less commonly, adrenal glands. Other complications are hypersplenism, venous thrombosis and osteoporosis.	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)
HBB	Dominant beta-thalassemia	Delta-beta-thalassemia is a form of beta-thalassemia (see this term) characterized by decreased or absent synthesis of the delta- and beta-globin chains with a compensatory increase in expression of fetal gamma-chain synthesis.	The heterozygous form of the condition is clinically asymptomatic with mild microcytosis and no elevation of HbA2 whereas the few homozygous patients have a mild clinical presentation. When inherited with heterozygous classical beta-thalassemia, patients usually have the thalassemia intermedia phenotype, but the thalassemia major phenotype has been described in some cases.	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)

HBB	Hemoglobin C disease	Dominant beta-thalassemia is a form of beta-thalassemia (see this term) resulting in moderate to severe anemia.	Patients present with moderate to severe anemia, jaundice and splenomegaly.	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)
HBB	Hemoglobin C-beta-thalassemia syndrome	Hemoglobin C disease (HbC) is a hemoglobinopathy characterized by production of abnormal variant hemoglobin known as hemoglobin C, with no or mild clinical manifestations (hemolytic anemia).	0	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)
HBB	Hemoglobin D disease	Hemoglobin C - beta-thalassemia (HbC - BT) is a form of beta-thalassemia (see this term) resulting in moderate hemolytic anemia.	Patients are usually asymptomatic and diagnosed during routine tests. When present, clinical manifestations are moderate anemia and splenomegaly.	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)
HBB	Hemoglobin E disease	Hemoglobin D disease(HbD) is a hemoglobinopathy characterized by production of abnormal variant hemoglobin known as hemoglobin D, with no or mild clinical manifestations (splenomegaly, very mild anemia).	0	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)
HBB	Hemoglobin E-beta-thalassemia syndrome	Hemoglobin E disease (HbE) is a hemoglobinopathy characterized by production of abnormal variant hemoglobin known as hemoglobin E, with a generally benign, asymptomatic presentation.	0	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)

HBB	Hemoglobin Lepore-beta-thalassemia syndrome	Hemoglobin E - beta-thalassemia (HbE - BT) is a form of beta-thalassemia (see this term) that results in a mild to severe clinical presentation ranging from a condition indistinguishable from beta-thalassemia major to a mild form of beta-thalassemia intermedia (see these terms).	Mild HbE - BT (about 15% of cases) is characterized by normal Hb levels (9-12 g/dl) and patients usually do not develop clinically significant symptoms. No treatment is required. Moderately severe forms (most cases) are characterized by decreased Hb levels (6-8 g/dl) and the clinical manifestations are similar to those of beta-thalassemia intermedia. Transfusions are not required unless infections precipitate further anemia. Iron overload may occur. Severe forms are characterized by very low Hb levels (4-5 g/dl) and patients present with manifestations similar to beta-thalassemia major and are treated as thalassemia major patients.	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)
HBB	Hemoglobin M disease	A rare beta-thalassemia associated with another hemoglobin anomaly characterized by the presence of the hemoglobin Lepore variant in association with beta-thalassemia. Clinical presentation is highly variable, depending on the type of beta-thalassemia, and ranges from severe hypochromic microcytic anemia and complete transfusion dependency to moderate, compensated anemia without a need for regular blood transfusions.	Delta-beta thalassemia is a hemoglobin disorder characterized by decreased or absent synthesis of the delta- and beta-globin chains with a compensatory increase in expression of fetal gamma-chain synthesis from the affected chromosome. Individuals with delta-beta thalassemia have hypochromic, microcytic anemia and increased HbF, which may mitigate the anemia depending on the level of HbF. Delta-beta thalassemia and some forms of HPFH result from deletions within the beta-globin gene cluster on chromosome 11p15; this has been referred to as 'deletional' HPFH. HPFH can also result from point mutations in the promoter regions of the gamma globulin genes HBG1 and HBG2; this has been referred to as 'non-deletional' HPFH.	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)

HBB	Hereditary persistence of fetal hemoglobin-beta-thalassemia syndrome	A rare hemoglobinopathy characterized by the presence of hemoglobin variants with structural abnormalities in the globin portion of the molecule which lead to auto-oxidation of heme iron, resulting in methemoglobinemia. Patients present with cyanosis for which no treatment is necessary. Mode of inheritance is autosomal dominant.	Methemoglobinemia is a clinical condition in which more than 1% of hemoglobin is oxidized to methemoglobin, a type of hemoglobin that contains the ferric (Fe3+) form of iron. Patients with hemoglobin M are cyanotic but otherwise asymptomatic. If the mutation occurs in the hemoglobin alpha subunit, cyanosis is apparent at birth, whereas if the beta chain is affected, cyanosis appears later or intensifies when beta subunit production increases. If a newborn carries a fetal M hemoglobin (gamma subunit), cyanosis disappears when the complete gamma-beta-switch occurs.	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)
HBB	Hereditary persistence of fetal hemoglobin-sickle cell disease syndrome	Hereditary persistence of fetal hemoglobin (HPFH) associated with beta-thalassemia (see this term) is characterized by high hemoglobin (Hb) F levels and an increased number of fetal-Hb-containing-cells.	The association of HPFH with beta-thalassemia mitigates the clinical manifestations which vary from a normal state to beta-thalassemia intermedia (see this term).	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)
HBB	Sickle cell anemia	Sickle cell anemia is a multisystem disease associated with episodes of acute illness and progressive organ damage. Hemoglobin polymerization, leading to erythrocyte rigidity and vasoocclusion, is central to the pathophysiology of the disease, but the importance of chronic anemia, hemolysis, and vasculopathy has been established.	A rare, genetic, hemoglobinopathy characterized by generally mild clinical phenotype, high fetal hemoglobin levels and mild microcytosis and hypochromia. In some cases, acute sickle cell disease manifestations were reported, namely acute chest syndrome and acute pain crisis. The genotype is characterized by the combination of an HbS and HbF allele; symptoms depend on the degree of HbF:HbS expressivity with patients with more than 35% pancellular HbF expression being asymptomatic. Symptomatic patients have heterocellular expression of HbF.	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)

HBB	Sickle cell-beta-thalassemia disease syndrome	A severe form of sickle cell disease (SCD) characterized by homozygosity for the sickle hemoglobin (HbS) gene and which acutely manifests with severe anemia, susceptibility to severe bacterial infections, and ischemic vasoocclusive accidents (VOA). It is a red cell disease of genetic origin which manifests with hemolytic disease and loss of red cell deformability leading to other occlusive events.	The disease does not manifest during fetal life or up to the first three months of life due to the presence of high levels of fetal hemoglobin. Clinical manifestations evolve with age and are extremely variable between individuals and at different times. In addition to anemia and bacterial infections, VOAs cause hyperalgic focal ischemia (and sometimes infarction) when they occur in the abdomen, chest or skeleton. Over the course of time, VOAs may compromise the integrity of tissues or organs.	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)
HBB	Sickle cell-hemoglobin C disease syndrome	Beta-thalassemia is characterized by a reduced production of hemoglobin A (HbA, alpha-2/beta-2), which results from the reduced synthesis of beta-globin chains relative to alpha-globin chains, thus causing an imbalance in globin chain production and hence abnormal erythropoiesis. The disorder is clinically heterogeneous	A rare, genetic hemoglobinopathy that affects red blood cells both in the production of abnormal hemoglobin, as well as the decreased synthesis of beta globin chains. Clinical manifestations depend on the amount of residual beta globin chains production, and are similar to sickle cell disease, including anemia, vascular occlusion and its complications, acute episodes of pain, acute chest syndrome, pulmonary hypertension, sepsis, ischemic brain injury, splenic sequestration crisis and splenomegaly.	NM_000518.5(HBB):c.217dup (p.Ser73Lysfs) ; NC_000011.10:g.5226765_5226768del ; NM_000518.5(HBB):c.92+5G>A ; NM_000518.5(HBB):c.85dup (p.Leu29Profs) ; NM_000518.5(HBB):c.82G>T (p.Ala28Ser) ; NM_000518.4(HBB):c.364G>A (p.Glu122Lys) ; NM_000518.5(HBB):c.315+1G>A ; NM_000518.4(HBB):c.135delC (p.Phe46Leufs) ; NM_000518.5(HBB):c.118C>T (p.Gln40Ter) ; NM_000518.4(HBB):c.112delT (p.Trp38Glyfs) ; NM_000518.5(HBB):c.93-21G>A ; NM_000518.5(HBB):c.92+6T>C ; NM_000518.5(HBB):c.92+5G>C ; NM_000518.5(HBB):c.92+1G>A ; NM_000518.5(HBB):c.79G>A (p.Glu27Lys) ; NM_000518.5(HBB):c.59A>G (p.Asn20Ser) ; NM_000518.5(HBB):c.52A>T (p.Lys18Ter) ; NM_000518.4(HBB):c.27dupG (p.Ser10Valfs*14) ; NM_000518.5(HBB):c.20A>T (p.Glu7Val) ; NM_000518.4(HBB):c.19G>A (p.Glu7Lys)

HEXA	Tay-Sachs disease, B variant, adult form	A rare, genetic hemoglobinopathy characterized by anemia, reticulocytosis and erythrocyte abnormalities including target cells, irreversibly sickled cells and crystal-containing cells. Clinical course is similar to sickle cell disease, but less severe and with less complications. Signs and symptoms may include acute episodes of pain, splenic infarction and splenic sequestration crisis, acute chest syndrome, focal segmental glomerulosclerosis, ischemic brain injury, peripheral retinopathy, and osteonecrosis.	0	NM_000520.5(HEXA):c.805+1G>A ; NM_000520.6:c.1274_1277dupTATC ; NM_000520.5(HEXA):c.78G>A ; c.1278_1281dup ; NM_000520.5(HEXA):c.629C>T ; NM_000520.5(HEXA):c.1214_1215delAAinsG ; NM_000520.5(HEXA):c.538T>C ; NM_000520.5(HEXA):c.459+5G>A ; NM_000520.4:c.1499delT ; NM_000520.5(HEXA):c.1528C>T ; c.77G>A ; NM_000520.5(HEXA):c.508C>T ; NM_000520.5(HEXA):c.533G>A ; NM_000520.5(HEXA):c.532C>T ; NM_000520.5(HEXA):c.632T>C ; NM_000520.5(HEXA):c.1495C>T ; NM_183050.4:c.509G>A ; NM_000520.5(HEXA):c.772G>C ; NM_000083.3:c.1444G>A ; c.759_774dup ; NM_000520.5(HEXA):c.1176G>A ; NM_000520.5(HEXA):c.672+1G>A ; NM_001318825.1(HEXA):c.1544G>A ; c.254-1G>C ; NM_000520.5(HEXA):c.1510C>T ; NM_000520.5(HEXA):c.533G>T ; NM_000520.5(HEXA):c.1177C>T ; NM_000520.5(HEXA):c.805+1G>C ; NM_000520.5(HEXA):c.1A>G ; NM_000520.5(HEXA):c.1260G>C ; NM_000520.6:c.915_917delCTT ; c.1537C>T ; NM_000520.5(HEXA):c.380T>G ; NM_000520.5(HEXA):c.749G>A ; NM_000520.5(HEXA):c.987G>A ; NM_000520.5(HEXA):c.1A>T ; NM_000520.6:c.805G>A ; NM_000520.5(HEXA):c.986+3A>G ; NM_000520.5(HEXA):c.1510del ; NM_000520.5(HEXA):c.173G>A ; NM_000520.6:c.540C>G ; NM_000520.5(HEXA):c.2T>C ; NM_000520.5(HEXA):c.1422G>C ; NM_000520.5(HEXA):c.116T>G ; NM_000520.5(HEXA):c.805+1G>A ; NM_000520.6:c.1274_1277dupTATC ; NM_000520.5(HEXA):c.78G>A ; c.1278_1281dup ; NM_000520.5(HEXA):c.629C>T ; NM_000520.5(HEXA):c.1214_1215delAAinsG ; NM_000520.5(HEXA):c.538T>C ; NM_000520.5(HEXA):c.459+5G>A ; NM_000520.4:c.1499delT ; NM_000520.5(HEXA):c.1528C>T ; c.77G>A ; NM_000520.5(HEXA):c.508C>T ; NM_000520.5(HEXA):c.533G>A ; NM_000520.5(HEXA):c.532C>T ; NM_000520.5(HEXA):c.632T>C ; NM_000520.5(HEXA):c.1495C>T ; NM_183050.4:c.509G>A ; NM_000520.5(HEXA):c.772G>C ; NM_000083.3:c.1444G>A ; c.759_774dup ; NM_000520.5(HEXA):c.1176G>A ; NM_000520.5(HEXA):c.672+1G>A ; NM_001318825.1(HEXA):c.1544G>A ; c.254-1G>C ; NM_000520.5(HEXA):c.1510C>T ; NM_000520.5(HEXA):c.533G>T ; NM_000520.5(HEXA):c.1177C>T ; NM_000520.5(HEXA):c.805+1G>C ; NM_000520.5(HEXA):c.1A>G ; NM_000520.5(HEXA):c.1260G>C ; NM_000520.6:c.915_917delCTT ; c.1537C>T ; NM_000520.5(HEXA):c.380T>G ; NM_000520.5(HEXA):c.749G>A ; NM_000520.5(HEXA):c.987G>A ; NM_000520.5(HEXA):c.1A>T ; NM_000520.6:c.805G>A ; NM_000520.5(HEXA):c.986+3A>G ; NM_000520.5(HEXA):c.1510del ; NM_000520.5(HEXA):c.173G>A ; NM_000520.6:c.540C>G ; NM_000520.5(HEXA):c.2T>C ; NM_000520.5(HEXA):c.1422G>C ; NM_000520.5(HEXA):c.116T>G

HEXA	Tay-Sachs disease, B variant, infantile form	A rare disorder characterized by accumulation of G2 gangliosides due to hexosaminidase A deficiency.	Three variants have been described according to age of onset. The infantile form (type 1) begins between 3 and 6 months of age. The earliest sign is an incessant startle response to noise. Psychomotor retardation appears after the age of 8 months with hypotonia, amaurosis, and megalencephaly. A cherry-red macular spot may be found but is not specific. Muscular weakness progresses and leads to paralysis. The disorder degenerates into a state of decerebration and is fatal during childhood. Enzymatic activity of the hexosaminidase A is either extremely low or totally absent in leucocytes and cultured in fibroblasts obtained by skin biopsy. In the juvenile form (type 2), onset is between ages 2 and 6 with locomotor ataxia, behavioural disorders, and progressive loss of intellectual capacities, leading to a state of decerebration and death at around the age of 15. The decrease in hexosaminidase A activity is less pronounced than in the infantile form. The adult or chronic form (type 3) may begin around the age of 10, but often the disorder is not diagnosed until adulthood. Two different clinical forms exist. The first is similar to atypical Friedreich disease, with spinocerebellar ataxia but no cardiac or osseous signs, such as scoliosis or flat feet. The second is that of juvenile spinal amyotrophy resembling Kugelberg-Welander's syndrome. Mental capacities and behaviour may or may not be affected. Hexosaminidase A deficiency is found.	NM_000520.5(HEXA):c.805+1G>A ; NM_000520.6:c.1274_1277dupTATC ; NM_000520.5(HEXA):c.78G>A ; c.1278_1281dup ; NM_000520.5(HEXA):c.629C>T ; NM_000520.5(HEXA):c.1214_1215delAAinsG ; NM_000520.5(HEXA):c.538T>C ; NM_000520.5(HEXA):c.459+5G>A ; NM_000520.4:c.1499delT ; NM_000520.5(HEXA):c.1528C>T ; c.77G>A ; NM_000520.5(HEXA):c.508C>T ; NM_000520.5(HEXA):c.533G>A ; NM_000520.5(HEXA):c.532C>T ; NM_000520.5(HEXA):c.632T>C ; NM_000520.5(HEXA):c.1495C>T ; NM_183050.4:c.509G>A ; NM_000520.5(HEXA):c.772G>C ; NM_000083.3:c.1444G>A ; c.759_774dup ; NM_000520.5(HEXA):c.1176G>A ; NM_000520.5(HEXA):c.672+1G>A ; NM_001318825.1(HEXA):c.1544G>A ; c.254-1G>C ; NM_000520.5(HEXA):c.1510C>T ; NM_000520.5(HEXA):c.533G>T ; NM_000520.5(HEXA):c.1177C>T ; NM_000520.5(HEXA):c.805+1G>C ; NM_000520.5(HEXA):c.1A>G ; NM_000520.5(HEXA):c.1260G>C ; NM_000520.6:c.915_917delCTT ; c.1537C>T ; NM_000520.5(HEXA):c.380T>G ; NM_000520.5(HEXA):c.749G>A ; NM_000520.5(HEXA):c.987G>A ; NM_000520.5(HEXA):c.1A>T ; NM_000520.6:c.805G>A ; NM_000520.5(HEXA):c.986+3A>G ; NM_000520.5(HEXA):c.1510del ; NM_000520.5(HEXA):c.173G>A ; NM_000520.6:c.540C>G ; NM_000520.5(HEXA):c.2T>C ; NM_000520.5(HEXA):c.1422G>C ; NM_000520.5(HEXA):c.116T>G ; NM_000520.5(HEXA):c.805+1G>A ; NM_000520.6:c.1274_1277dupTATC ; NM_000520.5(HEXA):c.78G>A ; c.1278_1281dup ; NM_000520.5(HEXA):c.629C>T ; NM_000520.5(HEXA):c.1214_1215delAAinsG ; NM_000520.5(HEXA):c.538T>C ; NM_000520.5(HEXA):c.459+5G>A ; NM_000520.4:c.1499delT ; NM_000520.5(HEXA):c.1528C>T ; c.77G>A ; NM_000520.5(HEXA):c.508C>T ; NM_000520.5(HEXA):c.533G>A ; NM_000520.5(HEXA):c.532C>T ; NM_000520.5(HEXA):c.632T>C ; NM_000520.5(HEXA):c.1495C>T ; NM_183050.4:c.509G>A ; NM_000520.5(HEXA):c.772G>C ; NM_000083.3:c.1444G>A ; c.759_774dup ; NM_000520.5(HEXA):c.1176G>A ; NM_000520.5(HEXA):c.672+1G>A ; NM_001318825.1(HEXA):c.1544G>A ; c.254-1G>C ; NM_000520.5(HEXA):c.1510C>T ; NM_000520.5(HEXA):c.533G>T ; NM_000520.5(HEXA):c.1177C>T ; NM_000520.5(HEXA):c.805+1G>C ; NM_000520.5(HEXA):c.1A>G ; NM_000520.5(HEXA):c.1260G>C ; NM_000520.6:c.915_917delCTT ; c.1537C>T ; NM_000520.5(HEXA):c.380T>G ; NM_000520.5(HEXA):c.749G>A ; NM_000520.5(HEXA):c.987G>A ; NM_000520.5(HEXA):c.1A>T ; NM_000520.6:c.805G>A ; NM_000520.5(HEXA):c.986+3A>G ; NM_000520.5(HEXA):c.1510del ; NM_000520.5(HEXA):c.173G>A ; NM_000520.6:c.540C>G ; NM_000520.5(HEXA):c.2T>C ; NM_000520.5(HEXA):c.1422G>C ; NM_000520.5(HEXA):c.116T>G

HEXA	Tay-Sachs disease, B variant, juvenile form	A rare disorder characterized by accumulation of G2 gangliosides due to hexosaminidase A deficiency.	Three variants have been described according to age of onset. The infantile form (type 1) begins between 3 and 6 months of age. The earliest sign is an incessant startle response to noise. Psychomotor retardation appears after the age of 8 months with hypotonia, amaurosis, and megalencephaly. A cherry-red macular spot may be found but is not specific. Muscular weakness progresses and leads to paralysis. The disorder degenerates into a state of decerebration and is fatal during childhood. Enzymatic activity of the hexosaminidase A is either extremely low or totally absent in leucocytes and cultured in fibroblasts obtained by skin biopsy. In the juvenile form (type 2), onset is between ages 2 and 6 with locomotor ataxia, behavioural disorders, and progressive loss of intellectual capacities, leading to a state of decerebration and death at around the age of 15. The decrease in hexosaminidase A activity is less pronounced than in the infantile form. The adult or chronic form (type 3) may begin around the age of 10, but often the disorder is not diagnosed until adulthood. Two different clinical forms exist. The first is similar to atypical Friedreich disease, with spinocerebellar ataxia but no cardiac or osseous signs, such as scoliosis or flat feet. The second is that of juvenile spinal amyotrophy resembling Kugelberg-Welander's syndrome. Mental capacities and behaviour may or may not be affected. Hexosaminidase A deficiency is found.	NM_000520.5(HEXA):c.805+1G>A ; NM_000520.6:c.1274_1277dupTATC ; NM_000520.5(HEXA):c.78G>A ; c.1278_1281dup ; NM_000520.5(HEXA):c.629C>T ; NM_000520.5(HEXA):c.1214_1215delAAinsG ; NM_000520.5(HEXA):c.538T>C ; NM_000520.5(HEXA):c.459+5G>A ; NM_000520.4:c.1499delT ; NM_000520.5(HEXA):c.1528C>T ; c.77G>A ; NM_000520.5(HEXA):c.508C>T ; NM_000520.5(HEXA):c.533G>A ; NM_000520.5(HEXA):c.532C>T ; NM_000520.5(HEXA):c.632T>C ; NM_000520.5(HEXA):c.1495C>T ; NM_183050.4:c.509G>A ; NM_000520.5(HEXA):c.772G>C ; NM_000083.3:c.1444G>A ; c.759_774dup ; NM_000520.5(HEXA):c.1176G>A ; NM_000520.5(HEXA):c.672+1G>A ; NM_001318825.1(HEXA):c.1544G>A ; c.254-1G>C ; NM_000520.5(HEXA):c.1510C>T ; NM_000520.5(HEXA):c.533G>T ; NM_000520.5(HEXA):c.1177C>T ; NM_000520.5(HEXA):c.805+1G>C ; NM_000520.5(HEXA):c.1A>G ; NM_000520.5(HEXA):c.1260G>C ; NM_000520.6:c.915_917delCTT ; c.1537C>T ; NM_000520.5(HEXA):c.380T>G ; NM_000520.5(HEXA):c.749G>A ; NM_000520.5(HEXA):c.987G>A ; NM_000520.5(HEXA):c.1A>T ; NM_000520.6:c.805G>A ; NM_000520.5(HEXA):c.986+3A>G ; NM_000520.5(HEXA):c.1510del ; NM_000520.5(HEXA):c.173G>A ; NM_000520.6:c.540C>G ; NM_000520.5(HEXA):c.2T>C ; NM_000520.5(HEXA):c.1422G>C ; NM_000520.5(HEXA):c.116T>G ; NM_000520.5(HEXA):c.805+1G>A ; NM_000520.6:c.1274_1277dupTATC ; NM_000520.5(HEXA):c.78G>A ; c.1278_1281dup ; NM_000520.5(HEXA):c.629C>T ; NM_000520.5(HEXA):c.1214_1215delAAinsG ; NM_000520.5(HEXA):c.538T>C ; NM_000520.5(HEXA):c.459+5G>A ; NM_000520.4:c.1499delT ; NM_000520.5(HEXA):c.1528C>T ; c.77G>A ; NM_000520.5(HEXA):c.508C>T ; NM_000520.5(HEXA):c.533G>A ; NM_000520.5(HEXA):c.532C>T ; NM_000520.5(HEXA):c.632T>C ; NM_000520.5(HEXA):c.1495C>T ; NM_183050.4:c.509G>A ; NM_000520.5(HEXA):c.772G>C ; NM_000083.3:c.1444G>A ; c.759_774dup ; NM_000520.5(HEXA):c.1176G>A ; NM_000520.5(HEXA):c.672+1G>A ; NM_001318825.1(HEXA):c.1544G>A ; c.254-1G>C ; NM_000520.5(HEXA):c.1510C>T ; NM_000520.5(HEXA):c.533G>T ; NM_000520.5(HEXA):c.1177C>T ; NM_000520.5(HEXA):c.805+1G>C ; NM_000520.5(HEXA):c.1A>G ; NM_000520.5(HEXA):c.1260G>C ; NM_000520.6:c.915_917delCTT ; c.1537C>T ; NM_000520.5(HEXA):c.380T>G ; NM_000520.5(HEXA):c.749G>A ; NM_000520.5(HEXA):c.987G>A ; NM_000520.5(HEXA):c.1A>T ; NM_000520.6:c.805G>A ; NM_000520.5(HEXA):c.986+3A>G ; NM_000520.5(HEXA):c.1510del ; NM_000520.5(HEXA):c.173G>A ; NM_000520.6:c.540C>G ; NM_000520.5(HEXA):c.2T>C ; NM_000520.5(HEXA):c.1422G>C ; NM_000520.5(HEXA):c.116T>G

HEXA	Tay-Sachs disease, B1 variant	A rare disorder characterized by accumulation of G2 gangliosides due to hexosaminidase A deficiency.	Three variants have been described according to age of onset. The infantile form (type 1) begins between 3 and 6 months of age. The earliest sign is an incessant startle response to noise. Psychomotor retardation appears after the age of 8 months with hypotonia, amaurosis, and megalencephaly. A cherry-red macular spot may be found but is not specific. Muscular weakness progresses and leads to paralysis. The disorder degenerates into a state of decerebration and is fatal during childhood. Enzymatic activity of the hexosaminidase A is either extremely low or totally absent in leucocytes and cultured in fibroblasts obtained by skin biopsy. In the juvenile form (type 2), onset is between ages 2 and 6 with locomotor ataxia, behavioural disorders, and progressive loss of intellectual capacities, leading to a state of decerebration and death at around the age of 15. The decrease in hexosaminidase A activity is less pronounced than in the infantile form. The adult or chronic form (type 3) may begin around the age of 10, but often the disorder is not diagnosed until adulthood. Two different clinical forms exist. The first is similar to atypical Friedreich disease, with spinocerebellar ataxia but no cardiac or osseous signs, such as scoliosis or flat feet. The second is that of juvenile spinal amyotrophy resembling Kugelberg-Welander's syndrome. Mental capacities and behaviour may or may not be affected. Hexosaminidase A deficiency is found.	NM_000520.5(HEXA):c.805+1G>A ; NM_000520.6:c.1274_1277dupTATC ; NM_000520.5(HEXA):c.78G>A ; c.1278_1281dup ; NM_000520.5(HEXA):c.629C>T ; NM_000520.5(HEXA):c.1214_1215delAAinsG ; NM_000520.5(HEXA):c.538T>C ; NM_000520.5(HEXA):c.459+5G>A ; NM_000520.4:c.1499delT ; NM_000520.5(HEXA):c.1528C>T ; c.77G>A ; NM_000520.5(HEXA):c.508C>T ; NM_000520.5(HEXA):c.533G>A ; NM_000520.5(HEXA):c.532C>T ; NM_000520.5(HEXA):c.632T>C ; NM_000520.5(HEXA):c.1495C>T ; NM_183050.4:c.509G>A ; NM_000520.5(HEXA):c.772G>C ; NM_000083.3:c.1444G>A ; c.759_774dup ; NM_000520.5(HEXA):c.1176G>A ; NM_000520.5(HEXA):c.672+1G>A ; NM_001318825.1(HEXA):c.1544G>A ; c.254-1G>C ; NM_000520.5(HEXA):c.1510C>T ; NM_000520.5(HEXA):c.533G>T ; NM_000520.5(HEXA):c.1177C>T ; NM_000520.5(HEXA):c.805+1G>C ; NM_000520.5(HEXA):c.1A>G ; NM_000520.5(HEXA):c.1260G>C ; NM_000520.6:c.915_917delCTT ; c.1537C>T ; NM_000520.5(HEXA):c.380T>G ; NM_000520.5(HEXA):c.749G>A ; NM_000520.5(HEXA):c.987G>A ; NM_000520.5(HEXA):c.1A>T ; NM_000520.6:c.805G>A ; NM_000520.5(HEXA):c.986+3A>G ; NM_000520.5(HEXA):c.1510del ; NM_000520.5(HEXA):c.173G>A ; NM_000520.6:c.540C>G ; NM_000520.5(HEXA):c.2T>C ; NM_000520.5(HEXA):c.1422G>C ; NM_000520.5(HEXA):c.116T>G ; NM_000520.5(HEXA):c.805+1G>A ; NM_000520.6:c.1274_1277dupTATC ; NM_000520.5(HEXA):c.78G>A ; c.1278_1281dup ; NM_000520.5(HEXA):c.629C>T ; NM_000520.5(HEXA):c.1214_1215delAAinsG ; NM_000520.5(HEXA):c.538T>C ; NM_000520.5(HEXA):c.459+5G>A ; NM_000520.4:c.1499delT ; NM_000520.5(HEXA):c.1528C>T ; c.77G>A ; NM_000520.5(HEXA):c.508C>T ; NM_000520.5(HEXA):c.533G>A ; NM_000520.5(HEXA):c.532C>T ; NM_000520.5(HEXA):c.632T>C ; NM_000520.5(HEXA):c.1495C>T ; NM_183050.4:c.509G>A ; NM_000520.5(HEXA):c.772G>C ; NM_000083.3:c.1444G>A ; c.759_774dup ; NM_000520.5(HEXA):c.1176G>A ; NM_000520.5(HEXA):c.672+1G>A ; NM_001318825.1(HEXA):c.1544G>A ; c.254-1G>C ; NM_000520.5(HEXA):c.1510C>T ; NM_000520.5(HEXA):c.533G>T ; NM_000520.5(HEXA):c.1177C>T ; NM_000520.5(HEXA):c.805+1G>C ; NM_000520.5(HEXA):c.1A>G ; NM_000520.5(HEXA):c.1260G>C ; NM_000520.6:c.915_917delCTT ; c.1537C>T ; NM_000520.5(HEXA):c.380T>G ; NM_000520.5(HEXA):c.749G>A ; NM_000520.5(HEXA):c.987G>A ; NM_000520.5(HEXA):c.1A>T ; NM_000520.6:c.805G>A ; NM_000520.5(HEXA):c.986+3A>G ; NM_000520.5(HEXA):c.1510del ; NM_000520.5(HEXA):c.173G>A ; NM_000520.6:c.540C>G ; NM_000520.5(HEXA):c.2T>C ; NM_000520.5(HEXA):c.1422G>C ; NM_000520.5(HEXA):c.116T>G

HEXB	Sandhoff disease, adult form	A rare disorder characterized by accumulation of G2 gangliosides due to hexosaminidase A deficiency.	Three variants have been described according to age of onset. The infantile form (type 1) begins between 3 and 6 months of age. The earliest sign is an incessant startle response to noise. Psychomotor retardation appears after the age of 8 months with hypotonia, amaurosis, and megalencephaly. A cherry-red macular spot may be found but is not specific. Muscular weakness progresses and leads to paralysis. The disorder degenerates into a state of decerebration and is fatal during childhood. Enzymatic activity of the hexosaminidase A is either extremely low or totally absent in leucocytes and cultured in fibroblasts obtained by skin biopsy. In the juvenile form (type 2), onset is between ages 2 and 6 with locomotor ataxia, behavioural disorders, and progressive loss of intellectual capacities, leading to a state of decerebration and death at around the age of 15. The decrease in hexosaminidase A activity is less pronounced than in the infantile form. The adult or chronic form (type 3) may begin around the age of 10, but often the disorder is not diagnosed until adulthood. Two different clinical forms exist. The first is similar to atypical Friedreich disease, with spinocerebellar ataxia but no cardiac or osseous signs, such as scoliosis or flat feet. The second is that of juvenile spinal amyotrophy resembling Kugelberg-Welander's syndrome. Mental capacities and behaviour may or may not be affected. Hexosaminidase A deficiency is found.	c.1539_1540del ; NM_000521.3(HEXB):c.1375G>T ; NM_000521.3(HEXB):c.850C>T ; NM_000521.3(HEXB):c.171delG ; NM_000521.3(HEXB):c.508C>T ; NM_000521.3:c.1619_1620insTTCATGTTATCTACAGACGTG ; NM_000521.4(HEXB):c.841C>T ; NM_000521.3:c.202_203insGG ; c.1345del ; NM_000521.3(HEXB):c.797A>G ; c.1310_1311del ; c.1380G>A ; NM_000521.3(HEXB):c.1517_1529dupCAAGTGCTGTTGG ; NM_000521.3(HEXB):c.298delC ; NM_000521.3(HEXB):c.1238_1242delCAAAG ; NM_000521.3(HEXB):c.1250C>T ; NM_000521.3(HEXB):c.115delG ; c.1539_1540del ; NM_000521.3(HEXB):c.1375G>T ; NM_000521.3(HEXB):c.850C>T ; NM_000521.3(HEXB):c.171delG ; NM_000521.3(HEXB):c.508C>T ; NM_000521.3:c.1619_1620insTTCATGTTATCTACAGACGTG ; NM_000521.4(HEXB):c.841C>T ; NM_000521.3:c.202_203insGG ; c.1345del ; NM_000521.3(HEXB):c.797A>G ; c.1310_1311del ; c.1380G>A ; NM_000521.3(HEXB):c.1517_1529dupCAAGTGCTGTTGG ; NM_000521.3(HEXB):c.298delC ; NM_000521.3(HEXB):c.1238_1242delCAAAG ; NM_000521.3(HEXB):c.1250C>T ; NM_000521.3(HEXB):c.115delG

HEXB	Sandhoff disease, infantile form	Sandhoff disease is a lysosomal storage disorder from the GM2 gangliosidosis family and is characterised by central nervous system degeneration.	The clinical picture is identical to that of Tay-Sachs disease, with startle reactions, early blindness, progressive motor and mental deterioration, macrocephaly and cherry-red spots on the macula. Patients may have a doll-like face, hepatosplenomegaly and recurring respiratory tract infections. High levels of urinary oligosaccharides are found. Children develop normally during the first 3-6 months of life, after which the disease appears and evolves quickly. In cases with later onset, or in adult cases, signs may be those of spinocerebellous ataxia or dystonia. Intellectual capacities may or may not be affected.	c.1539_1540del ; NM_000521.3(HEXB):c.1375G>T ; NM_000521.3(HEXB):c.850C>T ; NM_000521.3(HEXB):c.171delG ; NM_000521.3(HEXB):c.508C>T ; NM_000521.3:c.1619_1620insTTCATGTTATCTACAGACGTG ; NM_000521.4(HEXB):c.841C>T ; NM_000521.3:c.202_203insGG ; c.1345del ; NM_000521.3(HEXB):c.797A>G ; c.1310_1311del ; c.1380G>A ; NM_000521.3(HEXB):c.1517_1529dupCAAGTGCTGTTGG ; NM_000521.3(HEXB):c.298delC ; NM_000521.3(HEXB):c.1238_1242delCAAAG ; NM_000521.3(HEXB):c.1250C>T ; NM_000521.3(HEXB):c.115delG ; c.1539_1540del ; NM_000521.3(HEXB):c.1375G>T ; NM_000521.3(HEXB):c.850C>T ; NM_000521.3(HEXB):c.171delG ; NM_000521.3(HEXB):c.508C>T ; NM_000521.3:c.1619_1620insTTCATGTTATCTACAGACGTG ; NM_000521.4(HEXB):c.841C>T ; NM_000521.3:c.202_203insGG ; c.1345del ; NM_000521.3(HEXB):c.797A>G ; c.1310_1311del ; c.1380G>A ; NM_000521.3(HEXB):c.1517_1529dupCAAGTGCTGTTGG ; NM_000521.3(HEXB):c.298delC ; NM_000521.3(HEXB):c.1238_1242delCAAAG ; NM_000521.3(HEXB):c.1250C>T ; NM_000521.3(HEXB):c.115delG
HEXB	Sandhoff disease, juvenile form	Sandhoff disease is a lysosomal storage disorder from the GM2 gangliosidosis family and is characterised by central nervous system degeneration.	The clinical picture is identical to that of Tay-Sachs disease, with startle reactions, early blindness, progressive motor and mental deterioration, macrocephaly and cherry-red spots on the macula. Patients may have a doll-like face, hepatosplenomegaly and recurring respiratory tract infections. High levels of urinary oligosaccharides are found. Children develop normally during the first 3-6 months of life, after which the disease appears and evolves quickly. In cases with later onset, or in adult cases, signs may be those of spinocerebellous ataxia or dystonia. Intellectual capacities may or may not be affected.	c.1539_1540del ; NM_000521.3(HEXB):c.1375G>T ; NM_000521.3(HEXB):c.850C>T ; NM_000521.3(HEXB):c.171delG ; NM_000521.3(HEXB):c.508C>T ; NM_000521.3:c.1619_1620insTTCATGTTATCTACAGACGTG ; NM_000521.4(HEXB):c.841C>T ; NM_000521.3:c.202_203insGG ; c.1345del ; NM_000521.3(HEXB):c.797A>G ; c.1310_1311del ; c.1380G>A ; NM_000521.3(HEXB):c.1517_1529dupCAAGTGCTGTTGG ; NM_000521.3(HEXB):c.298delC ; NM_000521.3(HEXB):c.1238_1242delCAAAG ; NM_000521.3(HEXB):c.1250C>T ; NM_000521.3(HEXB):c.115delG ; c.1539_1540del ; NM_000521.3(HEXB):c.1375G>T ; NM_000521.3(HEXB):c.850C>T ; NM_000521.3(HEXB):c.171delG ; NM_000521.3(HEXB):c.508C>T ; NM_000521.3:c.1619_1620insTTCATGTTATCTACAGACGTG ; NM_000521.4(HEXB):c.841C>T ; NM_000521.3:c.202_203insGG ; c.1345del ; NM_000521.3(HEXB):c.797A>G ; c.1310_1311del ; c.1380G>A ; NM_000521.3(HEXB):c.1517_1529dupCAAGTGCTGTTGG ; NM_000521.3(HEXB):c.298delC ; NM_000521.3(HEXB):c.1238_1242delCAAAG ; NM_000521.3(HEXB):c.1250C>T ; NM_000521.3(HEXB):c.115delG

HFE	Familial porphyria cutanea tarda	Sandhoff disease is a lysosomal storage disorder from the GM2 gangliosidosis family and is characterised by central nervous system degeneration.	The clinical picture is identical to that of Tay-Sachs disease, with startle reactions, early blindness, progressive motor and mental deterioration, macrocephaly and cherry-red spots on the macula. Patients may have a doll-like face, hepatosplenomegaly and recurring respiratory tract infections. High levels of urinary oligosaccharides are found. Children develop normally during the first 3-6 months of life, after which the disease appears and evolves quickly. In cases with later onset, or in adult cases, signs may be those of spinocerebellous ataxia or dystonia. Intellectual capacities may or may not be affected.	NM_000410.3(HFE):c.277G>C ; c.252G>A ; NM_000410.3(HFE):c.989G>T ; NM_000410.3(HFE):c.314T>C ; NM_000410.3(HFE):c.277G>C ; c.252G>A ; NM_000410.3(HFE):c.989G>T ; NM_000410.3(HFE):c.314T>C
HFE	NON RARE IN EUROPE: Hemochromatosis type 1	Porphyria cutanea tarda (PCT) is the most common form of chronic hepatic porphyria (see this term). It is characterized by bullous photodermatitis.	The disease manifests in adulthood. PCT is acquired (75% of cases) or familial (25% of cases). Generally manifestations of the disease appear earlier in familial cases. Some risk factors can precipitate symptoms: excessive consumption of alcohol, hepatitis C, estrogen, and mutations of the genes that control iron metabolism, leading to iron overload (hemochromatosis). The main clinical symptoms include firstly, extremely fragile skin and, subsequently, bullous cutaneous lesions on the surface of skin exposed to the sun (hands, face). Scarring is slow and often followed by hyper and hypopigmentation. The presence of cutaneous lesions of varying ages is very characteristic of the disease. With age, the disease manifestations can be accompanied by hypertrichosis (mainly facial) and sclerodermic signs. Hepatic lesions can also develop (siderosis, steatosis, necrosis and chronic inflammatory disorders).	NM_000410.3(HFE):c.277G>C ; c.252G>A ; NM_000410.3(HFE):c.989G>T ; NM_000410.3(HFE):c.314T>C ; NM_000410.3(HFE):c.277G>C ; c.252G>A ; NM_000410.3(HFE):c.989G>T ; NM_000410.3(HFE):c.314T>C

HFE	Sporadic porphyria cutanea tarda	0	Hereditary hemochromatosis is an autosomal recessive disorder of iron metabolism wherein the body accumulates excess iron. Excess iron is deposited in a variety of organs leading to their failure, and resulting in serious illnesses including cirrhosis, hepatomas, diabetes, cardiomyopathy, arthritis, and hypogonadotropic hypogonadism. Severe effects of the disease usually do not appear until after decades of progressive iron loading. Removal of excess iron by therapeutic phlebotomy decreases morbidity and mortality if instituted early in the course of the disease. Classic hemochromatosis (HFE) is most often caused by mutation in a gene designated HFE on chromosome 6p21.3.Â	NM_000410.3(HFE):c.277G>C ; c.252G>A ; NM_000410.3(HFE):c.989G>T ; NM_000410.3(HFE):c.314T>C ; NM_000410.3(HFE):c.277G>C ; c.252G>A ; NM_000410.3(HFE):c.989G>T ; NM_000410.3(HFE):c.314T>C
HFE	Symptomatic form of hemochromatosis type 1	Porphyria cutanea tarda (PCT) is the most common form of chronic hepatic porphyria (see this term). It is characterized by bullous photodermatitis.	The disease manifests in adulthood. PCT is acquired (75% of cases) or familial (25% of cases). Generally manifestations of the disease appear earlier in familial cases. Some risk factors can precipitate symptoms: excessive consumption of alcohol, hepatitis C, estrogen, and mutations of the genes that control iron metabolism, leading to iron overload (hemochromatosis). The main clinical symptoms include firstly, extremely fragile skin and, subsequently, bullous cutaneous lesions on the surface of skin exposed to the sun (hands, face). Scarring is slow and often followed by hyper and hypopigmentation. The presence of cutaneous lesions of varying ages is very characteristic of the disease. With age, the disease manifestations can be accompanied by hypertrichosis (mainly facial) and sclerodermic signs. Hepatic lesions can also develop (siderosis, steatosis, necrosis and chronic inflammatory disorders).	NM_000410.3(HFE):c.277G>C ; c.252G>A ; NM_000410.3(HFE):c.989G>T ; NM_000410.3(HFE):c.314T>C ; NM_000410.3(HFE):c.277G>C ; c.252G>A ; NM_000410.3(HFE):c.989G>T ; NM_000410.3(HFE):c.314T>C

HGD	Alkaptonuria	Symptomatic form of hemochromatosis type 1 is a rare, hereditary hemochromatosis characterized by inappropriately regulated intestinal iron absorption which leads to excessive iron storage in various organs and manifests with a wide range of signs and symptoms, including abdominal pain, weakness, lethargy, weight loss, elevated serum aminotransferase levels, increase in skin pigmentation, and/or arthropathy in the metacarpophalangeal joints. Other commonly associated manifestations include hepatomegaly, cirrhosis, liver fibrosis, hepatocellular carcinoma, restrictive cardiomyopathy and/or diabetes mellitus.	Hereditary hemochromatosis is an autosomal recessive disorder of iron metabolism wherein the body accumulates excess iron. Excess iron is deposited in a variety of organs leading to their failure, and resulting in serious illnesses including cirrhosis, hepatomas, diabetes, cardiomyopathy, arthritis, and hypogonadotropic hypogonadism. Severe effects of the disease usually do not appear until after decades of progressive iron loading. Removal of excess iron by therapeutic phlebotomy decreases morbidity and mortality if instituted early in the course of the disease. Classic hemochromatosis (HFE) is most often caused by mutation in a gene designated HFE on chromosome 6p21.3.	NM_000187.3(HGD):c.1102A>G ; c.469+2T>C ; NM_000187.3(HGD):c.674G>A ; NM_000187.3(HGD):c.175delA ; NM_000187.3(HGD):c.688C>T ; NM_000187.3(HGD):c.140C>T ; NM_000187.3(HGD):c.1111dupC ; NM_000187.3(HGD):c.342+1G>A ; c.1189-2A>G ; c.172A>T ; NM_000187.3(HGD):c.16-1G>A ; NM_000187.3(HGD):c.808G>A ; NM_000187.3(HGD):c.899T>G ; NM_000187.3(HGD):c.481G>A ; NM_000187.3(HGD):c.1102A>G ; c.469+2T>C ; NM_000187.3(HGD):c.674G>A ; NM_000187.3(HGD):c.175delA ; NM_000187.3(HGD):c.688C>T ; NM_000187.3(HGD):c.140C>T ; NM_000187.3(HGD):c.1111dupC ; NM_000187.3(HGD):c.342+1G>A ; c.1189-2A>G ; c.172A>T ; NM_000187.3(HGD):c.16-1G>A ; NM_000187.3(HGD):c.808G>A ; NM_000187.3(HGD):c.899T>G ; NM_000187.3(HGD):c.481G>A

HGSNAT	Retinitis pigmentosa	A rare disorder of phenylalanine and tyrosine metabolism characterized by the accumulation of homogentisic acid (HGA) and its oxidized product, benzoquinone acetic acid (BQA), in various tissues (e.g. cartilage, connective tissue) and body fluids (urine, sweat), causing urine to darken when exposed to air as well as grey-blue coloration of the sclera and ear helix (ochronosis), and a disabling joint disease involving both the axial and peripheral joints (ochronotic arthropathy).	Many affected individuals are asymptomatic and unaware of their condition until adulthood, however, homogentisic aciduria may be recognized early in infancy by dark-stained diapers. After the third decade, unusual pigmentation of the sclera and the skin overlying cartilage begins to be observed, as well as muscular-skeletal symptoms such as back pain and stiffness. Involvement of the large peripheral joints usually occurs several years after spinal changes, often leading to end-stage joint disease. Ochronotic peripheral arthropathy is generally degenerative in nature. From the fourth decade, joint mobility diminishes. Ankylosis may be present. Fractures of the vertebrae and long bones are also possible. Other features may include genitourinary (e.g. renal, bladder, prostatic stones) and cardiac (mitral valvulitis, arrhythmias) complications as well as respiratory insufficiency due to musculoskeletal involvement.	NM_152419.2(HGSNAT):c.848C>T ; NM_152419.2(HGSNAT):c.607C>T ; c.1378-1G>A ; NM_152419.2(HGSNAT):c.1250+1G>A ; NM_152419.2(HGSNAT):c.1030C>T ; NM_152419.2(HGSNAT):c.1553C>T ; c.1503del ; NM_152419.2(HGSNAT):c.1464+1G>A ; NM_152419.2(HGSNAT):c.1622C>T ; NM_152419.2(HGSNAT):c.493+1G>A ; NM_152419.2(HGSNAT):c.848C>T ; NM_152419.2(HGSNAT):c.607C>T ; c.1378-1G>A ; NM_152419.2(HGSNAT):c.1250+1G>A ; NM_152419.2(HGSNAT):c.1030C>T ; NM_152419.2(HGSNAT):c.1553C>T ; c.1503del ; NM_152419.2(HGSNAT):c.1464+1G>A ; NM_152419.2(HGSNAT):c.1622C>T ; NM_152419.2(HGSNAT):c.493+1G>A

HGSNAT	Sanfilippo syndrome type C	Retinitis pigmentosa (RP) is an inherited retinal dystrophy leading to progressive loss of the photoreceptors and retinal pigment epithelium and resulting in blindness usually after several decades.	Retinitis pigmentosa is slowly progressive but relentless. There is however broad variability in age of onset, rate of progression and secondary clinical manifestations. Affected individuals generally first develop night blindness (nyctalopia) due to loss of rod function, often in adolescence or earlier. They then develop peripheral visual field impairment, and over time loss of central vision, usually at late stages, often around midlife. Central visual acuity loss may occur at any age as a result of cystoid macular edema or photoreceptor loss. Posterior subcapsular cataracts are common and severity is age dependent. Reduced color vision may also be found. Fundus examination reveals bone spicule pigment deposits, attenuated retinal vessels, retinal atrophy and waxy optic nerve pallor. Severity is partly correlated with the pattern of inheritance with X-linked cases having the most severe course, autosomal recessive and single occurrence cases having intermediate severity, and autosomal dominant the most favorable course.	NM_152419.2(HGSNAT):c.848C>T ; NM_152419.2(HGSNAT):c.607C>T ; c.1378-1G>A ; NM_152419.2(HGSNAT):c.1250+1G>A ; NM_152419.2(HGSNAT):c.1030C>T ; NM_152419.2(HGSNAT):c.1553C>T ; c.1503del ; NM_152419.2(HGSNAT):c.1464+1G>A ; NM_152419.2(HGSNAT):c.1622C>T ; NM_152419.2(HGSNAT):c.493+1G>A ; NM_152419.2(HGSNAT):c.848C>T ; NM_152419.2(HGSNAT):c.607C>T ; c.1378-1G>A ; NM_152419.2(HGSNAT):c.1250+1G>A ; NM_152419.2(HGSNAT):c.1030C>T ; NM_152419.2(HGSNAT):c.1553C>T ; c.1503del ; NM_152419.2(HGSNAT):c.1464+1G>A ; NM_152419.2(HGSNAT):c.1622C>T ; NM_152419.2(HGSNAT):c.493+1G>A
HMGCL	3-hydroxy-3-methylglutaric aciduria	Sanfilippo syndrome comprises several forms of lysosomal storage diseases due to impaired degradation of heparan sulfate. The deficient enzyme in Sanfilippo syndrome C, or MPS IIIC, is an acetyltransferase that catalyzes the conversion of alpha-glucosaminide residues to N-acetylglucosaminide in the presence of acetyl-CoA.	The Sanfilippo syndrome, or mucopolysaccharidosis III, is an autosomal recessive lysosomal storage disease due to impaired degradation of heparan sulfate. The disorder is characterized by severe central nervous system degeneration, but only mild somatic disease. Onset of clinical features usually occurs between 2 and 6 years; severe neurologic degeneration occurs in most patients between 6 and 10 years of age, and death occurs typically during the second or third decade of life. Type A has been reported to be the most severe, with earlier onset and rapid progression of symptoms and shorter survival.	c.230del ; NM_000191.3:c.122G>A ; NM_000191.2(HMGCL):c.206_207delCT ; NM_000191.2(HMGCL):c.835G>A ; NM_000191.2(HMGCL):c.698A>G ; NM_000191.2(HMGCL):c.505_506delTC ; c.230del ; NM_000191.3:c.122G>A ; NM_000191.2(HMGCL):c.206_207delCT ; NM_000191.2(HMGCL):c.835G>A ; NM_000191.2(HMGCL):c.698A>G ; NM_000191.2(HMGCL):c.505_506delTC

HPD	Hawkinsinuria	A rare organic aciduria, due to deficiency of 3-hydroxy-3-methylglutaryl-CoA lyase characterized by episodes of metabolic decompensation with hypoketotic hypoglycemia triggered by periods of fasting or infections.	The clinical presentation is heterogeneous, ranging from severe neonatal onset with potentially fatal outcome to presentation in adulthood. Most patients became symptomatic within the first year of life (50% in neonatal period) with episodes of metabolic decompensation triggered by periods of fasting or infections, which when left untreated may lead to neurological sequelae. Newborns or infants present with acidosis and hypoglycemia, accompanied by vomiting, dehydration, hypotonia and lethargy. Acute decompensation is triggered by infections, vaccinations, and dietary changes. The typical laboratory findings include hypoglycemia, acidosis, an increased anion gap, hyperammonemia and elevated transaminases. Long-term neurological complications are common. Half of the patients have a normal cognitive development while the remainder shows psychomotor deficits. Speech and motor developmental delay are frequent. Cerebral MRI frequently reveals diffuse abnormality in signal intensity of the cerebral white matter, thalami and basal ganglia. Other manifestations may include macrocephaly, dilated cardiomyopathy, arrhythmias, hepatomegaly and acute pancreatitis. Children are usually healthy between episodesÍ¾ subsequent acute crises may be preceded by anorexia, lethargy, behavioral changes, irritability and muscle weakness. Hypoketotic hypoglycemia is characteristic.	NM_001171993.1(HPD):c.483C>G ; c.987del ; NM_001171993.1(HPD):c.657T>G ; NM_001171993.1(HPD):c.483C>G ; c.987del ; NM_001171993.1(HPD):c.657T>G

HPD	Tyrosinemia type 3	Hawkinsinuria is an inborn error of tyrosine metabolism characterized by failure to thrive, persistent metabolic acidosis, fine and sparse hair, and excretion of the unusual cyclic amino acid metabolite, hawkinsin ((2-l-cystein-S-yl, 4-dihydroxycyclohex-5-en-1-yl)acetic acid), in the urine.	Symptoms manifest in infants fed on formula or cow's milk or after weaning from breast milk.	NM_001171993.1(HPD):c.483C>G ; c.987del ; NM_001171993.1(HPD):c.657T>G ; NM_001171993.1(HPD):c.483C>G ; c.987del ; NM_001171993.1(HPD):c.657T>G
HPS1	Hermansky-Pudlak syndrome with pulmonary fibrosis	Tyrosinemia type 3 is an inborn error of tyrosine metabolism characterised by mild hypertyrosinemia and increased urinary excretion of 4-hydroxyphenylpyruvate, 4-hydroxyphenyllactate and 4-hydroxyphenylacetate.	The clinical picture is highly variable ranging from asymptomatic in patients identified through neonatal screening program studies to patients with neurologic manifestations including intellectual deficit and ataxia.	NM_000195.4(HPS1):c.1472_1487dup16 ; NM_000195.4(HPS1):c.398+5G>A ; NM_000195.3(HPS1):c.1996G>T ; NM_000195.4(HPS1):c.397G>T ; NM_000195.4(HPS1):c.972delC ; NM_000195.4(HPS1):c.1472_1487dup16 ; NM_000195.4(HPS1):c.398+5G>A ; NM_000195.3(HPS1):c.1996G>T ; NM_000195.4(HPS1):c.397G>T ; NM_000195.4(HPS1):c.972delC
HSD17B4	Bifunctional enzyme deficiency	Hermansky-Pudlak syndrome with pulmonary fibrosis as a complication includes two types (HPS-1 and HPS-4) of Hermansky-Pudlak syndrome (HPS; see this term), a multi-system disorder characterized by oculocutaneous albinism, bleeding diathesis and, in some cases, pulmonary fibrosis or granulomatous colitis.	HPS-1 and HPS-4 present with features of HPS including oculocutaneous albinisim, reduced visual acuity, horizontal nystagmus, easy bruising of soft tissues, epistaxis, and prolonged bleeding after dental extraction, surgery or childbirth. Women may present with medically significant menstrual bleeding. Complications of HPS may include granulomatous colitis and pulmonary fibrosis. Pulmonary fibrosis is the most serious complication of HPS-1 and HPS-4 and usually presents in the fourth or fifth decade.	NM_000414.3(HSD17B4):c.317G>C ; c.1047+1G>T ; NM_000414.3(HSD17B4):c.1369A>T ; NM_000414.3(HSD17B4):c.650A>G ; NM_000414.3(HSD17B4):c.46G>A ; NM_000414.3(HSD17B4):c.317G>C ; c.1047+1G>T ; NM_000414.3(HSD17B4):c.1369A>T ; NM_000414.3(HSD17B4):c.650A>G ; NM_000414.3(HSD17B4):c.46G>A

HSD17B4	Perrault syndrome	A rare peroxisomal beta-oxidation disorder characterized by deficiency of peroxisomal D-bifunctional protein, type 1 being caused by deficiency of both dehydrogenase and hydratase activities of the enzyme, and types 2 and 3 by hydratase or dehydrogenase deficiency alone, while type 4 is due to compound heterozygous mutations affecting both units and represents a clinically milder phenotype. Types 1-3 are typically fatal in infancy. Patients present with early onset of generalized hypotonia, seizures, severe global developmental delay, craniofacial dysmorphism (large fontanel, high forehead, hypertelorism, epicanthal folds) and elevated plasma very long chain fatty acids. Variable features include hepatomegaly, polymicrogyria, and cerebral white matter abnormalities, among others.	D-bifunctional protein deficiency is a disorder of peroxisomal fatty acid beta-oxidation. The clinical manifestations of this deficiency is similar to those of disorders of peroxisomal assembly, including X-linked adrenoleukodystrophy, Zellweger cerebrohepatorenal syndrome and neonatal adrenoleukodystrophy.	NM_000414.3(HSD17B4):c.317G>C ; c.1047+1G>T ; NM_000414.3(HSD17B4):c.1369A>T ; NM_000414.3(HSD17B4):c.650A>G ; NM_000414.3(HSD17B4):c.46G>A ; NM_000414.3(HSD17B4):c.317G>C ; c.1047+1G>T ; NM_000414.3(HSD17B4):c.1369A>T ; NM_000414.3(HSD17B4):c.650A>G ; NM_000414.3(HSD17B4):c.46G>A

HYLS1	Hydrolethalus	Perrault syndrome (PS) is characterized by the association of ovarian dysgenesis in females with sensorineural hearing impairment. In more recent PS reports, some authors have described neurologic abnormalities, notably progressive cerebellar ataxia and intellectual deficit.	Mean age at diagnosis is 22 years following presentation with delayed puberty in females with sensorineural deafness. Hearing defects were noted in all but one of the reported cases (mean age at diagnosis of 8 years). The hearing loss is always sensorineural and bilateral but the severity is variable (mild to profound), even in affected patients from the same family. Ovarian dysgenesis has been reported in all female cases but no gonad defects are detected in males. Amenorrhea is generally primary but secondary amenorrhea has also been reported. Delayed growth (height below the third percentile) was reported in half the documented cases. The exact frequency of the neurological abnormalities is unknown, but nine females and two males (16-37 years old) lacking neurological abnormalities have been reported. Neurological signs are progressive and generally appear later in life, however, walking delay or early frequent falls have been noted in young PS patients. Common neurological signs are ataxia, dyspraxia, limited extraocular movements, and polyneuropathy. Some cases with scoliosis have also been reported.	c.669G>A ; NM_145014.2(HYLS1):c.632A>G ; c.724C>T ; c.669G>A ; NM_145014.2(HYLS1):c.632A>G ; c.724C>T

HYLS1	Joubert syndrome	Hydrolethalus (HLS) is a severe fetal malformation syndrome characterized by craniofacial dysmorphic features, central nervous system, cardiac, respiratory tract and limb abnormalities.	Micrognathia and retrognathia, cleft lip/palate, a poorly formed nose, posteriorly rotated ears and deep-set eyes are the main craniofacial dysmorphic features observed in HLS. A midline defect in the occipital bone dorsal to the foramen magnum is present, resulting in a keyhole-shaped defect. Brain abnormalities include hydrocephaly and agenesis of midline structures such as corpus callosum, cerebellar vermis and septum pellucidum, leading to a wide opened fluid-filled space between lateral ventricles. HLS is also characterized by postaxial and preaxial polydactyly, respectively in the hands and feet, the latter being clubbed. About half of the patients have large septal cardiac defect. Abnormal lobulation of the lungs, stenosis of the airways (larynx, trachea or bronchus), and abnormal genitalia (including uterus duplex in females and ectopic testis in males) are also found.	c.669G>A ; NM_145014.2(HYLS1):c.632A>G ; c.724C>T ; c.669G>A ; NM_145014.2(HYLS1):c.632A>G ; c.724C>T

IDS	Mucopolysaccharidosis type 2, attenuated form	A rare, autosomal recessive congenital cerebellar ataxia characterized by congenital malformation of the brainstem and agenesis or hypoplasia of the cerebellar vermis leading to an abnormal respiratory pattern, nystagmus, hypotonia, ataxia, and delay in achieving motor milestones.	Disease onset is antenatal, although clinical presentation is typically in the neonatal period with irregular breathing pattern (episodic tachypnea and/or apnea), and nystagmus. During infancy, hypotonia may appear. Cerebellar ataxia (staggering gait and imbalance) may develop later. Delayed acquisition of motor milestones is common. Cognitive abilities are variable, ranging from severe intellectual deficit to normal intelligence. Neuro-ophthalmologic examination may show oculomotor apraxia. In some cases, seizures occur. Careful examination of the face often shows a characteristic appearance: large head, prominent forehead, high rounded eyebrows, epicanthal folds, ptosis (occasionally), an upturned nose with prominent nostrils, an open mouth (which tends to have an oval shape early on, a 'rhomboid' appearance later, and finally can appear triangular with downturned angles), tongue protrusion and rhythmic tongue motions, and occasionally low-set and tilted ears. Other features sometimes present in Joubert syndrome include retinal dystrophy, hepatopathy, nephronophthisis, and polydactyly.	NM_000202.7(IDS):c.1505G>C ; c.278del ; NM_000202.7(IDS):c.317_318insTCAA ; NM_000202.6:c.388_389insG ; NM_000202.7(IDS):c.1122C>T ; NM_000202.7(IDS):c.597del ; NM_000202.7(IDS):c.208dupC ; NM_000202.7(IDS):c.1148delC ; NM_000202.7(IDS):c.514C>T ; NM_000202.7(IDS):c.690_691insT ; c.240+1G>A ; NM_000202.7(IDS):c.404A>G ; c.596_599del ; NM_000202.7(IDS):c.1508T>A ; NM_000202.7(IDS):c.998C>T ; NM_000202.7(IDS):c.587T>C ; NM_000202.7(IDS):c.1505G>C ; c.278del ; NM_000202.7(IDS):c.317_318insTCAA ; NM_000202.6:c.388_389insG ; NM_000202.7(IDS):c.1122C>T ; NM_000202.7(IDS):c.597del ; NM_000202.7(IDS):c.208dupC ; NM_000202.7(IDS):c.1148delC ; NM_000202.7(IDS):c.514C>T ; NM_000202.7(IDS):c.690_691insT ; c.240+1G>A ; NM_000202.7(IDS):c.404A>G ; c.596_599del ; NM_000202.7(IDS):c.1508T>A ; NM_000202.7(IDS):c.998C>T ; NM_000202.7(IDS):c.587T>C

IDS	Mucopolysaccharidosis type 2, severe form	Mucopolysaccharidosis type 2, attenuated form (MPS2att), the less severe form of MPS2 (see this term), leads to a massive accumulation of glycosaminoglycans and a wide variety of symptoms including distinctive facies, short stature, cardiorespiratory and skeletal findings. It is differentiated from mucopolysaccharidosis type 2, severe form (see this term) by the absence of cognitive decline.	MPS2att is clinically heterogeneous and its rate of progression is highly variable. Patients appear healthy at birth, with subtle initial symptoms appearing between 18 months and 4 years of age or even later, in particular umbilical or inguinal hernia. A distinctive facies (thickening of lips and nostrils, enlarged and protruding tongue), forms slowly and may first be observed at 2-4 years of age (often not evident until late). Swelling of the upper respiratory tract may be responsible for frequent infections, in particular otitis media; excessive snoring and sleep apnea; a distinctive hoarse voice and progressive loss of hearing. During early childhood growth is stunted and patients have a short stature with dysostosis multiplex and stiff joints that may make movement painful, hip dysplasia may also occur. Phalangeal joints are universally contracted resulting in claw-like hands; carpal tunnel syndrome is common. Spastic paresis due to spinal cord compression at the cranio-cervical region may also occur. Pressure exerted on the optic nerve may lead to loss of vision and retinal degeneration has also been reported in some cases. MPS2att patients, in general, have no cognitive impairments.	NM_000202.7(IDS):c.1505G>C ; c.278del ; NM_000202.7(IDS):c.317_318insTCAA ; NM_000202.6:c.388_389insG ; NM_000202.7(IDS):c.1122C>T ; NM_000202.7(IDS):c.597del ; NM_000202.7(IDS):c.208dupC ; NM_000202.7(IDS):c.1148delC ; NM_000202.7(IDS):c.514C>T ; NM_000202.7(IDS):c.690_691insT ; c.240+1G>A ; NM_000202.7(IDS):c.404A>G ; c.596_599del ; NM_000202.7(IDS):c.1508T>A ; NM_000202.7(IDS):c.998C>T ; NM_000202.7(IDS):c.587T>C ; NM_000202.7(IDS):c.1505G>C ; c.278del ; NM_000202.7(IDS):c.317_318insTCAA ; NM_000202.6:c.388_389insG ; NM_000202.7(IDS):c.1122C>T ; NM_000202.7(IDS):c.597del ; NM_000202.7(IDS):c.208dupC ; NM_000202.7(IDS):c.1148delC ; NM_000202.7(IDS):c.514C>T ; NM_000202.7(IDS):c.690_691insT ; c.240+1G>A ; NM_000202.7(IDS):c.404A>G ; c.596_599del ; NM_000202.7(IDS):c.1508T>A ; NM_000202.7(IDS):c.998C>T ; NM_000202.7(IDS):c.587T>C

IKBKAP	Familial dysautonomia	Mucopolysaccharidosis type 2 (MPS2, see this term), severe form (MPS2S), is associated with a massive accumulation of glycosaminoglycans and a wide variety of symptoms including a rapidly progressive cognitive decline; it is most often fatal in the second or third decade.	MPS2S presents with the spectrum of symptoms observed in all MSP2 (see this term) cases, often with an earlier presentation. MPS2S patients have a decrease in growth rate in early to mid-childhood, along with respiratory difficulties and a thickening of lips and nostrils as well as an enlarged and protruding tongue (distinctive facies), which may become evident between 2-4 years of age. Psychomotor milestones are delayed, and regression often occurs. Between the ages of 2-6 years patients begin to exhibit aggressive behavior and hyperactivity, often lacking any sense of danger as they follow a course of progressive cognitive decline. Vision may be affected, and progressive hearing loss occurs in most cases. Myocardial thickening and cardiac valve dysfunction are common. Approximately 60-80 % of patients with MPS2 have the severe form of the disease with neurological implications.	NM_003640.5:c.2087G>C ; c.2328del ; NM_003640.5:c.2204+6T>C ; c.3332del ; c.1460+2T>C ; NM_003640.5:c.2087G>C ; c.2328del ; NM_003640.5:c.2204+6T>C ; c.3332del ; c.1460+2T>C

IL2RG	Omenn syndrome	A rare hereditary sensory and autonomic neuropathy characterized by decreased pain and temperature perception, absent deep tendon reflexes, proprioceptive ataxia, afferent baroreflex failure and progressive optic neuropathy.	The disease is present at birth and is progressive. Initial symptoms (from birth to 3 years) include swallowing problems, aspiration pneumonia, hypotonia, temperature and blood pressure instability, and delayed development. Lack of fungiform papilla on the tongue and absence of tears with emotional crying are classic features, but not easily recognized (the tongue appears inconspicuous and lack of overflow tears is normal until about seven months of age). No obvious dysmorphism is present at birth, but a characteristic facial expression develops over time. Pain and temperature perception are decreased, but not absent. Proprioception and vibration sense are markedly decreased. Deep tendon reflexes are absent. Feeding difficulties due to gastrointestinal dysmotility (oropharyngeal incoordination, abnormal esophageal peristalsis, erratic gastric emptying, gastroesophageal reflux) occur early and may persist throughout life. Episodes of protracted vomiting attacks and hypertension termed 'autonomic crises" can be recurrent. Forty percent of the patients manifest a cyclical crisis pattern that can occur daily, weekly, or monthly with personality changes ranging from irritability and withdrawal to general excitation. Chronic lung disease (secondary to repeated aspirations), restrictive lung disease (imposed by scoliosis), and chemoreceptor dysfunction (resulting in blunted responses to hypoxemia) are frequent. Orthostatic hypotension without compensatory tachycardia is always present, as well as episodic hypertension in response to emotional stress or visceral pain. Chronic renal failure is common. Progressive optic neuropathy and neurotrophic keratopathy result in severe visual loss. There is ample phenotypic variation particularly in cognitive abilities. Severe kyphoscoliosis and short stature are common.	NM_000206.2(IL2RG):c.341G>A ; NM_000206.2(IL2RG):c.355A>T ; NM_000206.2(IL2RG):c.452T>C ; NM_000206.2(IL2RG):c.854G>A ; NM_000206.2(IL2RG):c.664C>T ; NM_000206.2(IL2RG):c.454+1G>A ; NM_000206.2(IL2RG):c.343T>C ; NM_000206.2(IL2RG):c.186T>A ; NM_000206.2(IL2RG):c.341G>A ; NM_000206.2(IL2RG):c.355A>T ; NM_000206.2(IL2RG):c.452T>C ; NM_000206.2(IL2RG):c.854G>A ; NM_000206.2(IL2RG):c.664C>T ; NM_000206.2(IL2RG):c.454+1G>A ; NM_000206.2(IL2RG):c.343T>C ; NM_000206.2(IL2RG):c.186T>A

IL2RG	T-B+ severe combined immunodeficiency due to gamma chain deficiency	Omenn syndrome (OS) is an inflammatory condition characterized by erythroderma, desquamation, alopecia, chronic diarrhea, failure to thrive, lymphadenopathy, and hepatosplenomegaly, associated with severe combined immunodeficiency (SCID; see this term).	OS presents during the first year of life with features of SCID including chronic diarrhea, pneumonitis and failure to thrive. In addition, patients present with inflammatory symptoms including lymphadenopathy, hepatosplenomegaly and generalized erythroderma, which may often cause alopecia and loss of eyebrows and eyelashes; protein loss may lead to generalized edema and metabolic disturbances. The signs and symptoms of OS can evolve over time and may not appear simultaneously. Some patients present with some but not all of these symptoms and may be described as having atypical Omenn syndrome. OS may also be associated with syndromic disorders including cartilage-hair hypoplasia (CHH), adenosine deaminase (ADA) deficiency, monosomy 22q11, coloboma of the eye, CHARGE syndrome and ligase 4 deficiency (see these terms).	NM_000206.2(IL2RG):c.341G>A ; NM_000206.2(IL2RG):c.355A>T ; NM_000206.2(IL2RG):c.452T>C ; NM_000206.2(IL2RG):c.854G>A ; NM_000206.2(IL2RG):c.664C>T ; NM_000206.2(IL2RG):c.454+1G>A ; NM_000206.2(IL2RG):c.343T>C ; NM_000206.2(IL2RG):c.186T>A ; NM_000206.2(IL2RG):c.341G>A ; NM_000206.2(IL2RG):c.355A>T ; NM_000206.2(IL2RG):c.452T>C ; NM_000206.2(IL2RG):c.854G>A ; NM_000206.2(IL2RG):c.664C>T ; NM_000206.2(IL2RG):c.454+1G>A ; NM_000206.2(IL2RG):c.343T>C ; NM_000206.2(IL2RG):c.186T>A
IVD	Isovaleric acidemia	Severe combined immunodeficiency (SCID) due to gamma chain deficiency, also called SCID-X1, is a form of SCID (see this term) characterized by severe and recurrent infections, associated with diarrhea and failure to thrive.	SCID-X1 manifests during the first months of life with severe and often life threatening viral, bacterial or fungal infections (e.g.Â Pneumocystis jiroveci pneumonitis, disseminated BCG infection if previously vaccinated), and failure to thrive. Chronic diarrhea is a frequent finding. Some patients may have skin rashes and abnormalities of liver function. Materno-fetal transfusion-associated graft versus host disease is also associated with the disease. Immunological findings are lymphopenia with the absence of T and NK cells, hypogammaglobulinemia, and normal or increased B cell count.	NM_002225.3(IVD):c.157C>T ; NM_002225.3(IVD):c.134T>C ; c.1057+5_1057+8del ; c.388_389insGT ; NM_002225.4(IVD):c.149G>C ; NM_002225.4(IVD):c.1199A>G ; NM_002225.3(IVD):c.559+1G>A ; c.503G>A ; c.904_905del ; NM_002225.3(IVD):c.507delG ; NM_002225.4(IVD):c.149G>A ; c.243+1G>A ; NM_002225.4(IVD):c.784+1G>A ; NM_002225.4(IVD):c.1183C>T ; NM_002225.3(IVD):c.367G>A ; c.1055_1057+4del ; NM_002225.4(IVD):c.1174C>T ; NM_002225.3(IVD):c.1141T>C ; NM_002225.3(IVD):c.390delT ; NM_002225.3(IVD):c.605G>T ; c.344_347dup ; NM_002225.3(IVD):c.406_407delTG ; NM_002225.3(IVD):c.465+2T>C ; NM_002225.3(IVD):c.941C>T ; NM_002225.3(IVD):c.1188delT ; NM_002225.3(IVD):c.157C>T ; NM_002225.3(IVD):c.134T>C ; c.1057+5_1057+8del ; c.388_389insGT ; NM_002225.4(IVD):c.149G>C ; NM_002225.4(IVD):c.1199A>G ; NM_002225.3(IVD):c.559+1G>A ; c.503G>A ; c.904_905del ; NM_002225.3(IVD):c.507delG ; NM_002225.4(IVD):c.149G>A ; c.243+1G>A ; NM_002225.4(IVD):c.784+1G>A ; NM_002225.4(IVD):c.1183C>T ; NM_002225.3(IVD):c.367G>A ; c.1055_1057+4del ; NM_002225.4(IVD):c.1174C>T ; NM_002225.3(IVD):c.1141T>C ; NM_002225.3(IVD):c.390delT ; NM_002225.3(IVD):c.605G>T ; c.344_347dup ; NM_002225.3(IVD):c.406_407delTG ; NM_002225.3(IVD):c.465+2T>C ; NM_002225.3(IVD):c.941C>T ; NM_002225.3(IVD):c.1188delT

LAMA2	Laminin subunit alpha 2-related congenital muscular dystrophy	A rare, autosomal recessive, organic aciduria that is characterized by variable clinical presentation ranging from acute neonatal onset of metabolic decompensation to later onset of chronic, non-specific manifestations including failure to thrive and/or developmental delay. All patients are prone to intermittent, acute metabolic decompensation. During metabolic episodes, urine analysis demonstrates elevated isovaleric acid derivatives.	Patients present along a spectrum. Acute, neonatal presentation is characterized by onset in the first two weeks of life with vomiting, seizures, and lethargy, progressing to coma. Metabolic acidosis with an increased anion gap is apparent on laboratory evaluation. Hyperammonemia may occur. Later onset is relatively non-specific with failure to thrive and/or developmental delay. Patients who survived an early acute presentation are subsequently indistinguishable from those with the chronic phenotype. All patients are prone to intermittent acute episodes of decompensation with minor illnesses. Childhood onset metabolic acidosis is typically brought on by prolonged fasting, increased intake of protein-rich food or infections, and can be fatal if not treated immediately. The characteristic smell of isovaleric acid may be present, and is likened to sweaty feet/body sweat. Though severe developmental delay and neurologic sequelae are present in some patients, they are likely related to severe biochemical presentations.	c.1612C>T ; c.9221del ; NM_000426.3(LAMA2):c.6955C>T ; NM_000426.3(LAMA2):c.3718C>T ; NM_000426.3(LAMA2):c.2962C>T ; c.8748del ; c.2323-2A>T ; NM_000426.3(LAMA2):c.3623_3645del23 ; NM_000426.3(LAMA2):c.4645C>T ; c.8705del ; NM_000426.3(LAMA2):c.7279_7280delCT ; c.5227G>T ; c.6617del ; NM_000426.3(LAMA2):c.112+1G>A ; c.2098_2099del ; c.1050del ; NM_000426.3(LAMA2):c.184G>T ; c.8314del ; NM_000426.3(LAMA2):c.5050G>T ; NM_000426.3(LAMA2):c.3976C>T ; NM_000426.3(LAMA2):c.2750-1G>C ; NM_000426.3(LAMA2):c.9101_9104dupAACA ; NM_000426.3(LAMA2):c.2451-2A>G ; NM_000426.3(LAMA2):c.3630delT ; NM_000426.3(LAMA2):c.825delC ; NM_000426.3(LAMA2):c.2901C>A ; NM_000426.3(LAMA2):c.6038delT ; NM_000426.3(LAMA2):c.6011delA ; c.6429+1G>A ; NM_000426.3(LAMA2):c.7810C>T ; c.6334A>T ; NM_000426.3(LAMA2):c.7732C>T ; NM_000426.3(LAMA2):c.3237C>A ; NM_000426.3(LAMA2):c.3215delG ; NM_000426.3(LAMA2):c.7147C>T ; NM_000426.3(LAMA2):c.7536delC ; c.1612C>T ; c.9221del ; NM_000426.3(LAMA2):c.6955C>T ; NM_000426.3(LAMA2):c.3718C>T ; NM_000426.3(LAMA2):c.2962C>T ; c.8748del ; c.2323-2A>T ; NM_000426.3(LAMA2):c.3623_3645del23 ; NM_000426.3(LAMA2):c.4645C>T ; c.8705del ; NM_000426.3(LAMA2):c.7279_7280delCT ; c.5227G>T ; c.6617del ; NM_000426.3(LAMA2):c.112+1G>A ; c.2098_2099del ; c.1050del ; NM_000426.3(LAMA2):c.184G>T ; c.8314del ; NM_000426.3(LAMA2):c.5050G>T ; NM_000426.3(LAMA2):c.3976C>T ; NM_000426.3(LAMA2):c.2750-1G>C ; NM_000426.3(LAMA2):c.9101_9104dupAACA ; NM_000426.3(LAMA2):c.2451-2A>G ; NM_000426.3(LAMA2):c.3630delT ; NM_000426.3(LAMA2):c.825delC ; NM_000426.3(LAMA2):c.2901C>A ; NM_000426.3(LAMA2):c.6038delT ; NM_000426.3(LAMA2):c.6011delA ; c.6429+1G>A ; NM_000426.3(LAMA2):c.7810C>T ; c.6334A>T ; NM_000426.3(LAMA2):c.7732C>T ; NM_000426.3(LAMA2):c.3237C>A ; NM_000426.3(LAMA2):c.3215delG ; NM_000426.3(LAMA2):c.7147C>T ; NM_000426.3(LAMA2):c.7536delC
LAMA3	Intermediate generalized junctional epidermolysis bullosa	Congenital muscular dystrophy type 1A (MCD1A) belongs to a group of neuromuscular disorders with onset at birth or infancy characterized by hypotonia, muscle weakness and muscle wasting.	The disease presents at birth or in the first few months of life with hypotonia and muscle weakness in the limbs and trunk. Respiratory and feeding disorders can also occur. Motor development is delayed and limited (sitting or standing is only possible with help). Infants present with early rigidity of the vertebral column, scoliosis, and respiratory insufficiency. There is facial involvement with a typical elongated myopathic face and ocular ophthalmoplegia disorders can appear later. Epileptic attacks are possible, although they occur in less than a third of patients. Intellectual development is normal.	c.4878dup ; c.4335dup ; NM_198129.2(LAMA3):c.6943A>T ; c.1182del ; c.335del ; NM_000227.4(LAMA3):c.2662C>T ; NM_000227.4(LAMA3):c.1981C>T ; NM_198129.2(LAMA3):c.8962C>T ; NM_000227.4(LAMA3):c.3350+2T>G ; c.4878dup ; c.4335dup ; NM_198129.2(LAMA3):c.6943A>T ; c.1182del ; c.335del ; NM_000227.4(LAMA3):c.2662C>T ; NM_000227.4(LAMA3):c.1981C>T ; NM_198129.2(LAMA3):c.8962C>T ; NM_000227.4(LAMA3):c.3350+2T>G

LAMA3	Laryngo-onycho-cutaneous syndrome	Generalized non-Herlitz-type junctional epidermolysis bullosa is a form of non-Herlitz-type junctional epidermolysis bullosa (JEB-nH, see this term) characterized by generalized skin blistering, atrophic scarring, nail dystrophy or nail absence, and enamel hypoplasia, with extracutaneous involvement.	The condition is clinically apparent at birth. Skin blistering is generalized and healing can occur either with atrophic scars, sometimes accompanied by hypopigmentation or hyperpigmentation or, less commonly, with the formation of exuberant granulation tissue. Nail dystrophy or loss is a constant feature, focal keratoderma can develop over time. Progressive and permanent hair loss is frequently present, affecting the scalp, eyelashes and eyebrows; pubic and axillary hair are scant or do not fully develop. Mucosal lesions mainly affect the oral and nasal cavity, although there is considerable individual variability. Ocular involvement has been reported in some patients and comprises corneal erosions and scars, and, rarely, ectropion. The teeth regularly show enamel hypoplasia, leading to severe caries. Chronic anemia of multifactorial etiology, although of varying severity, is frequent and may be associated with a growth delay.	c.4878dup ; c.4335dup ; NM_198129.2(LAMA3):c.6943A>T ; c.1182del ; c.335del ; NM_000227.4(LAMA3):c.2662C>T ; NM_000227.4(LAMA3):c.1981C>T ; NM_198129.2(LAMA3):c.8962C>T ; NM_000227.4(LAMA3):c.3350+2T>G ; c.4878dup ; c.4335dup ; NM_198129.2(LAMA3):c.6943A>T ; c.1182del ; c.335del ; NM_000227.4(LAMA3):c.2662C>T ; NM_000227.4(LAMA3):c.1981C>T ; NM_198129.2(LAMA3):c.8962C>T ; NM_000227.4(LAMA3):c.3350+2T>G
LAMA3	Severe generalized junctional epidermolysis bullosa	LOC syndrome is a subtype of junctional epidermolysis bullosa (JEB, see this term) characterized by an altered cry in the neonatal period and by aberrant production of granulation tissue in particular affecting the upper airway tract, conjunctiva and periungual/subungual sites.	The condition is present at birth. Characteristic cutaneous findings are transient blisters leaving slowly healing erosions with exuberant granulation tissue formation, mainly localized to the head and neck, hands, feet, elbows and knees. Extracutaneous manifestations are always observed: the progressive laryngeal involvement frequently leads to fatal respiratory obstruction in infancy, and the chronic conjunctival lesions cause symblepharon formation, and also total palpebral occlusion and blindness. Enamel hypoplasia is also always present and nail dystrophies are common.	c.4878dup ; c.4335dup ; NM_198129.2(LAMA3):c.6943A>T ; c.1182del ; c.335del ; NM_000227.4(LAMA3):c.2662C>T ; NM_000227.4(LAMA3):c.1981C>T ; NM_198129.2(LAMA3):c.8962C>T ; NM_000227.4(LAMA3):c.3350+2T>G ; c.4878dup ; c.4335dup ; NM_198129.2(LAMA3):c.6943A>T ; c.1182del ; c.335del ; NM_000227.4(LAMA3):c.2662C>T ; NM_000227.4(LAMA3):c.1981C>T ; NM_198129.2(LAMA3):c.8962C>T ; NM_000227.4(LAMA3):c.3350+2T>G

LAMA3	Hypoplastic amelogenesis imperfecta	Junctional epidermolysis bullosa, Herlitz-type is a severe subtype of junctional epidermolysis bullosa (JEB, see this term) characterized by blisters and extensive erosions, localized to the skin and mucous membranes.	The condition is present at birth. Exuberant granulation tissue is a characteristic manifestation, which usually arises within the first several months to one to two years of life, and may involve the skin (around nail folds, in a mask-like distribution on the face, and at sites of friction, such as shoulders and buttocks), and the upper airways. Involvement of mucous membranes may affect the entire gastrointestinal (GI) tract, genitourinary tract, and respiratory tract to the bronchioles. However, the most significant and frequent mucosal lesions are those in the upper part of the GI and respiratory tracts. The numerous erosions and ulcerations of the oral mucosa severely hamper feeding, and involvement of the laryngotracheal mucosa, manifesting as hoarseness, dyspnea and stridor, may lead to acute respiratory failure requiring tracheostomy. Other constant features include nail anomalies with paronychia, various degrees of onychodystrophy and nail shedding. Dental abnormalities, when survival enables their observation, include regularly marked hypoplasia or complete absence of enamel. Frequent ocular lesions comprise corneal blisters, erosions and scarring and ectropion formation. Failure to thrive is an almost constant finding in JEB-H, and multifactorial anemia is also common.	c.4878dup ; c.4335dup ; NM_198129.2(LAMA3):c.6943A>T ; c.1182del ; c.335del ; NM_000227.4(LAMA3):c.2662C>T ; NM_000227.4(LAMA3):c.1981C>T ; NM_198129.2(LAMA3):c.8962C>T ; NM_000227.4(LAMA3):c.3350+2T>G ; c.4878dup ; c.4335dup ; NM_198129.2(LAMA3):c.6943A>T ; c.1182del ; c.335del ; NM_000227.4(LAMA3):c.2662C>T ; NM_000227.4(LAMA3):c.1981C>T ; NM_198129.2(LAMA3):c.8962C>T ; NM_000227.4(LAMA3):c.3350+2T>G
LAMA3	Intermediate generalized junctional epidermolysis bullosa	A rare genetic odontal or periodontal disorder that represents a group of developmental conditions affecting the structure and clinical appearance of the enamel of all or nearly all the teeth in a more or less equal manner, and which may be associated with morphologic or biochemical changes elsewhere in the body.	The enamel may be hypoplastic, hypomineralised or both, and affected teeth may be discoloured, sensitive or prone to disintegration. Amelogenesis imperfecta (AI) exists in isolation or associated with other abnormalities as part of a syndrome.	c.4878dup ; c.4335dup ; NM_198129.2(LAMA3):c.6943A>T ; c.1182del ; c.335del ; NM_000227.4(LAMA3):c.2662C>T ; NM_000227.4(LAMA3):c.1981C>T ; NM_198129.2(LAMA3):c.8962C>T ; NM_000227.4(LAMA3):c.3350+2T>G ; c.4878dup ; c.4335dup ; NM_198129.2(LAMA3):c.6943A>T ; c.1182del ; c.335del ; NM_000227.4(LAMA3):c.2662C>T ; NM_000227.4(LAMA3):c.1981C>T ; NM_198129.2(LAMA3):c.8962C>T ; NM_000227.4(LAMA3):c.3350+2T>G

LAMA3	Severe generalized junctional epidermolysis bullosa	Generalized non-Herlitz-type junctional epidermolysis bullosa is a form of non-Herlitz-type junctional epidermolysis bullosa (JEB-nH, see this term) characterized by generalized skin blistering, atrophic scarring, nail dystrophy or nail absence, and enamel hypoplasia, with extracutaneous involvement.	The condition is clinically apparent at birth. Skin blistering is generalized and healing can occur either with atrophic scars, sometimes accompanied by hypopigmentation or hyperpigmentation or, less commonly, with the formation of exuberant granulation tissue. Nail dystrophy or loss is a constant feature, focal keratoderma can develop over time. Progressive and permanent hair loss is frequently present, affecting the scalp, eyelashes and eyebrows; pubic and axillary hair are scant or do not fully develop. Mucosal lesions mainly affect the oral and nasal cavity, although there is considerable individual variability. Ocular involvement has been reported in some patients and comprises corneal erosions and scars, and, rarely, ectropion. The teeth regularly show enamel hypoplasia, leading to severe caries. Chronic anemia of multifactorial etiology, although of varying severity, is frequent and may be associated with a growth delay.	c.4878dup ; c.4335dup ; NM_198129.2(LAMA3):c.6943A>T ; c.1182del ; c.335del ; NM_000227.4(LAMA3):c.2662C>T ; NM_000227.4(LAMA3):c.1981C>T ; NM_198129.2(LAMA3):c.8962C>T ; NM_000227.4(LAMA3):c.3350+2T>G ; c.4878dup ; c.4335dup ; NM_198129.2(LAMA3):c.6943A>T ; c.1182del ; c.335del ; NM_000227.4(LAMA3):c.2662C>T ; NM_000227.4(LAMA3):c.1981C>T ; NM_198129.2(LAMA3):c.8962C>T ; NM_000227.4(LAMA3):c.3350+2T>G

LAMA3	Hypoplastic amelogenesis imperfecta	Junctional epidermolysis bullosa, Herlitz-type is a severe subtype of junctional epidermolysis bullosa (JEB, see this term) characterized by blisters and extensive erosions, localized to the skin and mucous membranes.	The condition is present at birth. Exuberant granulation tissue is a characteristic manifestation, which usually arises within the first several months to one to two years of life, and may involve the skin (around nail folds, in a mask-like distribution on the face, and at sites of friction, such as shoulders and buttocks), and the upper airways. Involvement of mucous membranes may affect the entire gastrointestinal (GI) tract, genitourinary tract, and respiratory tract to the bronchioles. However, the most significant and frequent mucosal lesions are those in the upper part of the GI and respiratory tracts. The numerous erosions and ulcerations of the oral mucosa severely hamper feeding, and involvement of the laryngotracheal mucosa, manifesting as hoarseness, dyspnea and stridor, may lead to acute respiratory failure requiring tracheostomy. Other constant features include nail anomalies with paronychia, various degrees of onychodystrophy and nail shedding. Dental abnormalities, when survival enables their observation, include regularly marked hypoplasia or complete absence of enamel. Frequent ocular lesions comprise corneal blisters, erosions and scarring and ectropion formation. Failure to thrive is an almost constant finding in JEB-H, and multifactorial anemia is also common.	c.4878dup ; c.4335dup ; NM_198129.2(LAMA3):c.6943A>T ; c.1182del ; c.335del ; NM_000227.4(LAMA3):c.2662C>T ; NM_000227.4(LAMA3):c.1981C>T ; NM_198129.2(LAMA3):c.8962C>T ; NM_000227.4(LAMA3):c.3350+2T>G ; c.4878dup ; c.4335dup ; NM_198129.2(LAMA3):c.6943A>T ; c.1182del ; c.335del ; NM_000227.4(LAMA3):c.2662C>T ; NM_000227.4(LAMA3):c.1981C>T ; NM_198129.2(LAMA3):c.8962C>T ; NM_000227.4(LAMA3):c.3350+2T>G
LAMB3	Intermediate generalized junctional epidermolysis bullosa	A rare genetic odontal or periodontal disorder that represents a group of developmental conditions affecting the structure and clinical appearance of the enamel of all or nearly all the teeth in a more or less equal manner, and which may be associated with morphologic or biochemical changes elsewhere in the body.	The enamel may be hypoplastic, hypomineralised or both, and affected teeth may be discoloured, sensitive or prone to disintegration. Amelogenesis imperfecta (AI) exists in isolation or associated with other abnormalities as part of a syndrome.	NM_000228.2(LAMB3):c.2806C>T ; NM_000228.2(LAMB3):c.124C>T ; c.1357del ; c.628+1del ; c.3228+1G>A ; NM_000228.2(LAMB3):c.1830G>A ; c.3228+1G>T ; NM_000228.2(LAMB3):c.727C>T ; NM_000228.2(LAMB3):c.904del ; NM_000228.2(LAMB3):c.496C>T ; NM_000228.2(LAMB3):c.1903C>T ; c.1438_1442del ; NM_000228.2(LAMB3):c.1587_1588delAG ; NM_000228.2(LAMB3):c.565-2A>G ; NM_000228.2(LAMB3):c.628G>A ; NM_000228.2(LAMB3):c.2806C>T ; NM_000228.2(LAMB3):c.124C>T ; c.1357del ; c.628+1del ; c.3228+1G>A ; NM_000228.2(LAMB3):c.1830G>A ; c.3228+1G>T ; NM_000228.2(LAMB3):c.727C>T ; NM_000228.2(LAMB3):c.904del ; NM_000228.2(LAMB3):c.496C>T ; NM_000228.2(LAMB3):c.1903C>T ; c.1438_1442del ; NM_000228.2(LAMB3):c.1587_1588delAG ; NM_000228.2(LAMB3):c.565-2A>G ; NM_000228.2(LAMB3):c.628G>A

LAMB3	Severe generalized junctional epidermolysis bullosa	Generalized non-Herlitz-type junctional epidermolysis bullosa is a form of non-Herlitz-type junctional epidermolysis bullosa (JEB-nH, see this term) characterized by generalized skin blistering, atrophic scarring, nail dystrophy or nail absence, and enamel hypoplasia, with extracutaneous involvement.	The condition is clinically apparent at birth. Skin blistering is generalized and healing can occur either with atrophic scars, sometimes accompanied by hypopigmentation or hyperpigmentation or, less commonly, with the formation of exuberant granulation tissue. Nail dystrophy or loss is a constant feature, focal keratoderma can develop over time. Progressive and permanent hair loss is frequently present, affecting the scalp, eyelashes and eyebrows; pubic and axillary hair are scant or do not fully develop. Mucosal lesions mainly affect the oral and nasal cavity, although there is considerable individual variability. Ocular involvement has been reported in some patients and comprises corneal erosions and scars, and, rarely, ectropion. The teeth regularly show enamel hypoplasia, leading to severe caries. Chronic anemia of multifactorial etiology, although of varying severity, is frequent and may be associated with a growth delay.	NM_000228.2(LAMB3):c.2806C>T ; NM_000228.2(LAMB3):c.124C>T ; c.1357del ; c.628+1del ; c.3228+1G>A ; NM_000228.2(LAMB3):c.1830G>A ; c.3228+1G>T ; NM_000228.2(LAMB3):c.727C>T ; NM_000228.2(LAMB3):c.904del ; NM_000228.2(LAMB3):c.496C>T ; NM_000228.2(LAMB3):c.1903C>T ; c.1438_1442del ; NM_000228.2(LAMB3):c.1587_1588delAG ; NM_000228.2(LAMB3):c.565-2A>G ; NM_000228.2(LAMB3):c.628G>A ; NM_000228.2(LAMB3):c.2806C>T ; NM_000228.2(LAMB3):c.124C>T ; c.1357del ; c.628+1del ; c.3228+1G>A ; NM_000228.2(LAMB3):c.1830G>A ; c.3228+1G>T ; NM_000228.2(LAMB3):c.727C>T ; NM_000228.2(LAMB3):c.904del ; NM_000228.2(LAMB3):c.496C>T ; NM_000228.2(LAMB3):c.1903C>T ; c.1438_1442del ; NM_000228.2(LAMB3):c.1587_1588delAG ; NM_000228.2(LAMB3):c.565-2A>G ; NM_000228.2(LAMB3):c.628G>A

LAMC2	Intermediate generalized junctional epidermolysis bullosa	Junctional epidermolysis bullosa, Herlitz-type is a severe subtype of junctional epidermolysis bullosa (JEB, see this term) characterized by blisters and extensive erosions, localized to the skin and mucous membranes.	The condition is present at birth. Exuberant granulation tissue is a characteristic manifestation, which usually arises within the first several months to one to two years of life, and may involve the skin (around nail folds, in a mask-like distribution on the face, and at sites of friction, such as shoulders and buttocks), and the upper airways. Involvement of mucous membranes may affect the entire gastrointestinal (GI) tract, genitourinary tract, and respiratory tract to the bronchioles. However, the most significant and frequent mucosal lesions are those in the upper part of the GI and respiratory tracts. The numerous erosions and ulcerations of the oral mucosa severely hamper feeding, and involvement of the laryngotracheal mucosa, manifesting as hoarseness, dyspnea and stridor, may lead to acute respiratory failure requiring tracheostomy. Other constant features include nail anomalies with paronychia, various degrees of onychodystrophy and nail shedding. Dental abnormalities, when survival enables their observation, include regularly marked hypoplasia or complete absence of enamel. Frequent ocular lesions comprise corneal blisters, erosions and scarring and ectropion formation. Failure to thrive is an almost constant finding in JEB-H, and multifactorial anemia is also common.	NM_005562.2:c.3120_3121insA ; NM_005562.2(LAMC2):c.1659C>A ; NM_005562.2(LAMC2):c.2137_2143delCAGAACC ; c.3069+1G>A ; c.3512dup ; NM_005562.2(LAMC2):c.1782_1783delGC ; NM_005562.2(LAMC2):c.405-1G>A ; c.343C>T ; NM_005562.2(LAMC2):c.283C>T ; NM_005562.2:c.3120_3121insA ; NM_005562.2(LAMC2):c.1659C>A ; NM_005562.2(LAMC2):c.2137_2143delCAGAACC ; c.3069+1G>A ; c.3512dup ; NM_005562.2(LAMC2):c.1782_1783delGC ; NM_005562.2(LAMC2):c.405-1G>A ; c.343C>T ; NM_005562.2(LAMC2):c.283C>T

LAMC2	Junctional epidermolysis bullosa inversa	Generalized non-Herlitz-type junctional epidermolysis bullosa is a form of non-Herlitz-type junctional epidermolysis bullosa (JEB-nH, see this term) characterized by generalized skin blistering, atrophic scarring, nail dystrophy or nail absence, and enamel hypoplasia, with extracutaneous involvement.	The condition is clinically apparent at birth. Skin blistering is generalized and healing can occur either with atrophic scars, sometimes accompanied by hypopigmentation or hyperpigmentation or, less commonly, with the formation of exuberant granulation tissue. Nail dystrophy or loss is a constant feature, focal keratoderma can develop over time. Progressive and permanent hair loss is frequently present, affecting the scalp, eyelashes and eyebrows; pubic and axillary hair are scant or do not fully develop. Mucosal lesions mainly affect the oral and nasal cavity, although there is considerable individual variability. Ocular involvement has been reported in some patients and comprises corneal erosions and scars, and, rarely, ectropion. The teeth regularly show enamel hypoplasia, leading to severe caries. Chronic anemia of multifactorial etiology, although of varying severity, is frequent and may be associated with a growth delay.	NM_005562.2:c.3120_3121insA ; NM_005562.2(LAMC2):c.1659C>A ; NM_005562.2(LAMC2):c.2137_2143delCAGAACC ; c.3069+1G>A ; c.3512dup ; NM_005562.2(LAMC2):c.1782_1783delGC ; NM_005562.2(LAMC2):c.405-1G>A ; c.343C>T ; NM_005562.2(LAMC2):c.283C>T ; NM_005562.2:c.3120_3121insA ; NM_005562.2(LAMC2):c.1659C>A ; NM_005562.2(LAMC2):c.2137_2143delCAGAACC ; c.3069+1G>A ; c.3512dup ; NM_005562.2(LAMC2):c.1782_1783delGC ; NM_005562.2(LAMC2):c.405-1G>A ; c.343C>T ; NM_005562.2(LAMC2):c.283C>T
LAMC2	Severe generalized junctional epidermolysis bullosa	Junctional epidermolysis bullosa inversa is a rare severe subtype of junctional epidermolysis bullosa (JEB, see this term) characterized by blistering and erosions confined to intertriginous skin sites, the esophagus, and vagina.		NM_005562.2:c.3120_3121insA ; NM_005562.2(LAMC2):c.1659C>A ; NM_005562.2(LAMC2):c.2137_2143delCAGAACC ; c.3069+1G>A ; c.3512dup ; NM_005562.2(LAMC2):c.1782_1783delGC ; NM_005562.2(LAMC2):c.405-1G>A ; c.343C>T ; NM_005562.2(LAMC2):c.283C>T ; NM_005562.2:c.3120_3121insA ; NM_005562.2(LAMC2):c.1659C>A ; NM_005562.2(LAMC2):c.2137_2143delCAGAACC ; c.3069+1G>A ; c.3512dup ; NM_005562.2(LAMC2):c.1782_1783delGC ; NM_005562.2(LAMC2):c.405-1G>A ; c.343C>T ; NM_005562.2(LAMC2):c.283C>T

LIFR	Stï¿½ve-Wiedemann syndrome	Junctional epidermolysis bullosa, Herlitz-type is a severe subtype of junctional epidermolysis bullosa (JEB, see this term) characterized by blisters and extensive erosions, localized to the skin and mucous membranes.	The condition is present at birth. Exuberant granulation tissue is a characteristic manifestation, which usually arises within the first several months to one to two years of life, and may involve the skin (around nail folds, in a mask-like distribution on the face, and at sites of friction, such as shoulders and buttocks), and the upper airways. Involvement of mucous membranes may affect the entire gastrointestinal (GI) tract, genitourinary tract, and respiratory tract to the bronchioles. However, the most significant and frequent mucosal lesions are those in the upper part of the GI and respiratory tracts. The numerous erosions and ulcerations of the oral mucosa severely hamper feeding, and involvement of the laryngotracheal mucosa, manifesting as hoarseness, dyspnea and stridor, may lead to acute respiratory failure requiring tracheostomy. Other constant features include nail anomalies with paronychia, various degrees of onychodystrophy and nail shedding. Dental abnormalities, when survival enables their observation, include regularly marked hypoplasia or complete absence of enamel. Frequent ocular lesions comprise corneal blisters, erosions and scarring and ectropion formation. Failure to thrive is an almost constant finding in JEB-H, and multifactorial anemia is also common.	NM_002310.5(LIFR):c.2013dup ; NM_002310.5(LIFR):c.171_174delTAAC ; c.2503G>T ; c.1018_1022del ; NM_002310.5(LIFR):c.653dup ; NM_002310.5(LIFR):c.1789C>T ; NM_002310.5(LIFR):c.2013dup ; NM_002310.5(LIFR):c.171_174delTAAC ; c.2503G>T ; c.1018_1022del ; NM_002310.5(LIFR):c.653dup ; NM_002310.5(LIFR):c.1789C>T

LOXHD1	Autosomal recessive non-syndromic sensorineural deafness type DFNB	Stï¿½ve-Wiedemann syndrome (SWS) is a rare autosomal recessive congenital primary skeletal dysplasia, characterized by small stature, bowing of the long bones, camptodactyly, hyperthermic episodes, respiratory distress/apneic episodes and feeding difficulties that usually lead to early mortality.	SWS is characterized by short stature, bowing of extremities that affect the lower limbs more than the upper limbs, camptodactyly, respiratory distress/apneic spells and hyperthermic episodes frequently associated with feeding/swallowing difficulties. Other clinical findings are mask-like face, pursed mouth, hypoplastic midface, osteopenia, congenital contractures and muscular hypotonia. The condition is fatal in most cases as a result of respiratory distress or hyperthermia. However, survival beyond one year have been reported in few cases, and patients develop severe spinal deformities, along with streaky osteoporosis and spontaneous fractures, bowing of the lower limbs (with prominent joints) and dysautonomia (including temperature instability, absent corneal and patellar reflexes, and smooth tongue). Motor development is generally delayed but no intellectual deficit has been reported.	NM_144612.6:c.4714C>T ; c.512-1G>A ; c.1191_1192del ; c.457_461dup ; c.591C>A ; NM_144612.6(LOXHD1):c.2008C>T ; NM_144612.6:c.4714C>T ; c.512-1G>A ; c.1191_1192del ; c.457_461dup ; c.591C>A ; NM_144612.6(LOXHD1):c.2008C>T

LRPPRC	Congenital lactic acidosis, Saguenay-Lac-Saint-Jean type	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	c.3830_3839delinsAG ; NM_133259.3(LRPPRC):c.1061C>T ; c.3830_3839delinsAG ; NM_133259.3(LRPPRC):c.1061C>T

MAN2B1	Alpha-mannosidosis, adult form	Saguenay-Lac-St. Jean (SLSJ) type congenital lactic acidosis, a French Canadian form of Leigh syndrome (see this term), is a mitochondrial disease characterized by chronic metabolic acidosis, hypotonia, facial dysmorphism and delayed development.	Facial dysmorphism is characterized by a prominent forehead, wide nasal bridge, hypertelorism, broad anterior fontanelle, midfacial hypoplasia, broad midline, synophrys, and a characteristic arched form of the eyebrows, along with mild hirsutism. There are 3 forms of the disease corresponding to varying degrees of severity: a neonatal form, a classic form and a so-called "survivor" form. The neonatal form is characterized by fulminant acidotic states. The classic form can occur from birth with severe lactic acidosis, or manifest between 14 and 24 months by ataxic gait. This form is associated with episodes of lactic acidosis that can be triggered by physical exertion, emotional stress, infection or a heavy meal, and/or metabolic crises. Patients known as "survivors", i.e. those who have survived several episodes, cross a critical threshold and show less severe symptoms including hypotonia, asthenia, developmental delay (language acquisition and walking) and, in older patients, truncal ataxia, and a characteristic wide-based gait.	c.2116C>T ; NM_000528.3(MAN2B1):c.1830+1G>C ; NM_000528.3(MAN2B1):c.2398G>A ; c.2010del ; c.1777C>T ; c.2683_2684delinsG ; NM_000528.3(MAN2B1):c.2278C>T ; NM_000528.3(MAN2B1):c.2426T>C ; NM_000528.3(MAN2B1):c.1929G>A ; c.2365C>T ; NM_000528.3(MAN2B1):c.2436+2T>C ; NM_000528.3(MAN2B1):c.384G>A ; NM_000528.3(MAN2B1):c.1915C>T ; c.2116C>T ; NM_000528.3(MAN2B1):c.1830+1G>C ; NM_000528.3(MAN2B1):c.2398G>A ; c.2010del ; c.1777C>T ; c.2683_2684delinsG ; NM_000528.3(MAN2B1):c.2278C>T ; NM_000528.3(MAN2B1):c.2426T>C ; NM_000528.3(MAN2B1):c.1929G>A ; c.2365C>T ; NM_000528.3(MAN2B1):c.2436+2T>C ; NM_000528.3(MAN2B1):c.384G>A ; NM_000528.3(MAN2B1):c.1915C>T

MAN2B1	Alpha-mannosidosis, infantile form	An inherited lysosomal storage disorder characterized by immune deficiency, facial and skeletal abnormalities, hearing impairment, and intellectual deficit.	Affected infants often appear normal at birth but their condition worsens progressively. However, some children are born with ankle equinus or develop hydrocephalus in the first year of life. Main features are immune deficiency (manifested by recurrent infections, especially in the first decade of life), skeletal abnormalities (mild-to-moderate dysostosis multiplex, scoliosis and deformation of the sternum), hearing impairment (moderate-to-severe sensorineural hearing loss), gradual impairment of mental functions and speech, and often, periods of psychosis. Associated motor function disturbances include muscular weakness, joint abnormalities and ataxia. The facial dysmorphism is marked by a large head with a prominent forehead, rounded eyebrows, a flattened nasal bridge, macroglossia, widely spaced teeth, and prognathism. Slight strabismus is common. The clinical variability is significant, representing a continuum in severity.	c.2116C>T ; NM_000528.3(MAN2B1):c.1830+1G>C ; NM_000528.3(MAN2B1):c.2398G>A ; c.2010del ; c.1777C>T ; c.2683_2684delinsG ; NM_000528.3(MAN2B1):c.2278C>T ; NM_000528.3(MAN2B1):c.2426T>C ; NM_000528.3(MAN2B1):c.1929G>A ; c.2365C>T ; NM_000528.3(MAN2B1):c.2436+2T>C ; NM_000528.3(MAN2B1):c.384G>A ; NM_000528.3(MAN2B1):c.1915C>T ; c.2116C>T ; NM_000528.3(MAN2B1):c.1830+1G>C ; NM_000528.3(MAN2B1):c.2398G>A ; c.2010del ; c.1777C>T ; c.2683_2684delinsG ; NM_000528.3(MAN2B1):c.2278C>T ; NM_000528.3(MAN2B1):c.2426T>C ; NM_000528.3(MAN2B1):c.1929G>A ; c.2365C>T ; NM_000528.3(MAN2B1):c.2436+2T>C ; NM_000528.3(MAN2B1):c.384G>A ; NM_000528.3(MAN2B1):c.1915C>T
MAT1A	Brain demyelination due to methionine adenosyltransferase deficiency	An inherited lysosomal storage disorder characterized by immune deficiency, facial and skeletal abnormalities, hearing impairment, and intellectual deficit.	Affected infants often appear normal at birth but their condition worsens progressively. However, some children are born with ankle equinus or develop hydrocephalus in the first year of life. Main features are immune deficiency (manifested by recurrent infections, especially in the first decade of life), skeletal abnormalities (mild-to-moderate dysostosis multiplex, scoliosis and deformation of the sternum), hearing impairment (moderate-to-severe sensorineural hearing loss), gradual impairment of mental functions and speech, and often, periods of psychosis. Associated motor function disturbances include muscular weakness, joint abnormalities and ataxia. The facial dysmorphism is marked by a large head with a prominent forehead, rounded eyebrows, a flattened nasal bridge, macroglossia, widely spaced teeth, and prognathism. Slight strabismus is common. The clinical variability is significant, representing a continuum in severity.	NM_000429.2:c.827_828insG ; c.1043_1044del ; NM_000429.2(MAT1A):c.1006G>A ; NM_000429.2:c.538_539insTG ; NM_000429.2(MAT1A):c.914T>C ; NM_000429.2(MAT1A):c.791G>A ; NM_000429.2(MAT1A):c.966T>G ; NM_000429.2(MAT1A):c.790C>T ; NM_000429.2(MAT1A):c.1070C>T ; NM_000429.2:c.827_828insG ; c.1043_1044del ; NM_000429.2(MAT1A):c.1006G>A ; NM_000429.2:c.538_539insTG ; NM_000429.2(MAT1A):c.914T>C ; NM_000429.2(MAT1A):c.791G>A ; NM_000429.2(MAT1A):c.966T>G ; NM_000429.2(MAT1A):c.790C>T ; NM_000429.2(MAT1A):c.1070C>T

MCCC1	3-methylcrotonyl-CoA carboxylase deficiency	Hypermethioninemia due to methionine adenosyltransferase deficiency is a very rare metabolic disorder resulting in isolated hepatic hypermethioninemia that is usually benign due to partial inactivation of enzyme activity. Rarely patients have been found to have an odd odor or neurological disorders such as brain demyelination.	0	NM_020166.4(MCCC1):c.1526delG ; NM_020166.4(MCCC1):c.1310T>C ; NM_020166.4(MCCC1):c.1074del ; c.310C>T ; NC_000003.12:g.183071292del ; NM_020166.4(MCCC1):c.1905delA ; NM_020166.4(MCCC1):c.640-2A>G ; NM_020166.4(MCCC1):c.640-1G>A ; NM_020166.4(MCCC1):c.1380T>G ; NM_020166.4(MCCC1):c.343C>T ; NM_020166.4(MCCC1):c.1277T>C ; NM_020166.4(MCCC1):c.2079del ; NM_020166.4(MCCC1):c.1114C>T ; NM_020166.4(MCCC1):c.1155A>C ; NM_020166.4(MCCC1):c.1930G>T ; NM_020166.4(MCCC1):c.1526delG ; NM_020166.4(MCCC1):c.1310T>C ; NM_020166.4(MCCC1):c.1074del ; c.310C>T ; NC_000003.12:g.183071292del ; NM_020166.4(MCCC1):c.1905delA ; NM_020166.4(MCCC1):c.640-2A>G ; NM_020166.4(MCCC1):c.640-1G>A ; NM_020166.4(MCCC1):c.1380T>G ; NM_020166.4(MCCC1):c.343C>T ; NM_020166.4(MCCC1):c.1277T>C ; NM_020166.4(MCCC1):c.2079del ; NM_020166.4(MCCC1):c.1114C>T ; NM_020166.4(MCCC1):c.1155A>C ; NM_020166.4(MCCC1):c.1930G>T
MCCC2	3-methylcrotonyl-CoA carboxylase deficiency	A rare inherited disorder of leucine metabolism characterized by a highly variable clinical picture ranging from metabolic crisis in infancy to asymptomatic adults.	Patients with 3-methylcrotonyl-CoA carboxylase deficiency (3-MCCD) have a variable clinical phenotype with the vast majority of patients being asymptomatic and a small subgroup displaying symptoms of an organic aciduria, usually in association with environmental triggering factors. Many newborns now diagnosed through expanded newborn screening tests remain asymptomatic, indicating that the disease has a very low clinical penetrance. Most symptomatic patients have normal growth and development until presenting with an acute metabolic crisis, usually following a minor infection, fasting or introduction of a protein-rich diet, between the ages of 2-33 months. Symptoms include vomiting, coma and apnea. Rarely, neurological abnormalities (i.e. metabolic stroke, hemiparesis, and encephalopathy), weakness, muscular hypotonia and developmental delay have been reported. Between episodes of metabolic crisis patients are usually asymptomatic. Some patients with 3-MCCD may not develop symptoms until adulthood, manifesting with weakness and fatigue, while others may never show symptoms.	NM_022132.4(MCCC2):c.994C>T ; c.641del ; NM_022132.4(MCCC2):c.1065A>T ; NM_022132.4(MCCC2):c.735dup ; NM_022132.4(MCCC2):c.929C>G ; NM_022132.4(MCCC2):c.838G>T ; NM_022132.4(MCCC2):c.380C>G ; c.1072+1G>A ; NM_022132.4(MCCC2):c.295G>C ; NM_022132.4(MCCC2):c.464G>A ; c.1580G>A ; c.1577dup ; NM_022132.4(MCCC2):c.517dupT ; NM_022132.4(MCCC2):c.994C>T ; c.641del ; NM_022132.4(MCCC2):c.1065A>T ; NM_022132.4(MCCC2):c.735dup ; NM_022132.4(MCCC2):c.929C>G ; NM_022132.4(MCCC2):c.838G>T ; NM_022132.4(MCCC2):c.380C>G ; c.1072+1G>A ; NM_022132.4(MCCC2):c.295G>C ; NM_022132.4(MCCC2):c.464G>A ; c.1580G>A ; c.1577dup ; NM_022132.4(MCCC2):c.517dupT

MCOLN1	Mucolipidosis type IV	A rare inherited disorder of leucine metabolism characterized by a highly variable clinical picture ranging from metabolic crisis in infancy to asymptomatic adults.	Patients with 3-methylcrotonyl-CoA carboxylase deficiency (3-MCCD) have a variable clinical phenotype with the vast majority of patients being asymptomatic and a small subgroup displaying symptoms of an organic aciduria, usually in association with environmental triggering factors. Many newborns now diagnosed through expanded newborn screening tests remain asymptomatic, indicating that the disease has a very low clinical penetrance. Most symptomatic patients have normal growth and development until presenting with an acute metabolic crisis, usually following a minor infection, fasting or introduction of a protein-rich diet, between the ages of 2-33 months. Symptoms include vomiting, coma and apnea. Rarely, neurological abnormalities (i.e. metabolic stroke, hemiparesis, and encephalopathy), weakness, muscular hypotonia and developmental delay have been reported. Between episodes of metabolic crisis patients are usually asymptomatic. Some patients with 3-MCCD may not develop symptoms until adulthood, manifesting with weakness and fatigue, while others may never show symptoms.	NM_020533.3:c.964C>T ; NM_000159.4:c.1207C>T ; NM_020533.2(MCOLN1):c.304C>T ; NM_020533.2(MCOLN1):c.1084G>T ; NM_020533.3:c.964C>T ; NM_000159.4:c.1207C>T ; NM_020533.2(MCOLN1):c.304C>T ; NM_020533.2(MCOLN1):c.1084G>T
MECP2	Atypical Rett syndrome	Mucolipidosis type IV (ML IV) is a lysosomal storage disease characterised clinically by psychomotor retardation and visual abnormalities including corneal clouding, retinal degeneration, or strabismus.	In ML IV patients, phospholipids, gangliosides and mucopolysaccharides accumulate in lysosomal inclusions, some of which resemble membranous cytoplasmic bodies found in gangliosidoses. The condition seems to be caused by anomalies in the endocytosis of membrane components towards the lysosomes. The causative gene,Â MCOLN1, is located in the 19p13.3-p13.2 region and encodes mucolipin-1 (MLN1), a membrane protein from the transient receptor potential (TRP) channel family. Around 20 mutations have been described in the literature, two of which represent 95% of the alleles identified in the Ashkenazi population.	NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC ; NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC

MECP2	Autism	A rare genetic neurological disorder characterized by the presence of two or more of the main criteria for classic Rett syndrome (loss of acquired purposeful hand skills, loss of acquired spoken language, gait abnormalities, stereotypic hand movements), a period of regression followed by recovery or stabilization, and five out of eleven supportive criteria (breathing difficulties, bruxism, impaired sleep pattern, abnormal muscle tone, peripheral vasomotor disturbances, scoliosis/kyphosis, delayed growth, small cold hands and feet, inappropriate laughter or screaming spells, decreased pain sensation, and intense eye communication). Like classic Rett syndrome, it almost exclusively affects girls, while the disease course may be either milder or more severe.	Atypical forms may present with either a milder or more severe clinical picture than that seen in typical RTT. Several subvariants of atypical RTT have been defined. i) The early-onset seizure type (Hanefeld variant) is characterized by seizures in the first months of life with subsequent development of RTT features. ii) The congenital variant (Rolando variant) is the most severe form of atypical RTT, with onset of classic RTT features during the first three months of life. iii) The 'forme fruste' is a milder variant with onset in early childhood and an incomplete and protracted course. iv) The late childhood regression form is characterized by a normal head circumference and by a more gradual and later onset (late childhood) regression of language and motor skills. v) The preserved speech variant (PSD or Zappella variant) is marked by recovery of some verbal and manual skills.	NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC ; NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC

MECP2	Rett syndrome		Autism, the prototypic pervasive developmental disorder (PDD), is usually apparent by 3 years of age. It is characterized by a triad of limited or absent verbal communication, a lack of reciprocal social interaction or responsiveness, and restricted, stereotypic, and ritualized patterns of interests and behavior. 'Autism spectrum disorder,' sometimes referred to as ASD, is a broader phenotype encompassing the less severe disorders Asperger syndrome and pervasive developmental disorder, not otherwise specified (PDD-NOS). 'Broad autism phenotype' includes individuals with some symptoms of autism, but who do not meet the full criteria for autism or other disorders. Mental retardation coexists in approximately two-thirds of individuals with ASD, except for Asperger syndrome, in which mental retardation is conspicuously absent. Genetic studies in autism often include family members with these less stringent diagnoses.Â	NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC ; NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC

MECP2	Severe neonatal-onset encephalopathy with microcephaly	A rare severe, X-linked, neurodevelopmental disorder characterized by rapid developmental regression in infancy, partial or complete loss of purposeful hand movements, loss of speech, gait abnormalities, and stereotypic hand movements, commonly associated with deceleration of head growth, severe intellectual disability, seizures, and breathing abnormalities. The disorder has a progressive clinical course and may associate various comorbidities including gastrointestinal diseases, scoliosis, and behavioral disorders.	Classic or typical Rett syndrome (RTT) primarily affects girls and is characterized by apparently normal psychomotor development during the first 6-18 months of life followed by developmental stagnation with rapid regression in language and motor abilities, and subsequent long-term plateauing of skills. Repetitive, stereotypic hand movements replace purposeful hand use. Additional findings include autistic features, panic-like attacks, bruxism, episodic apnea and/or hyperpnea, gait ataxia and apraxia, tremors, seizures (60-80%), and acquired microcephaly. There is a wide variability in the rate of disease progression and severity. A number of males with a phenotype comparable to females with classical RTT have been described.	NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC ; NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC
MECP2	Systemic lupus erythematosus	Severe neonatal-onset encephalopathy with microcephaly is a rare monogenic disease with epilepsy characterized by neonatal-onset encephalopathy, microcephaly, severe developmental delay or absent development, breathing abnormalities (including central hypoventilation and/or respiratory insufficiency), intractable seizures, abnormal muscle tone and involuntary movements. Early death is usual.	The MECP2 gene is mutated in Rett syndrome (RTT), a severe neurodevelopmental disorder that almost always occurs in females. Although it was first thought that MECP2 mutations causing Rett syndrome were lethal in males, later reports identified a severe neonatal encephalopathy in surviving male sibs of patients with Rett syndrome.	NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC ; NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC

MECP2	Trisomy Xq28	Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by production of autoantibodies against nuclear, cytoplasmic, and cell surface molecules that transcend organ-specific boundaries. Tissue deposition of antibodies or immune complexes induces inflammation and subsequent injury of multiple organs and finally results in clinical manifestations of SLE, including glomerulonephritis, dermatitis, thrombosis, vasculitis, seizures, and arthritis.		NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC ; NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC
MECP2	X-linked intellectual disability-psychosis-macroorchidism syndrome	Distal Xq duplications refer to chromosomal disorders resulting from involvement of the long arm of the X chromosome (Xq). Clinical manifestations vary widely depending on the gender of the patient and on the gene content of the duplicated segment. The prevalence of Xq duplications remains unknown.	The most frequently reported distal duplications involve the Xq28 segment and yield a recognizable phenotype including distinctive facial features (premature closure of the fontanels or a ridged metopic suture, a broad face with full cheeks, epicanthal folds, large ears, a small and open mouth, ear anomalies, a pointed nose, an abnormal palate and facial hypotonia), major axial hypotonia, severe developmental delay, severe feeding difficulties, abnormal genitalia and susceptibility to infections.	NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC ; NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC

MECP2	X-linked non-syndromic intellectual disability	An X-linked syndromic intellectual disability characterized by developmental delay, variable degree of intellectual disability, speech delay or absent speech, pyramidal signs, tremor, macroorchidism and variable mood and behavior problems, including psychosis and autistic-like behavior. Males are predominantly affected, some females show lower cognitive abilities.	The MECP2 gene is mutated in Rett syndrome (RTT), a severe neurodevelopmental disorder that almost always occurs in females. Males with non-RTT mutations in the MECP2 gene can demonstrate a wide variety of phenotypes, including X-linked mental retardation with spasticity and other variable features, described here, and Lubs X-linked mental retardation syndrome (MRXSL). Males with RTT-associated MECP2 mutations have neonatal severe encephalopathy that is usually lethal (300673).	NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC ; NM_004992.3(MECP2):c.964C>T ; NM_004992.3(MECP2):c.916C>T ; NM_004992.3(MECP2):c.215dupC ; NM_004992.3(MECP2):c.611C>G ; NM_004992.3(MECP2):c.502C>T ; NM_004992.3(MECP2):c.763C>T ; NM_004992.3(MECP2):c.730C>T ; NM_004992.3(MECP2):c.965C>T ; NM_004992.3(MECP2):c.674C>T ; NM_001110792.1(MECP2):c.916C>T ; NM_004992.3(MECP2):c.806delG ; NM_004992.3(MECP2):c.808C>T ; NM_004992.3(MECP2):c.753delC
MEFV	BehÃ§et disease	MECP2 duplication syndrome is an X-linked neurodevelopmental disorder characterized by severe to profound mental retardation, infantile hypotonia, mild dysmorphic features, poor speech development, autistic features, seizures, progressive spasticity, and recurrent infections. Only males are affected, although female carriers may have some mild neuropsychiatric features, such as anxiety. Submicroscopic Xq28 duplications encompassing MECP2 are considered nonrecurrent events, because the breakpoint locations and rearrangement sizes vary among affected individuals.	0	NM_000243.2(MEFV):c.2082G>A ; c.163dup ; NM_000243.2(MEFV):c.1437C>G ; NM_000243.2(MEFV):c.2040G>A ; NM_000243.2(MEFV):c.2040G>C ; NM_000243.2(MEFV):c.2080A>G ; c.1141C>T ; NM_000243.2(MEFV):c.2282G>A ; NM_000243.2(MEFV):c.2076_2078delAAT ; c.656dup ; NM_000243.2(MEFV):c.1958G>A ; NM_000243.2(MEFV):c.2177T>C ; NM_000243.2(MEFV):c.2082G>A ; c.163dup ; NM_000243.2(MEFV):c.1437C>G ; NM_000243.2(MEFV):c.2040G>A ; NM_000243.2(MEFV):c.2040G>C ; NM_000243.2(MEFV):c.2080A>G ; c.1141C>T ; NM_000243.2(MEFV):c.2282G>A ; NM_000243.2(MEFV):c.2076_2078delAAT ; c.656dup ; NM_000243.2(MEFV):c.1958G>A ; NM_000243.2(MEFV):c.2177T>C

MEFV	Familial Mediterranean fever	A rare, chronic, relapsing, multisystemic vasculitis characterized by mucocutaneous lesions, as well as articular, vascular, ocular and central nervous system manifestations.	Onset most commonly occurs in adults (mean 30 years of age), but pediatric cases have been reported. Relapsing episodes of round oral aphthae with sharp erythematous and elevated borders (1-3 cm diameter) may be accompanied by genital aphthae (>50% of cases); cutaneous features may include pseudo-folliculitis and erythema nodosum. Ocular disorders (posterior uveitis, retinal vasculitis) occur in over 50% of BD patients. Arthralgia and/or non-erosive, asymmetric, arthritis affecting mainly large articulation (knees, ankles ect.) are frequent (45%) and can occur as an initial symptom. Vasculitis in BD is more frequent in the venous system where thromboses in femoro-iliac, superior and inferior vena cava and cerebral territories may occur. Rarer arterial thromboses and aneurysms primarily affect the pulmonary and aorta vessels. Neurological manifestations (neuro-BD) are frequent (>20%), and may include headache, fever, pyramidal signs with hemiparesis, cranial nerve damage, meningitis, behavioral changes and sphincter dysfunction. Aphthoid and/or ulcerative lesions may affect the whole digestive tract but mainly the ileo-caecum and ascending colon, potentially leading to hemorrhages and perforations.	NM_000243.2(MEFV):c.2082G>A ; c.163dup ; NM_000243.2(MEFV):c.1437C>G ; NM_000243.2(MEFV):c.2040G>A ; NM_000243.2(MEFV):c.2040G>C ; NM_000243.2(MEFV):c.2080A>G ; c.1141C>T ; NM_000243.2(MEFV):c.2282G>A ; NM_000243.2(MEFV):c.2076_2078delAAT ; c.656dup ; NM_000243.2(MEFV):c.1958G>A ; NM_000243.2(MEFV):c.2177T>C ; NM_000243.2(MEFV):c.2082G>A ; c.163dup ; NM_000243.2(MEFV):c.1437C>G ; NM_000243.2(MEFV):c.2040G>A ; NM_000243.2(MEFV):c.2040G>C ; NM_000243.2(MEFV):c.2080A>G ; c.1141C>T ; NM_000243.2(MEFV):c.2282G>A ; NM_000243.2(MEFV):c.2076_2078delAAT ; c.656dup ; NM_000243.2(MEFV):c.1958G>A ; NM_000243.2(MEFV):c.2177T>C

MEFV	Intermittent hydrarthrosis	Familial Mediterranean fever (FMF) is an autoinflammatory disorder characterized by recurrent short episodes of fever and serositis resulting in pain in the abdomen, chest, joints and muscles.	Disease onset usually occurs before the age of 30 with an earlier onset corresponding to a more severe phenotype. FMF can be divided into 2 types: FMF type 1 and 2. Type 1 is characterized by attacks (as often as once a week or every few years) of fever and serositis lasting 1-4 days and resolving spontaneously. Stress, exposure to cold, fat-rich meals, infections, certain drugs and menstrual cycles are possible attack triggers. Mild symptoms (myalgia, headache, nausea, dyspnea, arthralgia, low back pain, asthenia and anxiety) precede attacks and last about 17 hours. Attacks manifest as fever (38Â°C-40Â°C lasting 12-72 hours and not responding to antibiotics), diffuse or localized abdominal pain (often mimicking acute abdomen), constipation (diarrhea in children), arthralgias (in large joints), arthritis (in upper/lower limb/knee joints) and chest pain caused by pleuritis and/or pericarditis (see this term). In 7-40% of patients cutaneous involvement is also present. Amyloidosis type AA (see this term) can be a serious long term complication. FMF type 2 describes a phenotype where amyloidosis occurs as the first and only manifestation of the disease.	NM_000243.2(MEFV):c.2082G>A ; c.163dup ; NM_000243.2(MEFV):c.1437C>G ; NM_000243.2(MEFV):c.2040G>A ; NM_000243.2(MEFV):c.2040G>C ; NM_000243.2(MEFV):c.2080A>G ; c.1141C>T ; NM_000243.2(MEFV):c.2282G>A ; NM_000243.2(MEFV):c.2076_2078delAAT ; c.656dup ; NM_000243.2(MEFV):c.1958G>A ; NM_000243.2(MEFV):c.2177T>C ; NM_000243.2(MEFV):c.2082G>A ; c.163dup ; NM_000243.2(MEFV):c.1437C>G ; NM_000243.2(MEFV):c.2040G>A ; NM_000243.2(MEFV):c.2040G>C ; NM_000243.2(MEFV):c.2080A>G ; c.1141C>T ; NM_000243.2(MEFV):c.2282G>A ; NM_000243.2(MEFV):c.2076_2078delAAT ; c.656dup ; NM_000243.2(MEFV):c.1958G>A ; NM_000243.2(MEFV):c.2177T>C

MEFV	Sweet syndrome	A rare rheumatologic disease characterized by recurrent self-remitting episodes of acute monoarticular arthritis, often with a fixed periodicity, typically affecting the knee or another large joint, which develops an effusion over 12 to 24 hours with only mild to moderate pain and minimal signs of inflammation. Attacks last three to five days and may parallel menses in females. Systemic symptoms are absent, and no joint damage occurs.		NM_000243.2(MEFV):c.2082G>A ; c.163dup ; NM_000243.2(MEFV):c.1437C>G ; NM_000243.2(MEFV):c.2040G>A ; NM_000243.2(MEFV):c.2040G>C ; NM_000243.2(MEFV):c.2080A>G ; c.1141C>T ; NM_000243.2(MEFV):c.2282G>A ; NM_000243.2(MEFV):c.2076_2078delAAT ; c.656dup ; NM_000243.2(MEFV):c.1958G>A ; NM_000243.2(MEFV):c.2177T>C ; NM_000243.2(MEFV):c.2082G>A ; c.163dup ; NM_000243.2(MEFV):c.1437C>G ; NM_000243.2(MEFV):c.2040G>A ; NM_000243.2(MEFV):c.2040G>C ; NM_000243.2(MEFV):c.2080A>G ; c.1141C>T ; NM_000243.2(MEFV):c.2282G>A ; NM_000243.2(MEFV):c.2076_2078delAAT ; c.656dup ; NM_000243.2(MEFV):c.1958G>A ; NM_000243.2(MEFV):c.2177T>C

MFSD8	CLN7 disease	A rare inflammatory disease characterized by abrupt appearance of painful, edematous and erythematous papules, plaques and nodules on the skin, and frequently accompanied by fever and neutrophilia with a dense infiltration of mature neutrophils that are typically located in the upper dermis. The disease is classically associated with inflammatory disease, pregnancy, infection (mostly of the upper respiratory tract), or vaccination but may be idiopathic, associated with a hematological or visceral malignancy, or drug-induced.	Classical Sweet syndrome (CSS) usually presents in women between the age of 30 and 50 years, it is often preceded by an upper respiratory tract infection and may be associated with inflammatory bowel disease. It is characterized by the abrupt onset of painful erythematous plaques or nodules, but pustules and bullae are also described. Fever is observed in 30 to 80% of cases. Approximately one-third of patients with CSS experience recurrence of the dermatosis. Malignancy-associated Sweet syndrome (MASS) can occur as a paraneoplastic syndrome in patients with an established cancer or individuals whose Sweet syndrome-related hematologic dyscrasia or solid tumor was previously undiscovered; MASS is most commonly related to acute myelogenous leukemia. The dermatosis can precede, follow, or appear concurrently with the diagnosis of the patient's cancer. Hence, MASS can be the cutaneous harbinger of either an undiagnosed visceral malignancy in a previously cancer-free individual or an unsuspected cancer recurrence in an oncology patient. Drug-induced Sweet syndrome (DISS) most commonly occurs in patients who have been treated with granulocyte-colony stimulating factor, however, numerous medications have also be associated with DISS.	NM_152778.2(MFSD8):c.929G>A ; c.1090del ; NM_152778.2(MFSD8):c.894T>G ; NM_152778.2(MFSD8):c.881C>A ; NM_152778.2(MFSD8):c.1286G>A ; NM_152778.2(MFSD8):c.1235C>T ; c.1525_1526del ; c.999-2A>G ; NM_152778.2(MFSD8):c.929G>A ; c.1090del ; NM_152778.2(MFSD8):c.894T>G ; NM_152778.2(MFSD8):c.881C>A ; NM_152778.2(MFSD8):c.1286G>A ; NM_152778.2(MFSD8):c.1235C>T ; c.1525_1526del ; c.999-2A>G

MKKS	Bardet-Biedl syndrome	Late infantile neuronal ceroid lipofuscinoses (LINCLs) are a genetically heterogeneous group of neuronal ceroid lipofuscinoses (NCLs; see this term) typically characterized by onset during infancy or early childhood with decline of mental and motor capacities, epilepsy, and vision loss through retinal degeneration.	The initial clinical symptoms are motor or/and cognitive decline or epilepsy but the mean age of onset and speed of progression may vary depending on the underlying genetic defect. Patients with classic LINCL generally present with a standstill of mental development or the onset of severe epilepsy around the third year of life. The disorder progresses to complete loss of almost all motor and mental capacities before school age. As visual loss is not a prominent finding in the early stages of the disease course, it is frequently not recognized. Several variant forms have also been described in the literature (vLINCL) in which the mean ages of onset generally vary from 2-7 years and which commonly manifest with severe epilepsy followed by cognitive and motor decline and vision loss.	c.353del ; NC_000020.11:g.10407663_10407664del ; c.1436C>G ; c.353del ; NC_000020.11:g.10407663_10407664del ; c.1436C>G
MKKS	McKusick-Kaufman syndrome	Bardet-Biedl syndrome (BBS) is a ciliopathy with multisystem involvement.	This disorder is characterized by a combination of clinical signs: obesity, pigmentary retinopathy, post-axial polydactyly, polycystic kidneys, hypogenitalism, and learning disabilities, many of which appear several years after disease onset. Clinical expression is variable but most patients manifest the majority of clinical signs during the disease course. Pigmentary retinopathy is the only constant clinical sign after childhood. BBS may also be associated with several other manifestations including diabetes, hypertension, congenital cardiopathy and Hirschsprung disease (see this term).	c.353del ; NC_000020.11:g.10407663_10407664del ; c.1436C>G ; c.353del ; NC_000020.11:g.10407663_10407664del ; c.1436C>G

MKS1	Bardet-Biedl syndrome	McKusick-Kaufman syndrome is an autosomal recessive disorder characterized by genitourinary malformations, especially hydrometrocolpos, polydactyly, and, more rarely, heart or gastrointestinal malformations	A rare, genetic multiple congenital anomalies syndrome characterized by genitourinary malformations (hydrometrocolpos in females and in males, glanular hypospadias and prominent scrotal raphe) , postaxial polydactyly that may affect only one or several limbs, and to a lesser extent cardiac defects. Hydrometrocolpos is due to either a congenital obstruction, imperforate hymen or vaginal atresia, and causes a palpable mass and possibly hydronephrosis. Other anomalies occasionally reported include choanal atresia, pituitary dysplasia, esophageal atresia and distal tracheoesophageal fistula, Hirschsprung disease, vertebral anomalies, and hydrops fetalis. The disorder is allelic with Bardet-Biedl, and as some phenotypic overlap has been observed, patients should be reevaluated in later childhood for retinistis pigmentosas and other signs of Bardet-Biedl syndrome.	NM_017777.3(MKS1):c.1024+1G>A ; NM_017777.3(MKS1):c.508C>T ; NM_017777.3(MKS1):c.1024+1G>A ; NM_017777.3(MKS1):c.508C>T
MKS1	Joubert syndrome	Bardet-Biedl syndrome (BBS) is a ciliopathy with multisystem involvement.	This disorder is characterized by a combination of clinical signs: obesity, pigmentary retinopathy, post-axial polydactyly, polycystic kidneys, hypogenitalism, and learning disabilities, many of which appear several years after disease onset. Clinical expression is variable but most patients manifest the majority of clinical signs during the disease course. Pigmentary retinopathy is the only constant clinical sign after childhood. BBS may also be associated with several other manifestations including diabetes, hypertension, congenital cardiopathy and Hirschsprung disease (see this term).	NM_017777.3(MKS1):c.1024+1G>A ; NM_017777.3(MKS1):c.508C>T ; NM_017777.3(MKS1):c.1024+1G>A ; NM_017777.3(MKS1):c.508C>T

MKS1	Joubert syndrome with ocular defect	A rare, autosomal recessive congenital cerebellar ataxia characterized by congenital malformation of the brainstem and agenesis or hypoplasia of the cerebellar vermis leading to an abnormal respiratory pattern, nystagmus, hypotonia, ataxia, and delay in achieving motor milestones.	Disease onset is antenatal, although clinical presentation is typically in the neonatal period with irregular breathing pattern (episodic tachypnea and/or apnea), and nystagmus. During infancy, hypotonia may appear. Cerebellar ataxia (staggering gait and imbalance) may develop later. Delayed acquisition of motor milestones is common. Cognitive abilities are variable, ranging from severe intellectual deficit to normal intelligence. Neuro-ophthalmologic examination may show oculomotor apraxia. In some cases, seizures occur. Careful examination of the face often shows a characteristic appearance: large head, prominent forehead, high rounded eyebrows, epicanthal folds, ptosis (occasionally), an upturned nose with prominent nostrils, an open mouth (which tends to have an oval shape early on, a 'rhomboid' appearance later, and finally can appear triangular with downturned angles), tongue protrusion and rhythmic tongue motions, and occasionally low-set and tilted ears. Other features sometimes present in Joubert syndrome include retinal dystrophy, hepatopathy, nephronophthisis, and polydactyly.	NM_017777.3(MKS1):c.1024+1G>A ; NM_017777.3(MKS1):c.508C>T ; NM_017777.3(MKS1):c.1024+1G>A ; NM_017777.3(MKS1):c.508C>T
MKS1	Meckel syndrome	Joubert syndrome with ocular defect is, along with pure JS, the most frequent subtype of Joubert syndrome and related disorders (JSRD, see these terms) characterized by the neurological features of JS associated with retinal dystrophy.	Age of onset and severity of retinal involvement are variable, ranging from congenital blindness in patients with Leber congenital amaurosis (LCA, see this term) to progressive retinopathy with partial conservation of vision.	NM_017777.3(MKS1):c.1024+1G>A ; NM_017777.3(MKS1):c.508C>T ; NM_017777.3(MKS1):c.1024+1G>A ; NM_017777.3(MKS1):c.508C>T

MLC1	Megalencephalic leukoencephalopathy with subcortical cysts	A rare, lethal, genetic, multiple congenital anomaly disorder characterized by the triad of brain malformation (mainly occipital encephalocele), large polycystic kidneys, and polydactyly, as well as associated abnormalities that may include cleft lip/palate, cardiac and genital anomalies, central nervous system (CNS) malformations, liver fibrosis, and bone dysplasia.	Fetuses affected by Meckel syndrome (MKS) survive only a few days to a few weeks at the most, or dieÃ in utero. The main CNS features include occipital encephalocele, hydrocephalus, anencephaly, holoprosencephaly, as well as Dandy-Walker. Large polycystic kidneys with cystic dysplasia are a constant feature of Meckel syndrome. Hepatic dysgenesis and liver fibrosis are frequent. Polydactyly may affect all four extremities and is typically postaxial (80%) or very rarely preaxial. Affected individuals have pulmonary hypoplasia secondary to oligohydramnios. Cleft lip and palate, microphthalmia and micrognathia may be observed. Cardiac malformations may include atrial septal defect, aorta coarctation, patent arterial duct, and valvular pulmonary stenosis. Incomplete development of internal and external genitalia, and cryptorchidism in males are common.	NM_015166.3:c.274C>T ; NM_015166.3(MLC1):c.206C>T ; NM_015166.3(MLC1):c.423C>A ; NM_015166.3(MLC1):c.135dupC ; c.33dup ; c.424-2A>C ; NM_015166.3(MLC1):c.278C>T ; NM_015166.3(MLC1):c.422A>G ; NM_015166.3:c.274C>T ; NM_015166.3(MLC1):c.206C>T ; NM_015166.3(MLC1):c.423C>A ; NM_015166.3(MLC1):c.135dupC ; c.33dup ; c.424-2A>C ; NM_015166.3(MLC1):c.278C>T ; NM_015166.3(MLC1):c.422A>G
MLYCD	Malonic aciduria	Megalencephalic leukoencephalopathy with subcortical cysts is a leukodystrophy characterized by early-onset macrocephaly and delayed-onset neurologic deterioration, including cerebellar ataxia, spasticity, epilepsy, and mild cognitive decline.	Megalencephalic leukoencephalopathy with subcortical cysts (MLC) is a form of leukodystrophy that is characterized by infantile-onset macrocephaly, often with mild neurologic signs at presentation (such as mild motor delay), which worsen with time, leading to poor ambulation, falls, ataxia, spasticity, increasing seizures and cognitive decline. Brain magnetic resonance imaging reveals diffusely abnormal and mildly swollen white matter as well as subcortical cysts in the anterior temporal and frontoparietal regions.	c.758del ; NM_012213.2(MLYCD):c.560C>G ; NM_012213.2(MLYCD):c.679_680insTGAAGC ; c.758del ; NM_012213.2(MLYCD):c.560C>G ; NM_012213.2(MLYCD):c.679_680insTGAAGC
MMAA	Vitamin B12-responsive methylmalonic acidemia type cblA	Malonic aciduria is a metabolic disorder caused by deficiency of malonyl-CoA decarboxylase (MCD).	This condition usually presents in early childhood and the manifestations are variable. The majority of patients are developmentally delayed with other features that include hypotonia, seizures, hypoglycaemia, metabolic acidosis, cardiomyopathy and diarrhoea.	NM_172250.2(MMAA):c.503delC ; c.811G>T ; NM_172250.3(MMAA):c.450dup ; NM_172250.2(MMAA):c.586C>T ; NM_172250.2(MMAA):c.620A>G ; NM_172250.2(MMAA):c.455delC ; NM_172250.2(MMAA):c.1034delT ; NM_172250.2(MMAA):c.387C>A ; NM_172250.3(MMAA):c.283C>T ; NM_172250.2(MMAA):c.503delC ; c.811G>T ; NM_172250.3(MMAA):c.450dup ; NM_172250.2(MMAA):c.586C>T ; NM_172250.2(MMAA):c.620A>G ; NM_172250.2(MMAA):c.455delC ; NM_172250.2(MMAA):c.1034delT ; NM_172250.2(MMAA):c.387C>A ; NM_172250.3(MMAA):c.283C>T

MMAB	Vitamin B12-responsive methylmalonic acidemia type cblB	Methylmalonic aciduria is a genetically heterogeneous disorder of methylmalonate and cobalamin (cbl; vitamin B12) metabolism. Different forms of isolated methylmalonic aciduria have been classified according to complementation groups of cells in vitro. Patients with defects in the synthesis of AdoCbl are usually responsive to vitamin B12 therapy and are classified as 'cbl' type: these include cblA and cblB, which is caused by mutation in the MMAB gene on 12q24. See also cblH, which may be a subset of cblA. The 'mut' form of MMA is caused by mutation in the MUT gene on chromosome 6p. In general, the mut form of MMA is unresponsive to vitamin B12 therapy.		NM_052845.3(MMAB):c.568C>T ; c.220G>T ; NM_052845.3(MMAB):c.197-1G>T ; c.197-1G>A ; NM_052845.3(MMAB):c.556C>T ; NM_052845.3(MMAB):c.700C>T ; NM_052845.3(MMAB):c.568C>T ; c.220G>T ; NM_052845.3(MMAB):c.197-1G>T ; c.197-1G>A ; NM_052845.3(MMAB):c.556C>T ; NM_052845.3(MMAB):c.700C>T

MMACHC	Methylmalonic acidemia with homocystinuria, type cblC	Methylmalonic aciduria is a genetically heterogeneous disorder of methylmalonate and cobalamin (cbl; vitamin B12) metabolism. Different forms of isolated methylmalonic aciduria have been classified according to complementation groups of cells in vitro. Patients with defects in the synthesis of AdoCbl are usually responsive to vitamin B12 therapy and are classified as 'cbl' type: these include cblB and cblA (251100). The cblA type is caused by mutation in the MMAA gene (607481). The 'mut' type (251000) is caused by mutation in the MUT gene; in general, the mut form of MMA is unresponsive to vitamin B12 therapy.		NM_015506.2(MMACHC):c.482G>A ; NM_015506.2(MMACHC):c.440G>C ; NM_015506.2(MMACHC):c.615C>G ; NM_015506.2(MMACHC):c.394C>T ; NM_015506.2(MMACHC):c.547_548delGT ; NM_015506.2(MMACHC):c.331C>T ; NM_015506.2(MMACHC):c.609G>A ; NM_015506.2(MMACHC):c.347T>C ; NM_015506.2(MMACHC):c.658_660delAAG ; NM_015506.2(MMACHC):c.481C>T ; NM_015506.2(MMACHC):c.688C>T ; NM_015506.2(MMACHC):c.608G>A ; NM_015506.2(MMACHC):c.388_390delTAC ; NM_015506.2(MMACHC):c.619dup ; NM_015506.2(MMACHC):c.615C>A ; NM_015506.2(MMACHC):c.482G>A ; NM_015506.2(MMACHC):c.440G>C ; NM_015506.2(MMACHC):c.615C>G ; NM_015506.2(MMACHC):c.394C>T ; NM_015506.2(MMACHC):c.547_548delGT ; NM_015506.2(MMACHC):c.331C>T ; NM_015506.2(MMACHC):c.609G>A ; NM_015506.2(MMACHC):c.347T>C ; NM_015506.2(MMACHC):c.658_660delAAG ; NM_015506.2(MMACHC):c.481C>T ; NM_015506.2(MMACHC):c.688C>T ; NM_015506.2(MMACHC):c.608G>A ; NM_015506.2(MMACHC):c.388_390delTAC ; NM_015506.2(MMACHC):c.619dup ; NM_015506.2(MMACHC):c.615C>A
MMACHC	Methylcobalamin deficiency type cblDv1	cblC type methylmalonic acidemia with homocystinuria is a form of methylmalonic acidemia with homocystinuria (see this term), an inborn error of vitamin B12 (cobalamin) metabolism characterized by megaloblastic anemia, lethargy, failure to thrive, developmental delay, intellectual deficit and seizures.	The disease typically presents with failure to thrive, acute neurological deterioration, intellectual deficit, lethargy, seizures, microcephaly, a salt-and-pepper retinopathy, and signs of megaloblastic anemia (pallor, fatigue, anorexia). Severe brain abnormalities including hydrocephalus, white matter abnormalities, cerebral atrophy, and unusual basal ganglia lesions are common. Onset of the disorder can be early (infantile) or late (juvenile or adult), with the late-onset form characterized by ataxia, dementia and psychosis.	NM_015506.2(MMACHC):c.482G>A ; NM_015506.2(MMACHC):c.440G>C ; NM_015506.2(MMACHC):c.615C>G ; NM_015506.2(MMACHC):c.394C>T ; NM_015506.2(MMACHC):c.547_548delGT ; NM_015506.2(MMACHC):c.331C>T ; NM_015506.2(MMACHC):c.609G>A ; NM_015506.2(MMACHC):c.347T>C ; NM_015506.2(MMACHC):c.658_660delAAG ; NM_015506.2(MMACHC):c.481C>T ; NM_015506.2(MMACHC):c.688C>T ; NM_015506.2(MMACHC):c.608G>A ; NM_015506.2(MMACHC):c.388_390delTAC ; NM_015506.2(MMACHC):c.619dup ; NM_015506.2(MMACHC):c.615C>A ; NM_015506.2(MMACHC):c.482G>A ; NM_015506.2(MMACHC):c.440G>C ; NM_015506.2(MMACHC):c.615C>G ; NM_015506.2(MMACHC):c.394C>T ; NM_015506.2(MMACHC):c.547_548delGT ; NM_015506.2(MMACHC):c.331C>T ; NM_015506.2(MMACHC):c.609G>A ; NM_015506.2(MMACHC):c.347T>C ; NM_015506.2(MMACHC):c.658_660delAAG ; NM_015506.2(MMACHC):c.481C>T ; NM_015506.2(MMACHC):c.688C>T ; NM_015506.2(MMACHC):c.608G>A ; NM_015506.2(MMACHC):c.388_390delTAC ; NM_015506.2(MMACHC):c.619dup ; NM_015506.2(MMACHC):c.615C>A

MMACHC	Methylmalonic acidemia with homocystinuria, type cblD	Homocystinuria without methylmalonic aciduria is an inborn error of vitamin B12 (cobalamin) metabolism characterized by megaloblastic anemia, encephalopathy and, sometimes, developmental delay, and associated with homocystinuria and hyperhomocysteinemia. There are three types of homocystinuria without methylmalonic aciduria;Â cblE, cblGÂ andÂ cblD-variant 1 (cblDv1).	Homocystinuria without methylmalonic aciduria manifests mainly in early childhood with failure to thrive, megaloblastic anemia, developmental delay, hypotonia, seizures and cerebral atrophy with white matter abnormalities. Some patients may have an acute expression in the first few months of life, with vomiting, poor feeding and lethargy. Patients develop homocystinuria, hyperhomocysteinemia and, sometimes, hypomethioninemia. A mild clinical phenotype and late-onset disease in the absence of neurological involvement have also been described for the cblE disorder. Presentation in adulthood with ataxia, dementia or psychosis has been observed in cblG.	NM_015506.2(MMACHC):c.482G>A ; NM_015506.2(MMACHC):c.440G>C ; NM_015506.2(MMACHC):c.615C>G ; NM_015506.2(MMACHC):c.394C>T ; NM_015506.2(MMACHC):c.547_548delGT ; NM_015506.2(MMACHC):c.331C>T ; NM_015506.2(MMACHC):c.609G>A ; NM_015506.2(MMACHC):c.347T>C ; NM_015506.2(MMACHC):c.658_660delAAG ; NM_015506.2(MMACHC):c.481C>T ; NM_015506.2(MMACHC):c.688C>T ; NM_015506.2(MMACHC):c.608G>A ; NM_015506.2(MMACHC):c.388_390delTAC ; NM_015506.2(MMACHC):c.619dup ; NM_015506.2(MMACHC):c.615C>A ; NM_015506.2(MMACHC):c.482G>A ; NM_015506.2(MMACHC):c.440G>C ; NM_015506.2(MMACHC):c.615C>G ; NM_015506.2(MMACHC):c.394C>T ; NM_015506.2(MMACHC):c.547_548delGT ; NM_015506.2(MMACHC):c.331C>T ; NM_015506.2(MMACHC):c.609G>A ; NM_015506.2(MMACHC):c.347T>C ; NM_015506.2(MMACHC):c.658_660delAAG ; NM_015506.2(MMACHC):c.481C>T ; NM_015506.2(MMACHC):c.688C>T ; NM_015506.2(MMACHC):c.608G>A ; NM_015506.2(MMACHC):c.388_390delTAC ; NM_015506.2(MMACHC):c.619dup ; NM_015506.2(MMACHC):c.615C>A
MMACHC	Vitamin B12-responsive methylmalonic acidemia, type cblDv2	cblD type methylmalonic acidemia with homocystinuria is a form of methylmalonic acidemia with homocystinuria (see this term), an inborn error of vitamin B12 (cobalamin) metabolism characterized by variable biochemical, neurological and hematological manifestations.	Three different presentations have been described: the classic form with combined methylmalonic aciduria and homocystinuria;Â cblDÂ variant 1 (cblDv1) with isolated homocystinuria; andÂ cblDÂ variant 2 (cblDv2) with isolated methylmalonic aciduria. Clinical presentation is extremely variable. The disorder can present from early infancy to late childhood. Presenting signs are variable depending on which aspect(s) of cobalamin metabolism are affected and can include developmental delay, severe learning difficulties, seizures, movement and gait abnormalities, behavioral problems and signs of megaloblastic anemia (pallor, fatigue, anorexia).	NM_015506.2(MMACHC):c.482G>A ; NM_015506.2(MMACHC):c.440G>C ; NM_015506.2(MMACHC):c.615C>G ; NM_015506.2(MMACHC):c.394C>T ; NM_015506.2(MMACHC):c.547_548delGT ; NM_015506.2(MMACHC):c.331C>T ; NM_015506.2(MMACHC):c.609G>A ; NM_015506.2(MMACHC):c.347T>C ; NM_015506.2(MMACHC):c.658_660delAAG ; NM_015506.2(MMACHC):c.481C>T ; NM_015506.2(MMACHC):c.688C>T ; NM_015506.2(MMACHC):c.608G>A ; NM_015506.2(MMACHC):c.388_390delTAC ; NM_015506.2(MMACHC):c.619dup ; NM_015506.2(MMACHC):c.615C>A ; NM_015506.2(MMACHC):c.482G>A ; NM_015506.2(MMACHC):c.440G>C ; NM_015506.2(MMACHC):c.615C>G ; NM_015506.2(MMACHC):c.394C>T ; NM_015506.2(MMACHC):c.547_548delGT ; NM_015506.2(MMACHC):c.331C>T ; NM_015506.2(MMACHC):c.609G>A ; NM_015506.2(MMACHC):c.347T>C ; NM_015506.2(MMACHC):c.658_660delAAG ; NM_015506.2(MMACHC):c.481C>T ; NM_015506.2(MMACHC):c.688C>T ; NM_015506.2(MMACHC):c.608G>A ; NM_015506.2(MMACHC):c.388_390delTAC ; NM_015506.2(MMACHC):c.619dup ; NM_015506.2(MMACHC):c.615C>A

MMADHC	Methylmalonic acidemia with homocystinuria, type cblC	An inborn error of vitamin B12 (cobalamin) metabolism characterized by recurrent ketoacidotic comas or transient vomiting, dehydration, hypotonia and intellectual deficit, which responds to vitamin B12. There are three types:Â cblA, cblBÂ andÂ cblD-variant 2 (cblDv2).	Patients usually present in infancy or early childhood with features including lethargy, failure to thrive, recurrent vomiting, dehydration, respiratory distress, muscle hypotonia, hepatomegaly and coma. They may also show signs of anemia (not megaloblastic), have potentially life-threatening ketoacidosis and/or hyperammonemia, and developmental delay and intellectual deficit, with metabolic stroke affecting the brain stem. MA frequently leads to end-stage renal failure by adolescence or adulthood. Patients withÂ cblBÂ are usually more severely affected than patients withÂ cblA.	NM_015702.2(MMADHC):c.776T>C ; NM_015702.2(MMADHC):c.748C>T ; NM_015702.2(MMADHC):c.545C>A ; c.478+1G>T ; NM_015702.3(MMADHC):c.419dup ; c.795dup ; NM_015702.2(MMADHC):c.746A>G ; NM_015702.2(MMADHC):c.57_64delCTCTTTAG ; NM_015702.2(MMADHC):c.776T>C ; NM_015702.2(MMADHC):c.748C>T ; NM_015702.2(MMADHC):c.545C>A ; c.478+1G>T ; NM_015702.3(MMADHC):c.419dup ; c.795dup ; NM_015702.2(MMADHC):c.746A>G ; NM_015702.2(MMADHC):c.57_64delCTCTTTAG
MMADHC	Methylcobalamin deficiency type cblDv1	cblC type methylmalonic acidemia with homocystinuria is a form of methylmalonic acidemia with homocystinuria (see this term), an inborn error of vitamin B12 (cobalamin) metabolism characterized by megaloblastic anemia, lethargy, failure to thrive, developmental delay, intellectual deficit and seizures.	The disease typically presents with failure to thrive, acute neurological deterioration, intellectual deficit, lethargy, seizures, microcephaly, a salt-and-pepper retinopathy, and signs of megaloblastic anemia (pallor, fatigue, anorexia). Severe brain abnormalities including hydrocephalus, white matter abnormalities, cerebral atrophy, and unusual basal ganglia lesions are common. Onset of the disorder can be early (infantile) or late (juvenile or adult), with the late-onset form characterized by ataxia, dementia and psychosis.	NM_015702.2(MMADHC):c.776T>C ; NM_015702.2(MMADHC):c.748C>T ; NM_015702.2(MMADHC):c.545C>A ; c.478+1G>T ; NM_015702.3(MMADHC):c.419dup ; c.795dup ; NM_015702.2(MMADHC):c.746A>G ; NM_015702.2(MMADHC):c.57_64delCTCTTTAG ; NM_015702.2(MMADHC):c.776T>C ; NM_015702.2(MMADHC):c.748C>T ; NM_015702.2(MMADHC):c.545C>A ; c.478+1G>T ; NM_015702.3(MMADHC):c.419dup ; c.795dup ; NM_015702.2(MMADHC):c.746A>G ; NM_015702.2(MMADHC):c.57_64delCTCTTTAG

MMADHC	Methylmalonic acidemia with homocystinuria, type cblD	Homocystinuria without methylmalonic aciduria is an inborn error of vitamin B12 (cobalamin) metabolism characterized by megaloblastic anemia, encephalopathy and, sometimes, developmental delay, and associated with homocystinuria and hyperhomocysteinemia. There are three types of homocystinuria without methylmalonic aciduria;Â cblE, cblGÂ andÂ cblD-variant 1 (cblDv1).	Homocystinuria without methylmalonic aciduria manifests mainly in early childhood with failure to thrive, megaloblastic anemia, developmental delay, hypotonia, seizures and cerebral atrophy with white matter abnormalities. Some patients may have an acute expression in the first few months of life, with vomiting, poor feeding and lethargy. Patients develop homocystinuria, hyperhomocysteinemia and, sometimes, hypomethioninemia. A mild clinical phenotype and late-onset disease in the absence of neurological involvement have also been described for the cblE disorder. Presentation in adulthood with ataxia, dementia or psychosis has been observed in cblG.	NM_015702.2(MMADHC):c.776T>C ; NM_015702.2(MMADHC):c.748C>T ; NM_015702.2(MMADHC):c.545C>A ; c.478+1G>T ; NM_015702.3(MMADHC):c.419dup ; c.795dup ; NM_015702.2(MMADHC):c.746A>G ; NM_015702.2(MMADHC):c.57_64delCTCTTTAG ; NM_015702.2(MMADHC):c.776T>C ; NM_015702.2(MMADHC):c.748C>T ; NM_015702.2(MMADHC):c.545C>A ; c.478+1G>T ; NM_015702.3(MMADHC):c.419dup ; c.795dup ; NM_015702.2(MMADHC):c.746A>G ; NM_015702.2(MMADHC):c.57_64delCTCTTTAG
MMADHC	Vitamin B12-responsive methylmalonic acidemia, type cblDv2	cblD type methylmalonic acidemia with homocystinuria is a form of methylmalonic acidemia with homocystinuria (see this term), an inborn error of vitamin B12 (cobalamin) metabolism characterized by variable biochemical, neurological and hematological manifestations.	Three different presentations have been described: the classic form with combined methylmalonic aciduria and homocystinuria;Â cblDÂ variant 1 (cblDv1) with isolated homocystinuria; andÂ cblDÂ variant 2 (cblDv2) with isolated methylmalonic aciduria. Clinical presentation is extremely variable. The disorder can present from early infancy to late childhood. Presenting signs are variable depending on which aspect(s) of cobalamin metabolism are affected and can include developmental delay, severe learning difficulties, seizures, movement and gait abnormalities, behavioral problems and signs of megaloblastic anemia (pallor, fatigue, anorexia).	NM_015702.2(MMADHC):c.776T>C ; NM_015702.2(MMADHC):c.748C>T ; NM_015702.2(MMADHC):c.545C>A ; c.478+1G>T ; NM_015702.3(MMADHC):c.419dup ; c.795dup ; NM_015702.2(MMADHC):c.746A>G ; NM_015702.2(MMADHC):c.57_64delCTCTTTAG ; NM_015702.2(MMADHC):c.776T>C ; NM_015702.2(MMADHC):c.748C>T ; NM_015702.2(MMADHC):c.545C>A ; c.478+1G>T ; NM_015702.3(MMADHC):c.419dup ; c.795dup ; NM_015702.2(MMADHC):c.746A>G ; NM_015702.2(MMADHC):c.57_64delCTCTTTAG

MMUT	Vitamin B12-unresponsive methylmalonic acidemia type mut-	An inborn error of vitamin B12 (cobalamin) metabolism characterized by recurrent ketoacidotic comas or transient vomiting, dehydration, hypotonia and intellectual deficit, which responds to vitamin B12. There are three types:Â cblA, cblBÂ andÂ cblD-variant 2 (cblDv2).	Patients usually present in infancy or early childhood with features including lethargy, failure to thrive, recurrent vomiting, dehydration, respiratory distress, muscle hypotonia, hepatomegaly and coma. They may also show signs of anemia (not megaloblastic), have potentially life-threatening ketoacidosis and/or hyperammonemia, and developmental delay and intellectual deficit, with metabolic stroke affecting the brain stem. MA frequently leads to end-stage renal failure by adolescence or adulthood. Patients withÂ cblBÂ are usually more severely affected than patients withÂ cblA.	NM_000255.3(MMUT):c.2150G>T ; NM_000255.3(MMUT):c.1867G>A ; NM_000255.3(MMUT):c.91C>T ; NM_000255.3(MMUT):c.1106G>A ; NM_000255.3(MMUT):c.2080C>T ; NM_000255.3(MMUT):c.643G>A ; NM_000255.3(MMUT):c.278G>A ; NM_000255.3(MMUT):c.313T>C ; NM_000255.3(MMUT):c.1280G>A ; c.1181T>A ; NM_000255.3(MMUT):c.1399C>T ; NM_000255.3(MMUT):c.1741C>T ; NM_000255.3(MMUT):c.1924G>C ; NM_000255.3(MMUT):c.280G>A ; NM_000255.3(MMUT):c.914T>C ; NM_000255.3(MMUT):c.572C>A ; c.1658del ; NM_000255.3(MMUT):c.1207C>T ; NM_000255.3(MMUT):c.607G>A ; NM_000255.3(MMUT):c.1445-2A>G ; NM_000255.3(MMUT):c.671_678dup ; NM_000255.3(MMUT):c.655A>T ; NM_000255.3(MMUT):c.1420C>T ; NM_000255.3(MMUT):c.682C>T ; NM_000255.3(MMUT):c.2150G>T ; NM_000255.3(MMUT):c.1867G>A ; NM_000255.3(MMUT):c.91C>T ; NM_000255.3(MMUT):c.1106G>A ; NM_000255.3(MMUT):c.2080C>T ; NM_000255.3(MMUT):c.643G>A ; NM_000255.3(MMUT):c.278G>A ; NM_000255.3(MMUT):c.313T>C ; NM_000255.3(MMUT):c.1280G>A ; c.1181T>A ; NM_000255.3(MMUT):c.1399C>T ; NM_000255.3(MMUT):c.1741C>T ; NM_000255.3(MMUT):c.1924G>C ; NM_000255.3(MMUT):c.280G>A ; NM_000255.3(MMUT):c.914T>C ; NM_000255.3(MMUT):c.572C>A ; c.1658del ; NM_000255.3(MMUT):c.1207C>T ; NM_000255.3(MMUT):c.607G>A ; NM_000255.3(MMUT):c.1445-2A>G ; NM_000255.3(MMUT):c.671_678dup ; NM_000255.3(MMUT):c.655A>T ; NM_000255.3(MMUT):c.1420C>T ; NM_000255.3(MMUT):c.682C>T
MOCS1	Sulfite oxidase deficiency due to molybdenum cofactor deficiency type A	Vitamin B12-unresponsive methylmalonic acidemia type mut- is an inborn error of metabolism characterized by recurrent ketoacidotic comas or transient vomiting, dehydration, hypotonia and intellectual deficit, which does not respond to administration of vitamin B12.	The disease typically presents very early in life (<1 to 4 weeks), although later onset cases have been observed, with features including lethargy, failure to thrive, recurrent vomiting, dehydration, respiratory distress, muscle hypotonia, developmental delay, intellectual deficit, hepatomegaly and coma. Patients may show signs of anemia. They may also have potentially life-threatening ketoacidosis and/or hyperammonemia, renal and neurological complications, metabolic stroke and cardiomyopathy. mut- is generally less severe than vitamin B12-unresponsive methylmalonic acidemia type mut0 (see this term) and may in some cases respond to vitamin B12 therapy. Long term complications include metabolic stroke and development of end stage renal failure. These complications are more frequent in mut0 than in mut-.	c.397_406del ; NM_001075098.3(MOCS1):c.217C>T ; c.1027C>T ; NM_001075098.3(MOCS1):c.956G>A ; c.397_406del ; NM_001075098.3(MOCS1):c.217C>T ; c.1027C>T ; NM_001075098.3(MOCS1):c.956G>A

MPI	MPI-CDG	Encephalopathy due to sulfite oxidase deficiency is a rare neurometabolic disorder characterized by seizures, progressive encephalopathy and lens dislocation.	Symptoms usually occur within the first week after birth with feeding difficulties, vomiting and seizures which are difficult to control. The majority of patients exhibit facial dysmorphism (prominent forehead, narrow bifrontal diameter, sunken eyes, elongated palpebral fissures, puffy cheeks, small nose and long philtrum and thick lips). The course is progressive, with spasticity, severe intellectual deficit, and microcephaly seen in survivors. Lens dislocation usually occurs late in infancy but has been observed as early as two months of age. A late onset form with a milder phenotype has also been described.	NM_002435.1(MPI):c.656G>A ; c.833_836del ; NM_002435.2(MPI):c.413T>C ; NM_002435.2(MPI):c.884G>A ; NM_002435.2(MPI):c.305C>T ; NM_002435.1(MPI):c.656G>A ; c.833_836del ; NM_002435.2(MPI):c.413T>C ; NM_002435.2(MPI):c.884G>A ; NM_002435.2(MPI):c.305C>T
MPV17	Navajo neurohepatopathy	CDG Ib is clinically distinct from most other CDGs by the lack of significant central nervous system involvement. The predominant symptoms are chronic diarrhea with failure to thrive and protein-losing enteropathy with coagulopathy. Some patients develop hepatic fibrosis. CDG Ib is also different from other CDGs in that it can be treated effectively with oral mannose supplementation, but can be fatal if untreated. Thus, CDG Ib should be considered in the differential diagnosis of patients with unexplained hypoglycemia, chronic diarrhea, liver disease, or coagulopathy in order to allow early diagnosis and effective therapy.	MPI-CDG is a form of congenital disorders of N-linked glycosylation, characterized by cyclic vomiting, profound hypoglycemia, failure to thrive, liver fibrosis, gastrointestinal complications (protein-losing enteropathy with hypoalbuminaemia, life-threatening intestinal bleeding of diffuse origin), and thrombotic events (protein C and S deficiency, low anti-thrombine III levels), whereas neurological development and cognitive capacity is usually normal. The clinical course is variable even within families. The disease is caused by loss of function of the gene MPI (15q24.1).	NM_002437.4(MPV17):c.498C>A ; NM_002437.4(MPV17):c.70G>T ; NM_002437.4(MPV17):c.284dupG ; NM_002437.4(MPV17):c.359G>A ; c.462-2A>C ; NM_002437.4(MPV17):c.263_265delAGA ; NM_002437.4(MPV17):c.148C>T ; NM_002437.4(MPV17):c.149G>A ; NM_002437.4(MPV17):c.498C>A ; NM_002437.4(MPV17):c.70G>T ; NM_002437.4(MPV17):c.284dupG ; NM_002437.4(MPV17):c.359G>A ; c.462-2A>C ; NM_002437.4(MPV17):c.263_265delAGA ; NM_002437.4(MPV17):c.148C>T ; NM_002437.4(MPV17):c.149G>A

MTHFR	Cervical spina bifida aperta	Mitochondrial DNA depletion syndrome-6 is an autosomal recessive disorder characterized by infantile onset of progressive liver failure, often leading to death in the first year of life. Those that survive develop progressive neurologic involvement, including ataxia, hypotonia, dystonia, and psychomotor regression.	A rare, life-threatening, mitochondrial DNA depletion syndrome disease characterized by severe, progressive sensorimotor neuropathy associated with corneal ulceration, scarring or anesthesia, acral mutilation, metabolic and immunologic derangement, and hepatopathy (which can manifest with fulminant hepatic failure, a Reye-like syndrome or indolent progression to liver cirrhosis, depending on clinical form involved), present in the Navajo Native American population. Clinical presentation includes failure to thrive, distal limb weakness with reduced sensation, limb contractures with loss of funtion, areflexia, recurrent metabolic acidosis with intercurrent illness, immunologic anomalies manifesting with severe systemic infections, and sexual infantilism.	c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G
MTHFR	Cervical spina bifida cystica			c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G
MTHFR	Cervicothoracic spina bifida aperta			c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G
MTHFR	Cervicothoracic spina bifida cystica			c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G
MTHFR	Homocystinuria due to methylene tetrahydrofolate reductase deficiency			c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G
MTHFR	Isolated anencephaly	Homocystinuria due to methylene tetrahydrofolate reductase (MTHFR) deficiency is a metabolic disorder characterised by neurological manifestations.	Onset usually occurs during the first year of life with severe neurological signs, recurrent apnoea, microcephaly and convulsions. There is no megaloblastic anaemia. There are some forms with onset during childhood, adolescence, or adulthood beginning with mental regression, ataxia, and, most often, common psychiatric disorders of the schizophrenic type that may be linked to cerebrovascular accidents. Other symptoms such as subacute degeneration of the spinal chord have been reported.	c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G

MTHFR	Isolated exencephaly	A neural tube defect. This malformation is characterized by the total or partial absence of the cranial vault and the covering skin, the brain being missing or reduced to a small mass. Most cases are stillborn, although some infants have been reported to survive for a few hours or even a few days.	Neural tube defects have a birth incidence of approximately 1 in 1,000 in American Caucasians and are the second most common type of birth defect after congenital heart defects. The most common NTDs are open spina bifida (myelomeningocele) and anencephaly.Â Women with elevated plasma homocysteine, low folate, or low vitamin B12 (cobalamin) are at increased risk of having a child with a neural tube defect.	c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G
MTHFR	Lumbosacral spina bifida aperta	A neural tube defect. This malformation is characterized by the total or partial absence of the cranial vault and the covering skin, the brain being missing or reduced to a small mass. Most cases are stillborn, although some infants have been reported to survive for a few hours or even a few days.	Neural tube defects have a birth incidence of approximately 1 in 1,000 in American Caucasians and are the second most common type of birth defect after congenital heart defects. The most common NTDs are open spina bifida (myelomeningocele) and anencephaly.Â Women with elevated plasma homocysteine, low folate, or low vitamin B12 (cobalamin) are at increased risk of having a child with a neural tube defect.	c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G
MTHFR	Lumbosacral spina bifida cystica			c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G
MTHFR	NON RARE IN EUROPE: Non rare thrombophilia			c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G

MTHFR	Thoracolumbosacral spina bifida aperta	Thrombophilia is a multifactorial disorder of inappropriate clot formation resulting from an interaction of genetic, acquired, and circumstantial predisposing factors. Venous thromboembolism most commonly manifests as deep vein thrombosis, which may progress to pulmonary embolism if the clot dislodges and travels to the lung. Other manifestations include thromboses of the cerebral or visceral veins and recurrent pregnancy lossÂ .		c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G
MTHFR	Thoracolumbosacral spina bifida cystica			c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G
MTHFR	Total spina bifida aperta			c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G
MTHFR	Total spina bifida cystica			c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G
MTHFR	Upper thoracic spina bifida aperta			c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G
MTHFR	Upper thoracic spina bifida cystica			c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G ; c.3G>A ; NM_005957.4(MTHFR):c.968T>C ; c.562C>T ; NM_005957.4(MTHFR):c.547C>T ; c.1891del ; NM_005957.4(MTHFR):c.1743G>A ; NM_005957.4(MTHFR):c.971A>G
MTM1	X-linked centronuclear myopathy			NM_000252.2(MTM1):c.1261-10A>G ; NM_000252.2(MTM1):c.969del ; c.461T>G ; NM_000252.2(MTM1):c.70C>T ; c.780T>A ; NM_000252.2(MTM1):c.595_599delCCTGC ; NM_000252.2(MTM1):c.1306_1310dupCCTAT ; NM_000252.2(MTM1):c.670C>T ; NM_000252.2(MTM1):c.721C>T ; NM_000252.2(MTM1):c.969dup ; NM_000252.2(MTM1):c.1357_1358delCC ; NM_000252.2(MTM1):c.1415_1416delGT ; NM_000252.2(MTM1):c.420C>G ; NM_000252.2(MTM1):c.1261-10A>G ; NM_000252.2(MTM1):c.969del ; c.461T>G ; NM_000252.2(MTM1):c.70C>T ; c.780T>A ; NM_000252.2(MTM1):c.595_599delCCTGC ; NM_000252.2(MTM1):c.1306_1310dupCCTAT ; NM_000252.2(MTM1):c.670C>T ; NM_000252.2(MTM1):c.721C>T ; NM_000252.2(MTM1):c.969dup ; NM_000252.2(MTM1):c.1357_1358delCC ; NM_000252.2(MTM1):c.1415_1416delGT ; NM_000252.2(MTM1):c.420C>G

MTM1	X-linked myotubular myopathy-abnormal genitalia syndrome	A rare X-linked congenital myopathy characterized by numerous centrally placed nuclei on muscle biopsy and that presents at birth with marked weakness, hypotonia and respiratory failure.	The disease is characterized by a severe phenotype in males presenting at birth with marked weakness, hypotonia and respiratory failure. Signs of antenatal onset are frequent and comprise reduced fetal movements and polyhydramnios. Thinning of the ribs is observed on chest radiographs of the newborn. Birth asphyxia may be the presenting feature. A family history of either male neonatal deaths or miscarriages is common. Affected infants are often macrosomic, with a body length above the 90th centile and large head circumference. External ophthalmoplegia is commonly associated. Testes are frequently undescended. Pyloric stenosis and cavernous hemangiomas of the liver have been reported in some long-term survivors.	NM_000252.2(MTM1):c.1261-10A>G ; NM_000252.2(MTM1):c.969del ; c.461T>G ; NM_000252.2(MTM1):c.70C>T ; c.780T>A ; NM_000252.2(MTM1):c.595_599delCCTGC ; NM_000252.2(MTM1):c.1306_1310dupCCTAT ; NM_000252.2(MTM1):c.670C>T ; NM_000252.2(MTM1):c.721C>T ; NM_000252.2(MTM1):c.969dup ; NM_000252.2(MTM1):c.1357_1358delCC ; NM_000252.2(MTM1):c.1415_1416delGT ; NM_000252.2(MTM1):c.420C>G ; NM_000252.2(MTM1):c.1261-10A>G ; NM_000252.2(MTM1):c.969del ; c.461T>G ; NM_000252.2(MTM1):c.70C>T ; c.780T>A ; NM_000252.2(MTM1):c.595_599delCCTGC ; NM_000252.2(MTM1):c.1306_1310dupCCTAT ; NM_000252.2(MTM1):c.670C>T ; NM_000252.2(MTM1):c.721C>T ; NM_000252.2(MTM1):c.969dup ; NM_000252.2(MTM1):c.1357_1358delCC ; NM_000252.2(MTM1):c.1415_1416delGT ; NM_000252.2(MTM1):c.420C>G
MTTP	Abetalipoproteinemia	X-linked myotubular myopathy-abnormal genitalia syndrome is a rare chromosomal anomaly, partial deletion of the long arm of chromosome X, characterized by a combination of clinical manifestations of X-linked myotubular myopathy and a 46,XY disorder of sex development. Patients present with severe form of congenital myopathy and abnormal male genitalia.	Facial diplegia and often external ophthalmoplegia are frequent. The newborn cases resemble those of congenital myotonic dystrophy; the distinction can be made by examination of their mother who in the latter situation will invariably show mild facial weakness and clinical or electrical myotonia. Polyhydramnios is a feature of both forms of congenital myopathy, i.e., myotonic dystrophy and X-linked myotubular myopathy.Â	c.1867+1G>A ; NM_000253.3:c.2593G>T ; c.2031del ; NM_000253.3(MTTP):c.1769G>T ; NM_000253.3(MTTP):c.1619G>A ; NM_000253.3(MTTP):c.708_709del ; c.1867+1G>A ; NM_000253.3:c.2593G>T ; c.2031del ; NM_000253.3(MTTP):c.1769G>T ; NM_000253.3(MTTP):c.1619G>A ; NM_000253.3(MTTP):c.708_709del

MTTP	NON RARE IN EUROPE: Familial hypobetalipoproteinemia	A severe, familial hypobetalipoproteinemia characterized by permanently low levels (below the 5th percentile) of apolipoprotein B and LDL cholesterol, and by growth delay, malabsorption, hepatomegaly, and neurological and neuromuscular manifestations.	Abetalipoproteinemia manifests during the first year of life or in young childhood. It is often associated with growth delay, hepatomegaly with steatosis, diarrhea with steatorrhea, and fat malabsorption. Spastic ataxia, atypical retinitis pigmentosa, acanthocytosis, a low level of liposoluble vitamins, and major cytolysis and even cirrhosis can occur.	c.1867+1G>A ; NM_000253.3:c.2593G>T ; c.2031del ; NM_000253.3(MTTP):c.1769G>T ; NM_000253.3(MTTP):c.1619G>A ; NM_000253.3(MTTP):c.708_709del ; c.1867+1G>A ; NM_000253.3:c.2593G>T ; c.2031del ; NM_000253.3(MTTP):c.1769G>T ; NM_000253.3(MTTP):c.1619G>A ; NM_000253.3(MTTP):c.708_709del
MYO15A	Autosomal recessive non-syndromic sensorineural deafness type DFNB	Features are celiac syndrome, pigmentary degeneration of the retina, progressive ataxic neuropathy, and a peculiar 'burr-cell' malformation of the red cells called acanthocytosis. Intestinal absorption of lipids is defective, serum cholesterol very low, and serum beta lipoprotein absent.	Abetalipoproteinemia and familial hypobetalipoproteinemia are rare diseases characterized by hypocholesterolemia and malabsorption of lipid-soluble vitamins leading to retinal degeneration, neuropathy, and coagulopathy. Hepatic steatosis is also common. The root cause of both disorders is improper packaging and secretion of apolipoprotein B-containing particles. Obligate heterozygous parents of ABL patients usually have normal lipids consistent with autosomal recessive inheritance, whereas obligate heterozygous parents of FBHL patients typically have half normal levels of apoB-containing lipoproteins consistent with autosomal codominant inheritance.	NM_016239.4(MYO15A):c.3756+1G>T ; c.6046+2T>G ; NM_016239.4(MYO15A):c.10573del ; NM_016239.4(MYO15A):c.9958_9961del ; c.4751_4752dup ; NM_016239.3(MYO15A):c.3385C>T ; c.755dup ; NM_016239.3(MYO15A):c.8148G>T ; NM_016239.3(MYO15A):c.5492G>T ; c.8548C>T ; NM_016239.3(MYO15A):c.625G>T ; c.3693-2A>G ; NM_016239.4(MYO15A):c.3336del ; c.8410A>T ; c.6864_6874del ; c.8432_8450del ; c.5326C>T ; c.6004del ; NM_016239.3(MYO15A):c.3313G>T ; NM_016239.4(MYO15A):c.3756+1G>T ; c.6046+2T>G ; NM_016239.4(MYO15A):c.10573del ; NM_016239.4(MYO15A):c.9958_9961del ; c.4751_4752dup ; NM_016239.3(MYO15A):c.3385C>T ; c.755dup ; NM_016239.3(MYO15A):c.8148G>T ; NM_016239.3(MYO15A):c.5492G>T ; c.8548C>T ; NM_016239.3(MYO15A):c.625G>T ; c.3693-2A>G ; NM_016239.4(MYO15A):c.3336del ; c.8410A>T ; c.6864_6874del ; c.8432_8450del ; c.5326C>T ; c.6004del ; NM_016239.3(MYO15A):c.3313G>T

MYO7A	Autosomal dominant non-syndromic sensorineural deafness type DFNA	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	c.1344-1G>A ; NM_000260.4:c.2476G>A ; NM_000260.3(MYO7A):c.133-2A>G ; NM_000260.3(MYO7A):c.634C>T ; NM_000260.3(MYO7A):c.6025delG ; NM_000260.3(MYO7A):c.494C>T ; NM_000260.3(MYO7A):c.3508G>A ; NM_000260.3(MYO7A):c.635G>A ; NM_000260.3(MYO7A):c.5824G>T ; NM_000260.3(MYO7A):c.5886_5889delCTTT ; NM_000260.3(MYO7A):c.5392C>T ; NM_000260.3(MYO7A):c.1996C>T ; NM_000260.3(MYO7A):c.731G>C ; NM_000260.3(MYO7A):c.4024delT ; c.3596dup ; NM_000260.3(MYO7A):c.1884C>A ; NM_000260.3(MYO7A):c.448C>T ; NM_000260.3(MYO7A):c.3504-1G>C ; c.5967C>G ; NM_000260.4:c.640G>A ; NM_000260.3(MYO7A):c.1184G>A ; NM_000260.3(MYO7A):c.3G>A ; NM_000260.3(MYO7A):c.3719G>A ; NM_000260.3(MYO7A):c.1797G>A ; c.1344-1G>A ; NM_000260.4:c.2476G>A ; NM_000260.3(MYO7A):c.133-2A>G ; NM_000260.3(MYO7A):c.634C>T ; NM_000260.3(MYO7A):c.6025delG ; NM_000260.3(MYO7A):c.494C>T ; NM_000260.3(MYO7A):c.3508G>A ; NM_000260.3(MYO7A):c.635G>A ; NM_000260.3(MYO7A):c.5824G>T ; NM_000260.3(MYO7A):c.5886_5889delCTTT ; NM_000260.3(MYO7A):c.5392C>T ; NM_000260.3(MYO7A):c.1996C>T ; NM_000260.3(MYO7A):c.731G>C ; NM_000260.3(MYO7A):c.4024delT ; c.3596dup ; NM_000260.3(MYO7A):c.1884C>A ; NM_000260.3(MYO7A):c.448C>T ; NM_000260.3(MYO7A):c.3504-1G>C ; c.5967C>G ; NM_000260.4:c.640G>A ; NM_000260.3(MYO7A):c.1184G>A ; NM_000260.3(MYO7A):c.3G>A ; NM_000260.3(MYO7A):c.3719G>A ; NM_000260.3(MYO7A):c.1797G>A

MYO7A	Autosomal recessive non-syndromic sensorineural deafness type DFNB	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	c.1344-1G>A ; NM_000260.4:c.2476G>A ; NM_000260.3(MYO7A):c.133-2A>G ; NM_000260.3(MYO7A):c.634C>T ; NM_000260.3(MYO7A):c.6025delG ; NM_000260.3(MYO7A):c.494C>T ; NM_000260.3(MYO7A):c.3508G>A ; NM_000260.3(MYO7A):c.635G>A ; NM_000260.3(MYO7A):c.5824G>T ; NM_000260.3(MYO7A):c.5886_5889delCTTT ; NM_000260.3(MYO7A):c.5392C>T ; NM_000260.3(MYO7A):c.1996C>T ; NM_000260.3(MYO7A):c.731G>C ; NM_000260.3(MYO7A):c.4024delT ; c.3596dup ; NM_000260.3(MYO7A):c.1884C>A ; NM_000260.3(MYO7A):c.448C>T ; NM_000260.3(MYO7A):c.3504-1G>C ; c.5967C>G ; NM_000260.4:c.640G>A ; NM_000260.3(MYO7A):c.1184G>A ; NM_000260.3(MYO7A):c.3G>A ; NM_000260.3(MYO7A):c.3719G>A ; NM_000260.3(MYO7A):c.1797G>A ; c.1344-1G>A ; NM_000260.4:c.2476G>A ; NM_000260.3(MYO7A):c.133-2A>G ; NM_000260.3(MYO7A):c.634C>T ; NM_000260.3(MYO7A):c.6025delG ; NM_000260.3(MYO7A):c.494C>T ; NM_000260.3(MYO7A):c.3508G>A ; NM_000260.3(MYO7A):c.635G>A ; NM_000260.3(MYO7A):c.5824G>T ; NM_000260.3(MYO7A):c.5886_5889delCTTT ; NM_000260.3(MYO7A):c.5392C>T ; NM_000260.3(MYO7A):c.1996C>T ; NM_000260.3(MYO7A):c.731G>C ; NM_000260.3(MYO7A):c.4024delT ; c.3596dup ; NM_000260.3(MYO7A):c.1884C>A ; NM_000260.3(MYO7A):c.448C>T ; NM_000260.3(MYO7A):c.3504-1G>C ; c.5967C>G ; NM_000260.4:c.640G>A ; NM_000260.3(MYO7A):c.1184G>A ; NM_000260.3(MYO7A):c.3G>A ; NM_000260.3(MYO7A):c.3719G>A ; NM_000260.3(MYO7A):c.1797G>A

MYO7A	Usher syndrome type 1	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	c.1344-1G>A ; NM_000260.4:c.2476G>A ; NM_000260.3(MYO7A):c.133-2A>G ; NM_000260.3(MYO7A):c.634C>T ; NM_000260.3(MYO7A):c.6025delG ; NM_000260.3(MYO7A):c.494C>T ; NM_000260.3(MYO7A):c.3508G>A ; NM_000260.3(MYO7A):c.635G>A ; NM_000260.3(MYO7A):c.5824G>T ; NM_000260.3(MYO7A):c.5886_5889delCTTT ; NM_000260.3(MYO7A):c.5392C>T ; NM_000260.3(MYO7A):c.1996C>T ; NM_000260.3(MYO7A):c.731G>C ; NM_000260.3(MYO7A):c.4024delT ; c.3596dup ; NM_000260.3(MYO7A):c.1884C>A ; NM_000260.3(MYO7A):c.448C>T ; NM_000260.3(MYO7A):c.3504-1G>C ; c.5967C>G ; NM_000260.4:c.640G>A ; NM_000260.3(MYO7A):c.1184G>A ; NM_000260.3(MYO7A):c.3G>A ; NM_000260.3(MYO7A):c.3719G>A ; NM_000260.3(MYO7A):c.1797G>A ; c.1344-1G>A ; NM_000260.4:c.2476G>A ; NM_000260.3(MYO7A):c.133-2A>G ; NM_000260.3(MYO7A):c.634C>T ; NM_000260.3(MYO7A):c.6025delG ; NM_000260.3(MYO7A):c.494C>T ; NM_000260.3(MYO7A):c.3508G>A ; NM_000260.3(MYO7A):c.635G>A ; NM_000260.3(MYO7A):c.5824G>T ; NM_000260.3(MYO7A):c.5886_5889delCTTT ; NM_000260.3(MYO7A):c.5392C>T ; NM_000260.3(MYO7A):c.1996C>T ; NM_000260.3(MYO7A):c.731G>C ; NM_000260.3(MYO7A):c.4024delT ; c.3596dup ; NM_000260.3(MYO7A):c.1884C>A ; NM_000260.3(MYO7A):c.448C>T ; NM_000260.3(MYO7A):c.3504-1G>C ; c.5967C>G ; NM_000260.4:c.640G>A ; NM_000260.3(MYO7A):c.1184G>A ; NM_000260.3(MYO7A):c.3G>A ; NM_000260.3(MYO7A):c.3719G>A ; NM_000260.3(MYO7A):c.1797G>A

MYO7A	Usher syndrome type 2	Usher syndrome type I is an autosomal recessive condition characterized by profound congenital hearing impairment with unintelligible speech, early retinitis pigmentosa (usually evident within the first decade), and constant vestibular dysfunction. Type I is distinguished from type II on the basis of severity of hearing loss and the extent of vestibular involvement. Type I patients are profoundly deaf, whereas type II patients are 'hard of hearing.' Vestibular function is defective in type I patients, whereas type II patients have normal vestibular function. Patients with type III (USH3) have progressive hearing loss.	A rare ciliopathy characterized by profound congenital deafness, retinitis pigmentosa and vestibular dysfunction. Retinitis pigmentosa results in visual loss and generally manifests as night blindness, progressively constricted visual fields, and impaired visual acuity. Vestibular dysfunction a defining feature of this form, manifests as delayed motor development with affected infants taking longer to sit independently and to walk. Later on, vestibular dysfunction results in difficulty with activities requiring balance.	c.1344-1G>A ; NM_000260.4:c.2476G>A ; NM_000260.3(MYO7A):c.133-2A>G ; NM_000260.3(MYO7A):c.634C>T ; NM_000260.3(MYO7A):c.6025delG ; NM_000260.3(MYO7A):c.494C>T ; NM_000260.3(MYO7A):c.3508G>A ; NM_000260.3(MYO7A):c.635G>A ; NM_000260.3(MYO7A):c.5824G>T ; NM_000260.3(MYO7A):c.5886_5889delCTTT ; NM_000260.3(MYO7A):c.5392C>T ; NM_000260.3(MYO7A):c.1996C>T ; NM_000260.3(MYO7A):c.731G>C ; NM_000260.3(MYO7A):c.4024delT ; c.3596dup ; NM_000260.3(MYO7A):c.1884C>A ; NM_000260.3(MYO7A):c.448C>T ; NM_000260.3(MYO7A):c.3504-1G>C ; c.5967C>G ; NM_000260.4:c.640G>A ; NM_000260.3(MYO7A):c.1184G>A ; NM_000260.3(MYO7A):c.3G>A ; NM_000260.3(MYO7A):c.3719G>A ; NM_000260.3(MYO7A):c.1797G>A ; c.1344-1G>A ; NM_000260.4:c.2476G>A ; NM_000260.3(MYO7A):c.133-2A>G ; NM_000260.3(MYO7A):c.634C>T ; NM_000260.3(MYO7A):c.6025delG ; NM_000260.3(MYO7A):c.494C>T ; NM_000260.3(MYO7A):c.3508G>A ; NM_000260.3(MYO7A):c.635G>A ; NM_000260.3(MYO7A):c.5824G>T ; NM_000260.3(MYO7A):c.5886_5889delCTTT ; NM_000260.3(MYO7A):c.5392C>T ; NM_000260.3(MYO7A):c.1996C>T ;NM_000260.3(MYO7A):c.731G>C ; NM_000260.3(MYO7A):c.4024delT ; c.3596dup ; NM_000260.3(MYO7A):c.1884C>A ; NM_000260.3(MYO7A):c.448C>T ; NM_000260.3(MYO7A):c.3504-1G>C ; c.5967C>G ; NM_000260.4:c.640G>A ; NM_000260.3(MYO7A):c.1184G>A ; NM_000260.3(MYO7A):c.3G>A ; NM_000260.3(MYO7A):c.3719G>A ; NM_000260.3(MYO7A):c.1797G>A

NAGS	Hyperammonemia due to N-acetylglutamate synthase deficiency	Usher syndrome type I is an autosomal recessive condition characterized by profound congenital hearing impairment with unintelligible speech, early retinitis pigmentosa (usually evident within the first decade), and constant vestibular dysfunction. Type I is distinguished from type II on the basis of severity of hearing loss and the extent of vestibular involvement. Type I patients are profoundly deaf, whereas type II patients are 'hard of hearing.' Vestibular function is defective in type I patients, whereas type II patients have normal vestibular function. Patients with type III (USH3) have progressive hearing loss.	A rare ciliopathy characterized by congenital moderate-to-severe deafness, retinitis pigmentosa developing in the first or second decade, and normal vestibular function. Congenital bilateral sensorineural hearing loss is mild to moderate in the low frequencies and severe to profound in the higher frequencies. Additional manifestations include night blindness, constricted visual field (tunnel vision), and later on decreased visual acuity sometimes ending with bare light perception.	NM_153006.2(NAGS):c.1299G>C ; NM_153006.2(NAGS):c.1025del ; NM_153006.2(NAGS):c.916-2A>T ; NM_153006.3(NAGS):c.1307dup ; NM_153006.2(NAGS):c.1289T>C ; NM_153006.2(NAGS):c.971G>A ; NM_153006.2(NAGS):c.1299G>C ; NM_153006.2(NAGS):c.1025del ; NM_153006.2(NAGS):c.916-2A>T ; NM_153006.3(NAGS):c.1307dup ; NM_153006.2(NAGS):c.1289T>C ; NM_153006.2(NAGS):c.971G>A
NDRG1	Charcot-Marie-Tooth disease type 4D	N-acetylglutamate synthase (NAGS) deficiency is a urea cycle disorder leading to hyperammonaemia.	Onset occurs at any age, but neonatal presentation appears to be the most frequent. The clinical manifestations are variable but common features include vomiting, hyperactivity or lethargy, diarrhoea, poor feeding, seizures, hypotonia, delayed psychomotor development and respiratory distress. The hyperammonaemia is often severe and may lead to hyperammonaemic coma.	c.16C>T ; NM_001135242.1(NDRG1):c.442C>T ; c.928C>T ; c.-18-2_-18-1del ; c.16C>T ; NM_001135242.1(NDRG1):c.442C>T ; c.928C>T ; c.-18-2_-18-1del

NEB	Childhood-onset nemaline myopathy	By convention, the designation CMT4 is applied to autosomal recessive forms of demyelinating Charcot-Marie-Tooth disease, which is a peripheral neuropathy characterized by distal motor and sensory impairment resulting in gait difficulties and associated with foot deformities. Motor nerve conduction velocities are decreased, and sural nerve biopsies show loss of myelinated fibers. The age at onset and severity is variable.	Charcot-Marie-Tooth disease type 4D (CMT4D) is a subtype of Charcot-Marie-Tooth disease type 4 characterized by a childhood-onset of severe, progressive, demyelinating sensorimotor neuropathy manifesting with distal muscle weakness and atrophy, sensorineural hearing impairment leading to deafness (usually in third decade), severely reduced nerve conduction velocities, and skeletal, especially foot, deformities. Tongue atrophy has also been reported.	c.24874-1G>A ; c.843T>G ; c.2173G>T ; c.21945+1G>A ; c.6105dup ; NM_001271208.1(NEB):c.24770_24771delTT ; c.24687_24688del ; NM_001271208.1(NEB):c.8031_8041delAAATAAACGAG ; NM_001271208.1(NEB):c.24094C>T ; c.12203_12204del ; NM_001271208.1(NEB):c.25279G>T ; NM_001164507.1(NEB):c.21076C>T ; ENST00000397345.7:c.25404+1_25404+2insATGGA ; NM_001271208.1(NEB):c.23526_23527delAG ; c.24874-1G>A ; c.843T>G ; c.2173G>T ; c.21945+1G>A ; c.6105dup ; NM_001271208.1(NEB):c.24770_24771delTT ; c.24687_24688del ; NM_001271208.1(NEB):c.8031_8041delAAATAAACGAG ; NM_001271208.1(NEB):c.24094C>T ; c.12203_12204del ; NM_001271208.1(NEB):c.25279G>T ; NM_001164507.1(NEB):c.21076C>T ; ENST00000397345.7:c.25404+1_25404+2insATGGA ; NM_001271208.1(NEB):c.23526_23527delAG
NEB	Distal nebulin myopathy	Childhood onset nemaline myopathy, or mild nemaline myopathy is a type of nemaline myopathy (NM; see this terms) characterized by distal muscle weakness, and sometimes slowness of muscle contraction.	Childhood onset NM might represent 10-15% of total cases. Onset is around 10 years of age, with initial presentation of symmetric weakness of ankle dorsiflexion and foot drop, or a general slowness of muscle contraction. All movements at the ankle and more proximal limb muscles may be disturbed. Weakness is slowly progressive. Facial, respiratory and cardiac muscles are generally normal, but patients are unable to jump or run because of muscle weakness or slowness.	c.24874-1G>A ; c.843T>G ; c.2173G>T ; c.21945+1G>A ; c.6105dup ; NM_001271208.1(NEB):c.24770_24771delTT ; c.24687_24688del ; NM_001271208.1(NEB):c.8031_8041delAAATAAACGAG ; NM_001271208.1(NEB):c.24094C>T ; c.12203_12204del ; NM_001271208.1(NEB):c.25279G>T ; NM_001164507.1(NEB):c.21076C>T ; ENST00000397345.7:c.25404+1_25404+2insATGGA ; NM_001271208.1(NEB):c.23526_23527delAG ; c.24874-1G>A ; c.843T>G ; c.2173G>T ; c.21945+1G>A ; c.6105dup ; NM_001271208.1(NEB):c.24770_24771delTT ; c.24687_24688del ; NM_001271208.1(NEB):c.8031_8041delAAATAAACGAG ; NM_001271208.1(NEB):c.24094C>T ; c.12203_12204del ; NM_001271208.1(NEB):c.25279G>T ; NM_001164507.1(NEB):c.21076C>T ; ENST00000397345.7:c.25404+1_25404+2insATGGA ; NM_001271208.1(NEB):c.23526_23527delAG

NEB	Intermediate nemaline myopathy	Distal nebulin myopathy is a rare, slowly progressive, autosomal recessive distal myopathy characterized by early onset of predominantly distal muscle weakness and atrophy affecting lower leg extensor muscles, finger extensors and neck flexors. Muscle histology does not always show nemaline rods.	Distal nebulin myopathy manifests initially, in early childhood or young adulthood, by foot drop, but the first symptoms can be seen as early as one year of age. The most severely affected muscles include the ankle dorsiflexors, the finger extensors and the neck flexors. Patients are usually not able to walk on their heels and later in the disease course, there is a mild proximal muscle involvement. Additional features include early-onset moderate facial weakness and mild respiratory problems, such as shortness of breath on strenuous exercise (although only one patient presenting decreased vital capacity has been reported). Cardiac muscle is usually not affected, however cardiomyopathy has been described in one patient.	c.24874-1G>A ; c.843T>G ; c.2173G>T ; c.21945+1G>A ; c.6105dup ; NM_001271208.1(NEB):c.24770_24771delTT ; c.24687_24688del ; NM_001271208.1(NEB):c.8031_8041delAAATAAACGAG ; NM_001271208.1(NEB):c.24094C>T ; c.12203_12204del ; NM_001271208.1(NEB):c.25279G>T ; NM_001164507.1(NEB):c.21076C>T ; ENST00000397345.7:c.25404+1_25404+2insATGGA ; NM_001271208.1(NEB):c.23526_23527delAG ; c.24874-1G>A ; c.843T>G ; c.2173G>T ; c.21945+1G>A ; c.6105dup ; NM_001271208.1(NEB):c.24770_24771delTT ; c.24687_24688del ; NM_001271208.1(NEB):c.8031_8041delAAATAAACGAG ; NM_001271208.1(NEB):c.24094C>T ; c.12203_12204del ; NM_001271208.1(NEB):c.25279G>T ; NM_001164507.1(NEB):c.21076C>T ; ENST00000397345.7:c.25404+1_25404+2insATGGA ; NM_001271208.1(NEB):c.23526_23527delAG
NEB	Lethal multiple pterygium syndrome	Intermediate nemaline myopathy is a type of nemaline myopathy (NM; see this term) that shows features of typical NM (see this term) in neonates with a more severe progression.	Neonates with intermediate NM present with spontaneous anti-gravity movements and active respiratory muscles, but with a progressive generalized weakness which prevents achievement of gross motor milestones or leads to loss of ambulation and/or independent respiration by age 11 years. Children often develop joint contractures.	c.24874-1G>A ; c.843T>G ; c.2173G>T ; c.21945+1G>A ; c.6105dup ; NM_001271208.1(NEB):c.24770_24771delTT ; c.24687_24688del ; NM_001271208.1(NEB):c.8031_8041delAAATAAACGAG ; NM_001271208.1(NEB):c.24094C>T ; c.12203_12204del ; NM_001271208.1(NEB):c.25279G>T ; NM_001164507.1(NEB):c.21076C>T ; ENST00000397345.7:c.25404+1_25404+2insATGGA ; NM_001271208.1(NEB):c.23526_23527delAG ; c.24874-1G>A ; c.843T>G ; c.2173G>T ; c.21945+1G>A ; c.6105dup ; NM_001271208.1(NEB):c.24770_24771delTT ; c.24687_24688del ; NM_001271208.1(NEB):c.8031_8041delAAATAAACGAG ; NM_001271208.1(NEB):c.24094C>T ; c.12203_12204del ; NM_001271208.1(NEB):c.25279G>T ; NM_001164507.1(NEB):c.21076C>T ; ENST00000397345.7:c.25404+1_25404+2insATGGA ; NM_001271208.1(NEB):c.23526_23527delAG

NEB	Severe congenital nemaline myopathy	A rare genetic multiple pterygium syndrome characterized by intrauterine growth retardation, fetal akinesia, multiple joint contractures causing severe arthrogryposis and pterygia (webbing) across multiple joints. Cystic hygroma and/or fetal hydrops are almost invariably present.	Lethal multiple pterygium syndrome (LMPS) is characterized by growth deficiency of prenatal onset, pterygia present in multiple areas (chin to sternum, cervical, axillary, humero-ulnar, crural, popliteal and the ankles) and flexion contractures giving rise to severe arthrogryposis. Subcutaneous edema varies from mildly edematous skin to fetal hydrops with cystic hygroma, lung hypoplasia, and oligo or polyhydramnios. Facial anomalies include hypertelorism, down-slanting palpebral fissures, epicanthic folds, flat nasal root, microretrognathism, microstomia, low-set malformed ears and cleft palate. Other anomalies include a small chest, reduced muscle bulk, cryptorchidism, central nervous system abnormalities (in particular cerebellar hypoplasia, ventricular dilatation and polymicrogyria), hypoplastic dermal ridges and creases, and less frequently a mid-forehead hemangioma, intestinal malrotation, cardiac hypoplasia, diaphragmatic hernia, obstructive uropathy, rocker bottom feet, microcephaly and/or cerebellar and pontine hypoplasia.	c.24874-1G>A ; c.843T>G ; c.2173G>T ; c.21945+1G>A ; c.6105dup ; NM_001271208.1(NEB):c.24770_24771delTT ; c.24687_24688del ; NM_001271208.1(NEB):c.8031_8041delAAATAAACGAG ; NM_001271208.1(NEB):c.24094C>T ; c.12203_12204del ; NM_001271208.1(NEB):c.25279G>T ; NM_001164507.1(NEB):c.21076C>T ; ENST00000397345.7:c.25404+1_25404+2insATGGA ; NM_001271208.1(NEB):c.23526_23527delAG ; c.24874-1G>A ; c.843T>G ; c.2173G>T ; c.21945+1G>A ; c.6105dup ; NM_001271208.1(NEB):c.24770_24771delTT ; c.24687_24688del ; NM_001271208.1(NEB):c.8031_8041delAAATAAACGAG ; NM_001271208.1(NEB):c.24094C>T ; c.12203_12204del ; NM_001271208.1(NEB):c.25279G>T ; NM_001164507.1(NEB):c.21076C>T ; ENST00000397345.7:c.25404+1_25404+2insATGGA ; NM_001271208.1(NEB):c.23526_23527delAG
NEB	Typical nemaline myopathy	Severe congenital nemaline myopathy is a severe form of nemaline myopathy (NM; see this term) characterized by severe hypotonia with little spontaneous movement in neonates.	Neonates have sucking and swallowing difficulties, and gastroesophageal reflux, which leads to failure to thrive. Involvement of diaphragm and intercostal muscles contributes to respiratory insufficiency. Cardiomyopathy and arthrogryposis may occur.	c.24874-1G>A ; c.843T>G ; c.2173G>T ; c.21945+1G>A ; c.6105dup ; NM_001271208.1(NEB):c.24770_24771delTT ; c.24687_24688del ; NM_001271208.1(NEB):c.8031_8041delAAATAAACGAG ; NM_001271208.1(NEB):c.24094C>T ; c.12203_12204del ; NM_001271208.1(NEB):c.25279G>T ; NM_001164507.1(NEB):c.21076C>T ; ENST00000397345.7:c.25404+1_25404+2insATGGA ; NM_001271208.1(NEB):c.23526_23527delAG ; c.24874-1G>A ; c.843T>G ; c.2173G>T ; c.21945+1G>A ; c.6105dup ; NM_001271208.1(NEB):c.24770_24771delTT ; c.24687_24688del ; NM_001271208.1(NEB):c.8031_8041delAAATAAACGAG ; NM_001271208.1(NEB):c.24094C>T ; c.12203_12204del ; NM_001271208.1(NEB):c.25279G>T ; NM_001164507.1(NEB):c.21076C>T ; ENST00000397345.7:c.25404+1_25404+2insATGGA ; NM_001271208.1(NEB):c.23526_23527delAG

NPC1	Niemann-Pick disease type C, adult neurologic onset	Typical nemaline myopathy is a moderate neonatal form of nemaline myopathy (NM; see this term) characterized by facial and skeletal muscle weakness and mild respiratory involvement.	Disease onset is in the neonatal period. Patients have a long face, a high-arched palate and a tented upper lip. Skeletal anomalies may include kyphoscoliosis,Â pectus carinatumÃ andÂ pes cavus. In the first year of life, hypotonia and facial weakness are present and often contribute to failure to thrive and delayed motor development. Anti-gravity movements are present and respiratory muscle involvement is frequent. Nocturnal hypoxia and hypercarbia and lower respiratory tract infections are common manifestations. Joint hypermobility can be observed. In a minority of children weakness is more distal. Progression is very slow or absent and most patients are able to live an independent active life.	NM_000271.4(NPC1):c.3467A>G ; NM_000271.4(NPC1):c.3175C>T ; c.1042C>T ; NM_000271.4(NPC1):c.1628C>T ; NM_000271.4(NPC1):c.3611_3614del ; NM_000271.4(NPC1):c.2861C>T ; NM_000271.4(NPC1):c.2848G>A ; NM_000271.4(NPC1):c.3104C>T ; NM_000271.4(NPC1):c.530G>A ; NM_000271.4(NPC1):c.352_353delAG ; NM_000271.5:c.1211G>A ; NM_000271.4(NPC1):c.3662del ; NM_000271.4(NPC1):c.2324A>C ; NM_000271.4(NPC1):c.3182T>C ; NM_000271.4(NPC1):c.2932C>T ; NM_000271.4(NPC1):c.2974G>A ; NM_000271.4(NPC1):c.2072C>T ; NM_000271.4(NPC1):c.2873G>A ; NM_000271.4(NPC1):c.337T>C ; NM_000271.4(NPC1):c.2761C>T ; NM_000271.4(NPC1):c.2842G>A ; NM_000271.4(NPC1):c.3425T>C ; NM_000271.4(NPC1):c.3467A>G ; NM_000271.4(NPC1):c.3175C>T ; c.1042C>T ; NM_000271.4(NPC1):c.1628C>T ; NM_000271.4(NPC1):c.3611_3614del ; NM_000271.4(NPC1):c.2861C>T ; NM_000271.4(NPC1):c.2848G>A ; NM_000271.4(NPC1):c.3104C>T ; NM_000271.4(NPC1):c.530G>A ; NM_000271.4(NPC1):c.352_353delAG ; NM_000271.5:c.1211G>A ; NM_000271.4(NPC1):c.3662del ; NM_000271.4(NPC1):c.2324A>C ; NM_000271.4(NPC1):c.3182T>C ; NM_000271.4(NPC1):c.2932C>T ; NM_000271.4(NPC1):c.2974G>A ; NM_000271.4(NPC1):c.2072C>T ; NM_000271.4(NPC1):c.2873G>A ; NM_000271.4(NPC1):c.337T>C ; NM_000271.4(NPC1):c.2761C>T ; NM_000271.4(NPC1):c.2842G>A ; NM_000271.4(NPC1):c.3425T>C
NPC1	Niemann-Pick disease type C, juvenile neurologic onset	A rare lysosomal lipid storage disease characterized by variable clinical signs, depending on the age of onset, such as prolonged unexplained neonatal jaundice or cholestasis, isolated unexplained splenomegaly, and progressive, often severe neurological symptoms such as cognitive decline, cerebellar ataxia, vertical supranuclear gaze palsy (VSPG), dysarthria, dysphagia, dystonia, seizures, gelastic cataplexy, and psychiatric disorders.	The clinical onset and presentation is heterogeneous. NPDC is classically a neurovisceral condition with hepatosplenomegaly usually preceding the neurological symptoms, occurring in infancy or childhood but possibly occurring much later. Some patients exhibit lung disease early on and a small subset of patients can develop rapidly deteriorating hepatic or respiratory failure in early infancy. Neurological onset varies between early infancy to adulthood. Typically, neurologic involvement is progressive and consists mainly of dystonia, cerebellar ataxia, dysarthria, dysphagia, and progressive dementia. VSGP and cataplexy (with or without narcolepsy) are characteristic. Psychiatric disturbances are frequent in late-onset patients.	NM_000271.4(NPC1):c.3467A>G ; NM_000271.4(NPC1):c.3175C>T ; c.1042C>T ; NM_000271.4(NPC1):c.1628C>T ; NM_000271.4(NPC1):c.3611_3614del ; NM_000271.4(NPC1):c.2861C>T ; NM_000271.4(NPC1):c.2848G>A ; NM_000271.4(NPC1):c.3104C>T ; NM_000271.4(NPC1):c.530G>A ; NM_000271.4(NPC1):c.352_353delAG ; NM_000271.5:c.1211G>A ; NM_000271.4(NPC1):c.3662del ; NM_000271.4(NPC1):c.2324A>C ; NM_000271.4(NPC1):c.3182T>C ; NM_000271.4(NPC1):c.2932C>T ; NM_000271.4(NPC1):c.2974G>A ; NM_000271.4(NPC1):c.2072C>T ; NM_000271.4(NPC1):c.2873G>A ; NM_000271.4(NPC1):c.337T>C ; NM_000271.4(NPC1):c.2761C>T ; NM_000271.4(NPC1):c.2842G>A ; NM_000271.4(NPC1):c.3425T>C

NPC1	Niemann-Pick disease type C, late infantile neurologic onset	A rare lysosomal lipid storage disease characterized by variable clinical signs, depending on the age of onset, such as prolonged unexplained neonatal jaundice or cholestasis, isolated unexplained splenomegaly, and progressive, often severe neurological symptoms such as cognitive decline, cerebellar ataxia, vertical supranuclear gaze palsy (VSPG), dysarthria, dysphagia, dystonia, seizures, gelastic cataplexy, and psychiatric disorders.	The clinical onset and presentation is heterogeneous. NPDC is classically a neurovisceral condition with hepatosplenomegaly usually preceding the neurological symptoms, occurring in infancy or childhood but possibly occurring much later. Some patients exhibit lung disease early on and a small subset of patients can develop rapidly deteriorating hepatic or respiratory failure in early infancy. Neurological onset varies between early infancy to adulthood. Typically, neurologic involvement is progressive and consists mainly of dystonia, cerebellar ataxia, dysarthria, dysphagia, and progressive dementia. VSGP and cataplexy (with or without narcolepsy) are characteristic. Psychiatric disturbances are frequent in late-onset patients.	NM_000271.4(NPC1):c.3467A>G ; NM_000271.4(NPC1):c.3175C>T ; c.1042C>T ; NM_000271.4(NPC1):c.1628C>T ; NM_000271.4(NPC1):c.3611_3614del ; NM_000271.4(NPC1):c.2861C>T ; NM_000271.4(NPC1):c.2848G>A ; NM_000271.4(NPC1):c.3104C>T ; NM_000271.4(NPC1):c.530G>A ; NM_000271.4(NPC1):c.352_353delAG ; NM_000271.5:c.1211G>A ; NM_000271.4(NPC1):c.3662del ; NM_000271.4(NPC1):c.2324A>C ; NM_000271.4(NPC1):c.3182T>C ; NM_000271.4(NPC1):c.2932C>T ; NM_000271.4(NPC1):c.2974G>A ; NM_000271.4(NPC1):c.2072C>T ; NM_000271.4(NPC1):c.2873G>A ; NM_000271.4(NPC1):c.337T>C ; NM_000271.4(NPC1):c.2761C>T ; NM_000271.4(NPC1):c.2842G>A ; NM_000271.4(NPC1):c.3425T>C ; NM_000271.4(NPC1):c.3467A>G ; NM_000271.4(NPC1):c.3175C>T ; c.1042C>T ; NM_000271.4(NPC1):c.1628C>T ; NM_000271.4(NPC1):c.3611_3614del ; NM_000271.4(NPC1):c.2861C>T ; NM_000271.4(NPC1):c.2848G>A ; NM_000271.4(NPC1):c.3104C>T ; NM_000271.4(NPC1):c.530G>A ; NM_000271.4(NPC1):c.352_353delAG ; NM_000271.5:c.1211G>A ; NM_000271.4(NPC1):c.3662del ; NM_000271.4(NPC1):c.2324A>C ; NM_000271.4(NPC1):c.3182T>C ; NM_000271.4(NPC1):c.2932C>T ; NM_000271.4(NPC1):c.2974G>A ; NM_000271.4(NPC1):c.2072C>T ; NM_000271.4(NPC1):c.2873G>A ; NM_000271.4(NPC1):c.337T>C ; NM_000271.4(NPC1):c.2761C>T ; NM_000271.4(NPC1):c.2842G>A ; NM_000271.4(NPC1):c.3425T>C
NPC1	Niemann-Pick disease type C, severe early infantile neurologic onset	A rare lysosomal lipid storage disease characterized by variable clinical signs, depending on the age of onset, such as prolonged unexplained neonatal jaundice or cholestasis, isolated unexplained splenomegaly, and progressive, often severe neurological symptoms such as cognitive decline, cerebellar ataxia, vertical supranuclear gaze palsy (VSPG), dysarthria, dysphagia, dystonia, seizures, gelastic cataplexy, and psychiatric disorders.	The clinical onset and presentation is heterogeneous. NPDC is classically a neurovisceral condition with hepatosplenomegaly usually preceding the neurological symptoms, occurring in infancy or childhood but possibly occurring much later. Some patients exhibit lung disease early on and a small subset of patients can develop rapidly deteriorating hepatic or respiratory failure in early infancy. Neurological onset varies between early infancy to adulthood. Typically, neurologic involvement is progressive and consists mainly of dystonia, cerebellar ataxia, dysarthria, dysphagia, and progressive dementia. VSGP and cataplexy (with or without narcolepsy) are characteristic. Psychiatric disturbances are frequent in late-onset patients.	NM_000271.4(NPC1):c.3467A>G ; NM_000271.4(NPC1):c.3175C>T ; c.1042C>T ; NM_000271.4(NPC1):c.1628C>T ; NM_000271.4(NPC1):c.3611_3614del ; NM_000271.4(NPC1):c.2861C>T ; NM_000271.4(NPC1):c.2848G>A ; NM_000271.4(NPC1):c.3104C>T ; NM_000271.4(NPC1):c.530G>A ; NM_000271.4(NPC1):c.352_353delAG ; NM_000271.5:c.1211G>A ; NM_000271.4(NPC1):c.3662del ; NM_000271.4(NPC1):c.2324A>C ; NM_000271.4(NPC1):c.3182T>C ; NM_000271.4(NPC1):c.2932C>T ; NM_000271.4(NPC1):c.2974G>A ; NM_000271.4(NPC1):c.2072C>T ; NM_000271.4(NPC1):c.2873G>A ; NM_000271.4(NPC1):c.337T>C ; NM_000271.4(NPC1):c.2761C>T ; NM_000271.4(NPC1):c.2842G>A ; NM_000271.4(NPC1):c.3425T>C

NPC1	Niemann-Pick disease type C, severe perinatal form	A rare lysosomal lipid storage disease characterized by variable clinical signs, depending on the age of onset, such as prolonged unexplained neonatal jaundice or cholestasis, isolated unexplained splenomegaly, and progressive, often severe neurological symptoms such as cognitive decline, cerebellar ataxia, vertical supranuclear gaze palsy (VSPG), dysarthria, dysphagia, dystonia, seizures, gelastic cataplexy, and psychiatric disorders.	The clinical onset and presentation is heterogeneous. NPDC is classically a neurovisceral condition with hepatosplenomegaly usually preceding the neurological symptoms, occurring in infancy or childhood but possibly occurring much later. Some patients exhibit lung disease early on and a small subset of patients can develop rapidly deteriorating hepatic or respiratory failure in early infancy. Neurological onset varies between early infancy to adulthood. Typically, neurologic involvement is progressive and consists mainly of dystonia, cerebellar ataxia, dysarthria, dysphagia, and progressive dementia. VSGP and cataplexy (with or without narcolepsy) are characteristic. Psychiatric disturbances are frequent in late-onset patients.	NM_000271.4(NPC1):c.3467A>G ; NM_000271.4(NPC1):c.3175C>T ; c.1042C>T ; NM_000271.4(NPC1):c.1628C>T ; NM_000271.4(NPC1):c.3611_3614del ; NM_000271.4(NPC1):c.2861C>T ; NM_000271.4(NPC1):c.2848G>A ; NM_000271.4(NPC1):c.3104C>T ; NM_000271.4(NPC1):c.530G>A ; NM_000271.4(NPC1):c.352_353delAG ; NM_000271.5:c.1211G>A ; NM_000271.4(NPC1):c.3662del ; NM_000271.4(NPC1):c.2324A>C ; NM_000271.4(NPC1):c.3182T>C ; NM_000271.4(NPC1):c.2932C>T ; NM_000271.4(NPC1):c.2974G>A ; NM_000271.4(NPC1):c.2072C>T ; NM_000271.4(NPC1):c.2873G>A ; NM_000271.4(NPC1):c.337T>C ; NM_000271.4(NPC1):c.2761C>T ; NM_000271.4(NPC1):c.2842G>A ; NM_000271.4(NPC1):c.3425T>C ; NM_000271.4(NPC1):c.3467A>G ; NM_000271.4(NPC1):c.3175C>T ; c.1042C>T ; NM_000271.4(NPC1):c.1628C>T ; NM_000271.4(NPC1):c.3611_3614del ; NM_000271.4(NPC1):c.2861C>T ; NM_000271.4(NPC1):c.2848G>A ; NM_000271.4(NPC1):c.3104C>T ; NM_000271.4(NPC1):c.530G>A ; NM_000271.4(NPC1):c.352_353delAG ; NM_000271.5:c.1211G>A ; NM_000271.4(NPC1):c.3662del ; NM_000271.4(NPC1):c.2324A>C ; NM_000271.4(NPC1):c.3182T>C ; NM_000271.4(NPC1):c.2932C>T ; NM_000271.4(NPC1):c.2974G>A ; NM_000271.4(NPC1):c.2072C>T ; NM_000271.4(NPC1):c.2873G>A ; NM_000271.4(NPC1):c.337T>C ; NM_000271.4(NPC1):c.2761C>T ; NM_000271.4(NPC1):c.2842G>A ; NM_000271.4(NPC1):c.3425T>C
NPC2	Niemann-Pick disease type C, adult neurologic onset	A rare lysosomal lipid storage disease characterized by variable clinical signs, depending on the age of onset, such as prolonged unexplained neonatal jaundice or cholestasis, isolated unexplained splenomegaly, and progressive, often severe neurological symptoms such as cognitive decline, cerebellar ataxia, vertical supranuclear gaze palsy (VSPG), dysarthria, dysphagia, dystonia, seizures, gelastic cataplexy, and psychiatric disorders.	The clinical onset and presentation is heterogeneous. NPDC is classically a neurovisceral condition with hepatosplenomegaly usually preceding the neurological symptoms, occurring in infancy or childhood but possibly occurring much later. Some patients exhibit lung disease early on and a small subset of patients can develop rapidly deteriorating hepatic or respiratory failure in early infancy. Neurological onset varies between early infancy to adulthood. Typically, neurologic involvement is progressive and consists mainly of dystonia, cerebellar ataxia, dysarthria, dysphagia, and progressive dementia. VSGP and cataplexy (with or without narcolepsy) are characteristic. Psychiatric disturbances are frequent in late-onset patients.	NM_006432.4(NPC2):c.358C>T ; NM_006432.3(NPC2):c.436C>T ; NM_006432.4(NPC2):c.115G>A ; NM_006432.4(NPC2):c.352G>T ; NM_006432.3(NPC2):c.58G>T ; NM_006432.3(NPC2):c.27delG ; NM_006432.4(NPC2):c.295T>C ; NM_006432.4(NPC2):c.358C>T ; NM_006432.3(NPC2):c.436C>T ; NM_006432.4(NPC2):c.115G>A ; NM_006432.4(NPC2):c.352G>T ; NM_006432.3(NPC2):c.58G>T ; NM_006432.3(NPC2):c.27delG ; NM_006432.4(NPC2):c.295T>C

NPC2	Niemann-Pick disease type C, juvenile neurologic onset	A rare lysosomal lipid storage disease characterized by variable clinical signs, depending on the age of onset, such as prolonged unexplained neonatal jaundice or cholestasis, isolated unexplained splenomegaly, and progressive, often severe neurological symptoms such as cognitive decline, cerebellar ataxia, vertical supranuclear gaze palsy (VSPG), dysarthria, dysphagia, dystonia, seizures, gelastic cataplexy, and psychiatric disorders.	The clinical onset and presentation is heterogeneous. NPDC is classically a neurovisceral condition with hepatosplenomegaly usually preceding the neurological symptoms, occurring in infancy or childhood but possibly occurring much later. Some patients exhibit lung disease early on and a small subset of patients can develop rapidly deteriorating hepatic or respiratory failure in early infancy. Neurological onset varies between early infancy to adulthood. Typically, neurologic involvement is progressive and consists mainly of dystonia, cerebellar ataxia, dysarthria, dysphagia, and progressive dementia. VSGP and cataplexy (with or without narcolepsy) are characteristic. Psychiatric disturbances are frequent in late-onset patients.	NM_006432.4(NPC2):c.358C>T ; NM_006432.3(NPC2):c.436C>T ; NM_006432.4(NPC2):c.115G>A ; NM_006432.4(NPC2):c.352G>T ; NM_006432.3(NPC2):c.58G>T ; NM_006432.3(NPC2):c.27delG ; NM_006432.4(NPC2):c.295T>C ; NM_006432.4(NPC2):c.358C>T ; NM_006432.3(NPC2):c.436C>T ; NM_006432.4(NPC2):c.115G>A ; NM_006432.4(NPC2):c.352G>T ; NM_006432.3(NPC2):c.58G>T ; NM_006432.3(NPC2):c.27delG ; NM_006432.4(NPC2):c.295T>C
NPC2	Niemann-Pick disease type C, late infantile neurologic onset	A rare lysosomal lipid storage disease characterized by variable clinical signs, depending on the age of onset, such as prolonged unexplained neonatal jaundice or cholestasis, isolated unexplained splenomegaly, and progressive, often severe neurological symptoms such as cognitive decline, cerebellar ataxia, vertical supranuclear gaze palsy (VSPG), dysarthria, dysphagia, dystonia, seizures, gelastic cataplexy, and psychiatric disorders.	The clinical onset and presentation is heterogeneous. NPDC is classically a neurovisceral condition with hepatosplenomegaly usually preceding the neurological symptoms, occurring in infancy or childhood but possibly occurring much later. Some patients exhibit lung disease early on and a small subset of patients can develop rapidly deteriorating hepatic or respiratory failure in early infancy. Neurological onset varies between early infancy to adulthood. Typically, neurologic involvement is progressive and consists mainly of dystonia, cerebellar ataxia, dysarthria, dysphagia, and progressive dementia. VSGP and cataplexy (with or without narcolepsy) are characteristic. Psychiatric disturbances are frequent in late-onset patients.	NM_006432.4(NPC2):c.358C>T ; NM_006432.3(NPC2):c.436C>T ; NM_006432.4(NPC2):c.115G>A ; NM_006432.4(NPC2):c.352G>T ; NM_006432.3(NPC2):c.58G>T ; NM_006432.3(NPC2):c.27delG ; NM_006432.4(NPC2):c.295T>C ; NM_006432.4(NPC2):c.358C>T ; NM_006432.3(NPC2):c.436C>T ; NM_006432.4(NPC2):c.115G>A ; NM_006432.4(NPC2):c.352G>T ; NM_006432.3(NPC2):c.58G>T ; NM_006432.3(NPC2):c.27delG ; NM_006432.4(NPC2):c.295T>C

NPC2	Niemann-Pick disease type C, severe early infantile neurologic onset	A rare lysosomal lipid storage disease characterized by variable clinical signs, depending on the age of onset, such as prolonged unexplained neonatal jaundice or cholestasis, isolated unexplained splenomegaly, and progressive, often severe neurological symptoms such as cognitive decline, cerebellar ataxia, vertical supranuclear gaze palsy (VSPG), dysarthria, dysphagia, dystonia, seizures, gelastic cataplexy, and psychiatric disorders.	The clinical onset and presentation is heterogeneous. NPDC is classically a neurovisceral condition with hepatosplenomegaly usually preceding the neurological symptoms, occurring in infancy or childhood but possibly occurring much later. Some patients exhibit lung disease early on and a small subset of patients can develop rapidly deteriorating hepatic or respiratory failure in early infancy. Neurological onset varies between early infancy to adulthood. Typically, neurologic involvement is progressive and consists mainly of dystonia, cerebellar ataxia, dysarthria, dysphagia, and progressive dementia. VSGP and cataplexy (with or without narcolepsy) are characteristic. Psychiatric disturbances are frequent in late-onset patients.	NM_006432.4(NPC2):c.358C>T ; NM_006432.3(NPC2):c.436C>T ; NM_006432.4(NPC2):c.115G>A ; NM_006432.4(NPC2):c.352G>T ; NM_006432.3(NPC2):c.58G>T ; NM_006432.3(NPC2):c.27delG ; NM_006432.4(NPC2):c.295T>C ; NM_006432.4(NPC2):c.358C>T ; NM_006432.3(NPC2):c.436C>T ; NM_006432.4(NPC2):c.115G>A ; NM_006432.4(NPC2):c.352G>T ; NM_006432.3(NPC2):c.58G>T ; NM_006432.3(NPC2):c.27delG ; NM_006432.4(NPC2):c.295T>C
NPC2	Niemann-Pick disease type C, severe perinatal form	A rare lysosomal lipid storage disease characterized by variable clinical signs, depending on the age of onset, such as prolonged unexplained neonatal jaundice or cholestasis, isolated unexplained splenomegaly, and progressive, often severe neurological symptoms such as cognitive decline, cerebellar ataxia, vertical supranuclear gaze palsy (VSPG), dysarthria, dysphagia, dystonia, seizures, gelastic cataplexy, and psychiatric disorders.	The clinical onset and presentation is heterogeneous. NPDC is classically a neurovisceral condition with hepatosplenomegaly usually preceding the neurological symptoms, occurring in infancy or childhood but possibly occurring much later. Some patients exhibit lung disease early on and a small subset of patients can develop rapidly deteriorating hepatic or respiratory failure in early infancy. Neurological onset varies between early infancy to adulthood. Typically, neurologic involvement is progressive and consists mainly of dystonia, cerebellar ataxia, dysarthria, dysphagia, and progressive dementia. VSGP and cataplexy (with or without narcolepsy) are characteristic. Psychiatric disturbances are frequent in late-onset patients.	NM_006432.4(NPC2):c.358C>T ; NM_006432.3(NPC2):c.436C>T ; NM_006432.4(NPC2):c.115G>A ; NM_006432.4(NPC2):c.352G>T ; NM_006432.3(NPC2):c.58G>T ; NM_006432.3(NPC2):c.27delG ; NM_006432.4(NPC2):c.295T>C ; NM_006432.4(NPC2):c.358C>T ; NM_006432.3(NPC2):c.436C>T ; NM_006432.4(NPC2):c.115G>A ; NM_006432.4(NPC2):c.352G>T ; NM_006432.3(NPC2):c.58G>T ; NM_006432.3(NPC2):c.27delG ; NM_006432.4(NPC2):c.295T>C

NPHP1	Bardet-Biedl syndrome	A rare lysosomal lipid storage disease characterized by variable clinical signs, depending on the age of onset, such as prolonged unexplained neonatal jaundice or cholestasis, isolated unexplained splenomegaly, and progressive, often severe neurological symptoms such as cognitive decline, cerebellar ataxia, vertical supranuclear gaze palsy (VSPG), dysarthria, dysphagia, dystonia, seizures, gelastic cataplexy, and psychiatric disorders.	The clinical onset and presentation is heterogeneous. NPDC is classically a neurovisceral condition with hepatosplenomegaly usually preceding the neurological symptoms, occurring in infancy or childhood but possibly occurring much later. Some patients exhibit lung disease early on and a small subset of patients can develop rapidly deteriorating hepatic or respiratory failure in early infancy. Neurological onset varies between early infancy to adulthood. Typically, neurologic involvement is progressive and consists mainly of dystonia, cerebellar ataxia, dysarthria, dysphagia, and progressive dementia. VSGP and cataplexy (with or without narcolepsy) are characteristic. Psychiatric disturbances are frequent in late-onset patients.	c.1del ; NM_000272.3(NPHP1):c.1184dupC ; c.829C>T ; NM_000272.3(NPHP1):c.555dupA ; c.455C>G ; NM_000272.3(NPHP1):c.1884+1G>T ; NM_000272.3(NPHP1):c.80T>A ; c.1del ; NM_000272.3(NPHP1):c.1184dupC ; c.829C>T ; NM_000272.3(NPHP1):c.555dupA ; c.455C>G ; NM_000272.3(NPHP1):c.1884+1G>T ; NM_000272.3(NPHP1):c.80T>A
NPHP1	Joubert syndrome with renal defect	Bardet-Biedl syndrome (BBS) is a ciliopathy with multisystem involvement.	This disorder is characterized by a combination of clinical signs: obesity, pigmentary retinopathy, post-axial polydactyly, polycystic kidneys, hypogenitalism, and learning disabilities, many of which appear several years after disease onset. Clinical expression is variable but most patients manifest the majority of clinical signs during the disease course. Pigmentary retinopathy is the only constant clinical sign after childhood. BBS may also be associated with several other manifestations including diabetes, hypertension, congenital cardiopathy and Hirschsprung disease (see this term).	c.1del ; NM_000272.3(NPHP1):c.1184dupC ; c.829C>T ; NM_000272.3(NPHP1):c.555dupA ; c.455C>G ; NM_000272.3(NPHP1):c.1884+1G>T ; NM_000272.3(NPHP1):c.80T>A ; c.1del ; NM_000272.3(NPHP1):c.1184dupC ; c.829C>T ; NM_000272.3(NPHP1):c.555dupA ; c.455C>G ; NM_000272.3(NPHP1):c.1884+1G>T ; NM_000272.3(NPHP1):c.80T>A
NPHP1	Juvenile nephronophthisis	Joubert syndrome with renal defect is a rare subtype of Joubert syndrome and related disorders (JSRD, see this term) characterized by the neurological features of JS associated with renal disease, in the absence of retinopathy.	In most cases, renal disease manifests as juvenile nephronophthisis, with onset of clinical symptoms in the late first/early second decade of life, although in rare cases there may be infantile NPH, with onset in the first years of life.	c.1del ; NM_000272.3(NPHP1):c.1184dupC ; c.829C>T ; NM_000272.3(NPHP1):c.555dupA ; c.455C>G ; NM_000272.3(NPHP1):c.1884+1G>T ; NM_000272.3(NPHP1):c.80T>A ; c.1del ; NM_000272.3(NPHP1):c.1184dupC ; c.829C>T ; NM_000272.3(NPHP1):c.555dupA ; c.455C>G ; NM_000272.3(NPHP1):c.1884+1G>T ; NM_000272.3(NPHP1):c.80T>A

NPHP1	Senior-Loken syndrome	A rare, genetic, renal ciliopathy characterized by reduced ability of the kidneys to concentrate solutes, chronic tubulointerstitial nephritis, cystic renal disease and progression to end stage renal disease (ESRD). The three clinical subtypes are characterized by the age of onset of ESRD which includes infantile, juvenile and late onset.	Three main forms have been described. Juvenile NPHP, the most frequent form, progresses to end-stage renal failure at median age of 13 and is responsible for 15% of cases of childhood ESRD. Infantile NPHP can present in utero with oligohydramnios sequence or postnatally with reduced kidney function and progresses to ESRD before age 3. Late-onset NPHP is a rare form of the disease and presents clinical and histological signs similar to the juvenile form but with ESRD occurring later (median age of 19 years). The typical clinical symptoms include polyuria, polydipsia with regular fluid intake, impaired sodium reabsorption that cause hypovolemia and hyponatremia, anemia and growth delay. Renal ultrasonography in early stages is normal or shows unspecific changes with increased renal echogenicity, with advancing kidney disease poor cortico-medullary differentiation is described; corticomedullary cysts are present in the 70% of patients. Renal histopathology in NPHP is characterized by the triad of tubular cysts, tubular basement membrane disruption, and interstitial fibrosis with interstitial cell infiltration. Retinal degeneration is the most frequent extrarenal findings (10%), cerebellar vermis aplasia, liver fibrosis and skeletal defects could be also present. Extrarenal phenotypes are distinct but they overlap in some syndromic forms of NPHP (such as Joubert syndrome, Senior-Loken syndrome, Meckel-Gruber syndrome).	c.1del ; NM_000272.3(NPHP1):c.1184dupC ; c.829C>T ; NM_000272.3(NPHP1):c.555dupA ; c.455C>G ; NM_000272.3(NPHP1):c.1884+1G>T ; NM_000272.3(NPHP1):c.80T>A ; c.1del ; NM_000272.3(NPHP1):c.1184dupC ; c.829C>T ; NM_000272.3(NPHP1):c.555dupA ; c.455C>G ; NM_000272.3(NPHP1):c.1884+1G>T ; NM_000272.3(NPHP1):c.80T>A

NPHS1	Genetic steroid-resistant nephrotic syndrome	A rare autosomal recessive oculo-renal ciliopathy characterized by the association of nephronophthisis (NPHP), a chronic kidney disease, with retinal dystrophy.	The disease typically presents in the first two decades of life as a combination of nephronophthisis (NPH) with retinal degeneration. Depending on the genetic background either the visual disorder or chronic kidney disease determine the clinical picture. NPH typically presents with symptoms such as polyuria, polydipsia, secondary enuresis and anemia. Chronic kidney disease usually slowly progresses to end-stage kidney disease (ESKD). Ocular features include congenital or early-onset severe visual loss due to retinal dystrophy (Leber congenital amaurosis) or a milder phenotype determined by a slowly progressing tube-like restriction of visual fields and night blindness (tapeto-retinal degeneration). Funduscopy reveals various degrees of atrophic and pigmentary retinal alterations. In rare occasions, other additional clinical signs may be observed like liver fibrosis, obesity and neurologic disorders.	NM_004646.3(NPHS1):c.3478C>T ; c.3109+1G>A ; NM_004646.3(NPHS1):c.1307_1308dupAC ; NM_004646.3(NPHS1):c.3325C>T ; NM_004646.3(NPHS1):c.2491C>T ; NM_004646.3(NPHS1):c.1481delC ; NM_004646.3(NPHS1):c.121_122delCT ; NM_004646.3(NPHS1):c.1715G>A ; NM_004646.3(NPHS1):c.2928G>T ; NM_004646.3(NPHS1):c.3478C>T ; c.3109+1G>A ; NM_004646.3(NPHS1):c.1307_1308dupAC ; NM_004646.3(NPHS1):c.3325C>T ; NM_004646.3(NPHS1):c.2491C>T ; NM_004646.3(NPHS1):c.1481delC ; NM_004646.3(NPHS1):c.121_122delCT ; NM_004646.3(NPHS1):c.1715G>A ; NM_004646.3(NPHS1):c.2928G>T
NR0B1	46,XX testicular disorder of sex development	A rare, hereditary nephrotic syndrome characterized by proteinuria, hypoalbuminemia, edema, and hyperlipidemia, with an absence of response to an initial trial of corticosteroids (i.e. steroid-resistant nephrotic syndrome; SRNS) and a generally complicated course.	Disease onset may occur anywhere between birth and adulthood but predominantly presents in younger populations. The nephrotic syndrome is defined by severe proteinuria (Urinary Protein/Creatinine ration > 200 mg/mmol) with low serum albumin (<30 g/l) and possible edema. Biopsy shows minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS) or, more rarely, diffuse mesangial sclerosis (DMS), and podocyte foot process effacement by electron microscopy. It is multi-drug resistant and usually progresses to end-stage kidney failure; however, patients have a very low risk of recurrence after kidney transplantation.	NM_000475.4(NR0B1):c.788T>A ; NM_000475.4(NR0B1):c.704G>A ; NM_000475.4(NR0B1):c.591C>A ; NM_000475.4(NR0B1):c.847C>T ; NM_000475.4(NR0B1):c.513G>A ; NM_000475.4(NR0B1):c.873G>C ; c.388_389del ; NM_000475.4(NR0B1):c.813C>G ; NM_000475.4(NR0B1):c.1319A>T ; NM_000475.4(NR0B1):c.1316T>G ; NM_000475.4(NR0B1):c.800G>C ; NM_000475.4(NR0B1):c.1107G>A ; NM_000475.4(NR0B1):c.890T>C ; NM_000475.4(NR0B1):c.273C>A ; NM_000475.4(NR0B1):c.788T>A ; NM_000475.4(NR0B1):c.704G>A ; NM_000475.4(NR0B1):c.591C>A ; NM_000475.4(NR0B1):c.847C>T ; NM_000475.4(NR0B1):c.513G>A ; NM_000475.4(NR0B1):c.873G>C ; c.388_389del ; NM_000475.4(NR0B1):c.813C>G ; NM_000475.4(NR0B1):c.1319A>T ; NM_000475.4(NR0B1):c.1316T>G ; NM_000475.4(NR0B1):c.800G>C ; NM_000475.4(NR0B1):c.1107G>A ; NM_000475.4(NR0B1):c.890T>C ; NM_000475.4(NR0B1):c.273C>A

NR0B1	46,XY complete gonadal dysgenesis	A rare disorder of sex development (DSD) associated with a 46, XX karyotype and characterized by male external genitalia, ranging from normal to atypical with associated testosterone deficiency.	The clinical phenotype is variable, with features that include: normal male external to atypical genitalia, undescended testes with absent MÃ¼llerian structures and infertility. Presentation depends on the presence of the SRY gene (sex determining region of the Y chromosome). SRY positive cases (80-90%) are usually otherwise normal men who present after puberty with short stature, normal pubic hair and penile size but small testes, gynecomastia and azoospermia-related sterility. Undescended testes and hypospadias are also reported. There are usually no concerns about gender role and identity. SRY negative individuals (10-20%) usually present at birth with features such as penoscrotal hypospadias and undescended testes. Long-term complications due to male hypogonadism include: low libido, erectile dysfunction, decreased secondary sexual characteristics, osteopenia and depression.	NM_000475.4(NR0B1):c.788T>A ; NM_000475.4(NR0B1):c.704G>A ; NM_000475.4(NR0B1):c.591C>A ; NM_000475.4(NR0B1):c.847C>T ; NM_000475.4(NR0B1):c.513G>A ; NM_000475.4(NR0B1):c.873G>C ; c.388_389del ; NM_000475.4(NR0B1):c.813C>G ; NM_000475.4(NR0B1):c.1319A>T ; NM_000475.4(NR0B1):c.1316T>G ; NM_000475.4(NR0B1):c.800G>C ; NM_000475.4(NR0B1):c.1107G>A ; NM_000475.4(NR0B1):c.890T>C ; NM_000475.4(NR0B1):c.273C>A ; NM_000475.4(NR0B1):c.788T>A ; NM_000475.4(NR0B1):c.704G>A ; NM_000475.4(NR0B1):c.591C>A ; NM_000475.4(NR0B1):c.847C>T ; NM_000475.4(NR0B1):c.513G>A ; NM_000475.4(NR0B1):c.873G>C ; c.388_389del ; NM_000475.4(NR0B1):c.813C>G ; NM_000475.4(NR0B1):c.1319A>T ; NM_000475.4(NR0B1):c.1316T>G ; NM_000475.4(NR0B1):c.800G>C ; NM_000475.4(NR0B1):c.1107G>A ; NM_000475.4(NR0B1):c.890T>C ; NM_000475.4(NR0B1):c.273C>A
NR0B1	46,XY partial gonadal dysgenesis	A rare disorder of sex development (DSD) associated with anomalies in gonadal development that result in the presence of female external and internal genitalia despite the 46,XY karyotype.	Patients present during adolescence or early adulthood with normal female external genitalia but lack pubertal development although adrenarche is normal. Completely undeveloped streak gonads are present and are associated with an increased risk of abdominal tumours (most commonly dysgerminoma; see this term), which may be the presenting feature in some cases. Stature is normal or above normal, and features of Turner syndrome (see this term) are absent.	NM_000475.4(NR0B1):c.788T>A ; NM_000475.4(NR0B1):c.704G>A ; NM_000475.4(NR0B1):c.591C>A ; NM_000475.4(NR0B1):c.847C>T ; NM_000475.4(NR0B1):c.513G>A ; NM_000475.4(NR0B1):c.873G>C ; c.388_389del ; NM_000475.4(NR0B1):c.813C>G ; NM_000475.4(NR0B1):c.1319A>T ; NM_000475.4(NR0B1):c.1316T>G ; NM_000475.4(NR0B1):c.800G>C ; NM_000475.4(NR0B1):c.1107G>A ; NM_000475.4(NR0B1):c.890T>C ; NM_000475.4(NR0B1):c.273C>A ; NM_000475.4(NR0B1):c.788T>A ; NM_000475.4(NR0B1):c.704G>A ; NM_000475.4(NR0B1):c.591C>A ; NM_000475.4(NR0B1):c.847C>T ; NM_000475.4(NR0B1):c.513G>A ; NM_000475.4(NR0B1):c.873G>C ; c.388_389del ; NM_000475.4(NR0B1):c.813C>G ; NM_000475.4(NR0B1):c.1319A>T ; NM_000475.4(NR0B1):c.1316T>G ; NM_000475.4(NR0B1):c.800G>C ; NM_000475.4(NR0B1):c.1107G>A ; NM_000475.4(NR0B1):c.890T>C ; NM_000475.4(NR0B1):c.273C>A

NR0B1	X-linked adrenal hypoplasia congenita	46,XY partial gonadal dysgenesis (46,XY PGD) is a disorder of sex development (DSD) associated with anomalies in gonadal development that results in genital ambiguity of variable degree ranging from almost female phenotype to almost male phenotype in a patient carrying a male 46,XY karyotype.	46,XY PGD is characterized by ambiguous external genitalia with or without MÃ¼llerian structures. The degree of genital ambiguity varies along a spectrum, ranging from an almost female phenotype with clitoromegaly at one extreme to an almost male phenotype with isolated hypospadias at the other. Many patients present ambiguous genitalia or severe micropenis associated with complete regression of testicular tissue in one or both sides. Embryonic Testicular regression syndrome (ETRS; see this term) is considered as part of the clinical spectrum of PGD. Depending on the mutation, patients can have adrenal insufficiency or renal involvement (i.e. Wilms tumors or nephrotic syndrome). Gonadoblastomas or invasive germ cell tumors occur in around 20-30% of patients.	NM_000475.4(NR0B1):c.788T>A ; NM_000475.4(NR0B1):c.704G>A ; NM_000475.4(NR0B1):c.591C>A ; NM_000475.4(NR0B1):c.847C>T ; NM_000475.4(NR0B1):c.513G>A ; NM_000475.4(NR0B1):c.873G>C ; c.388_389del ; NM_000475.4(NR0B1):c.813C>G ; NM_000475.4(NR0B1):c.1319A>T ; NM_000475.4(NR0B1):c.1316T>G ; NM_000475.4(NR0B1):c.800G>C ; NM_000475.4(NR0B1):c.1107G>A ; NM_000475.4(NR0B1):c.890T>C ; NM_000475.4(NR0B1):c.273C>A ; NM_000475.4(NR0B1):c.788T>A ; NM_000475.4(NR0B1):c.704G>A ; NM_000475.4(NR0B1):c.591C>A ; NM_000475.4(NR0B1):c.847C>T ; NM_000475.4(NR0B1):c.513G>A ; NM_000475.4(NR0B1):c.873G>C ; c.388_389del ; NM_000475.4(NR0B1):c.813C>G ; NM_000475.4(NR0B1):c.1319A>T ; NM_000475.4(NR0B1):c.1316T>G ; NM_000475.4(NR0B1):c.800G>C ; NM_000475.4(NR0B1):c.1107G>A ; NM_000475.4(NR0B1):c.890T>C ; NM_000475.4(NR0B1):c.273C>A

NR2E3	Goldmann-Favre syndrome	A rare genetic adrenal disease characterized by primary adrenal insufficiency (AI) and/or hypogonadotropic hypogonadism (HH). Male patients typically present with AI with acute onset in infancy or insidious onset in childhood. Clinical features of AI include hyperpigmentation, vomiting, poor feeding, failure to thrive, seizures, vascular collapse, and sometimes sudden death. HH manifests later as delayed or arrested puberty. In rare cases, patients become symptomatic in early adulthood with delayed-onset AI, partial HH, and/or infertility. Histologically, the adrenal glands lack the permanent adult cortical zone. The remaining cells are larger than fetal adrenal cells ("cytomegalic") and contain characteristic nuclear inclusions.	Congenital adrenal hypoplasia (AHC) is a rare disorder that can be inherited in an X-linked or autosomal recessive pattern. In X-linked AHC, primary adrenocortical failure occurs because the adrenal glands lack the permanent adult cortical zone. The remaining cells are termed 'cytomegalic' because they are larger than typical fetal adrenal cells. Patients with AHC usually present in early infancy with primary adrenal failure. Hypogonadotropic hypogonadism (HHG) is a hallmark of the disorder, and is recognized during adolescence because of the absence or interruption of normal pubertal development. Abnormal spermatogenesis has also been observed in these patients. Milder forms of the disease have been described, with adrenal insufficiency sometimes occurring in childhood or even early adulthood.	NM_014249.3(NR2E3):c.226C>T ; NM_016346.4:c.119-2A>C ; c.298_299del ; NM_016346.3(NR2E3):c.1034_1038del ; NM_014249.4:c.932G>A ; NM_014249.3(NR2E3):c.226C>T ; NM_016346.4:c.119-2A>C ; c.298_299del ; NM_016346.3(NR2E3):c.1034_1038del ; NM_014249.4:c.932G>A

NR2E3	Retinitis pigmentosa	Goldmann-Favre syndrome (GFS) is a vitreoretinal dystrophy characterized by early onset of night blindness, reduced bilateral visual acuity, and typical fundus findings (progressive pigmentary degenerative changes, macular edema, retinoschisis).	The onset is usually in childhood. GFS manifests with progressive loss of visual acuity and night blindness. Peripheral vision can be decreased. Cataract is a frequent complication. Optic atrophy has been occasionally reported. The vitreous changes are degenerative and may include microfibrillar strands, liquefaction and posterior vitreous detachment. The fundus features include annular pigmentary changes (clumped pigment deposits), central or peripheral retinoschisis, cystoid macular edema. The GFS features are usually bilateral and symmetrical. The electroretinogram (ERG) is abnormal: both rod and cone ERGs are markedly diminished and may be non-detectable. Patients may have an increased sensitivity to blue light due to increased S-cone sensitivity.	NM_014249.3(NR2E3):c.226C>T ; NM_016346.4:c.119-2A>C ; c.298_299del ; NM_016346.3(NR2E3):c.1034_1038del ; NM_014249.4:c.932G>A ; NM_014249.3(NR2E3):c.226C>T ; NM_016346.4:c.119-2A>C ; c.298_299del ; NM_016346.3(NR2E3):c.1034_1038del ; NM_014249.4:c.932G>A
NTRK1	Differentiated thyroid carcinoma	Retinitis pigmentosa (RP) is an inherited retinal dystrophy leading to progressive loss of the photoreceptors and retinal pigment epithelium and resulting in blindness usually after several decades.	Retinitis pigmentosa is slowly progressive but relentless. There is however broad variability in age of onset, rate of progression and secondary clinical manifestations. Affected individuals generally first develop night blindness (nyctalopia) due to loss of rod function, often in adolescence or earlier. They then develop peripheral visual field impairment, and over time loss of central vision, usually at late stages, often around midlife. Central visual acuity loss may occur at any age as a result of cystoid macular edema or photoreceptor loss. Posterior subcapsular cataracts are common and severity is age dependent. Reduced color vision may also be found. Fundus examination reveals bone spicule pigment deposits, attenuated retinal vessels, retinal atrophy and waxy optic nerve pallor. Severity is partly correlated with the pattern of inheritance with X-linked cases having the most severe course, autosomal recessive and single occurrence cases having intermediate severity, and autosomal dominant the most favorable course.	NM_001012331.1:c.1908_1909insT ; NM_001007792.1(NTRK1):c.1621G>C ; NM_001007792.1(NTRK1):c.2231G>C ; NM_001007792.1:c.1976C>T ; NM_001007792.1(NTRK1):c.1651A>G ; c.1709del ; NM_001012331.1:c.1908_1909insT ; NM_001007792.1(NTRK1):c.1621G>C ; NM_001007792.1(NTRK1):c.2231G>C ; NM_001007792.1:c.1976C>T ; NM_001007792.1(NTRK1):c.1651A>G ; c.1709del

NTRK1	Familial medullary thyroid carcinoma	A rare, slow-growing, epithelial thyroid carcinoma typically presenting as an asymptomatic thyroid mass and is classed as either papillary thyroid cancer (PTC), follicular thyroid cancer (FTC) or Hurthle cell thyroid cancer (HCTC).	PTC, FTC, and HCTC have similar presentations, and constitute about 75, 20, and 5 percent of cases, respectively. About 10 percent of PTC are classified as tall cell variant, the most aggressive from of PTC. HCTC is generally considered slightly more aggressive than PTC and FTC. The age at diagnosis is usually over 30 years. Presentation is typically with an asymptomatic thyroid nodule. Rare but worrisome presentations include hoarseness due to vocal cord paralysis and obstruction of the airway or esophagus, and may suggest an aggressive variant of DTC or anaplastic thyroid carcinoma. DTC grows slowly, and distant metastases are rare at the time of presentation. The most common metastatic site is the cervical lymph nodes. Distant metastasis to lungs or bones is rare (about 5%). Pediatric cases are rare. They are more frequently present with lymph node involvement. Despite this apparently more aggressive presentation, the prognosis is excellent. Pathologically, PTC are usually composed of a mixture of papillae and follicles, frequently with relatively large nuclei containing folds and a clear center. About 50% contain calcium deposits. Different histological PTC subtypes have been described. FTC are characterized by microfollicles and presence of capsular and vascular invasion. HCTC, pathologically similar to FTC, are distinguished by mitochondria-rich, eosinophilic cytoplasm. Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) is a recently described variant; it is currently unclear if it is a pre-malignant lesion or a DTC variant.	NM_001012331.1:c.1908_1909insT ; NM_001007792.1(NTRK1):c.1621G>C ; NM_001007792.1(NTRK1):c.2231G>C ; NM_001007792.1:c.1976C>T ; NM_001007792.1(NTRK1):c.1651A>G ; c.1709del ; NM_001012331.1:c.1908_1909insT ; NM_001007792.1(NTRK1):c.1621G>C ; NM_001007792.1(NTRK1):c.2231G>C ; NM_001007792.1:c.1976C>T ; NM_001007792.1(NTRK1):c.1651A>G ; c.1709del

NTRK1	Hereditary sensory and autonomic neuropathy type 4	Multiple endocrine neoplasia type IIA is an autosomal dominant syndrome of multiple endocrine neoplasms, includingÂ medullaryÃ thyroidÂ carcinomaÂ (MTC), pheochromocytoma, and parathyroid adenomas. MEN2B, characterized by MTC with or without pheochromocytoma and with characteristic clinical abnormalities such as ganglioneuromas of the lips, tongue and colon, but without hyperparathyroidism, is also caused by mutation in the RET gene.		NM_001012331.1:c.1908_1909insT ; NM_001007792.1(NTRK1):c.1621G>C ; NM_001007792.1(NTRK1):c.2231G>C ; NM_001007792.1:c.1976C>T ; NM_001007792.1(NTRK1):c.1651A>G ; c.1709del ; NM_001012331.1:c.1908_1909insT ; NM_001007792.1(NTRK1):c.1621G>C ; NM_001007792.1(NTRK1):c.2231G>C ; NM_001007792.1:c.1976C>T ; NM_001007792.1(NTRK1):c.1651A>G ; c.1709del

NTRK1	Hereditary sensory and autonomic neuropathy type 5	A rare hereditary sensory and autonomic neuropathy characterized by anhidrosis, insensitivity to pain, self-mutilating behavior and episodes of fever.	The disease typically presents in early infancy, but may occasionally present during the neonatal period. Consanguinity has been reported in 50% of patients. Episodic fevers without obvious infections, extreme hyperpyrexia and febrile convulsions due to inability to dissipate heat as a result of anhidrosis as well as self-mutilation are usually the earliest signs of the disease. The cardinal feature is absence of sweating on the trunk and extremities, with occasional patients producing some moisture on the forehead, tip of the nose and gluteal sulcus. The skin becomes thick and callused with lichenification of palms, areas of hypotrichosis on the scalp and dystrophic nails. Deep tendon reflexes are usually present. Pain insensitivity is profound resulting in self-mutilation, auto-amputation, and corneal scarring but some patients retain temperature perception. Vibration sense and proprioception are normal or moderately decreased Bone fractures are slow to heal and large weight bearing joints are particularly susceptible to repeated trauma and frequently go on to the development of Charcot joints and osteomyelitis. Hypotonia and delayed developmental milestones are frequent in the early years, but sometimes normalize with age. Speech is usually clear, but patients have severe learning difficulties, irritability, hyperactivity, and cognitive impairment. Normal intelligence, however, has been reported in a few patients. Mild postural hypotension with compensatory tachycardia may be present, but not episodic hypertension. Around 20% of patients have scoliosis.	NM_001012331.1:c.1908_1909insT ; NM_001007792.1(NTRK1):c.1621G>C ; NM_001007792.1(NTRK1):c.2231G>C ; NM_001007792.1:c.1976C>T ; NM_001007792.1(NTRK1):c.1651A>G ; c.1709del ; NM_001012331.1:c.1908_1909insT ; NM_001007792.1(NTRK1):c.1621G>C ; NM_001007792.1(NTRK1):c.2231G>C ; NM_001007792.1:c.1976C>T ; NM_001007792.1(NTRK1):c.1651A>G ; c.1709del
OAT	Gyrate atrophy of choroid and retina	A disorder that is characterized by loss of pain perception and impaired temperature sensitivity, in the absence of any other major neurological anomalies.	Other findings include ulcers, self-mutilation and damaged joints. Intelligence is normal.	NM_000274.3(OAT):c.955C>T ; NM_000274.3(OAT):c.994G>A ; NM_000274.3(OAT):c.824G>A ; NM_000274.3(OAT):c.677C>T ; NM_000274.3(OAT):c.268C>G ; NM_000274.3(OAT):c.596C>A ; NM_000274.3(OAT):c.901-2A>G ; NM_000274.3(OAT):c.539G>C ; NM_000274.3(OAT):c.812G>A ; NM_000274.3(OAT):c.278G>T ; NM_000274.3(OAT):c.952G>A ; NM_000274.3(OAT):c.1250C>T ; NM_000274.3(OAT):c.1205T>C ; NM_000274.3(OAT):c.952delG ; NM_000274.3(OAT):c.533G>A ; NM_000274.3(OAT):c.159delC ; NM_000274.3(OAT):c.627T>A ; NM_000274.3(OAT):c.1276C>T ; NM_000274.3(OAT):c.955C>T ; NM_000274.3(OAT):c.994G>A ; NM_000274.3(OAT):c.824G>A ; NM_000274.3(OAT):c.677C>T ; NM_000274.3(OAT):c.268C>G ; NM_000274.3(OAT):c.596C>A ; NM_000274.3(OAT):c.901-2A>G ; NM_000274.3(OAT):c.539G>C ; NM_000274.3(OAT):c.812G>A ; NM_000274.3(OAT):c.278G>T ; NM_000274.3(OAT):c.952G>A ; NM_000274.3(OAT):c.1250C>T ; NM_000274.3(OAT):c.1205T>C ; NM_000274.3(OAT):c.952delG ; NM_000274.3(OAT):c.533G>A ; NM_000274.3(OAT):c.159delC ; NM_000274.3(OAT):c.627T>A ; NM_000274.3(OAT):c.1276C>T

OCRL	Dent disease type 2	Gyrate atrophy of the choroid and retina (GACR) is a very rare, inherited retinal dystrophy, characterized by progressive chorioretinal atrophy, myopia and early cataract.	Age at diagnosis is highly variable (1 month - 44 years). High phenotypic variability is noted among patients even within the same family, as well variable disease progression. The first complaints of the patients are night blindness (nyctalopia) and constriction of the visual field caused by multiple round areas of chorioretinal atrophy in the periphery. Over the years, the atrophic areas increase, coalesce and spread towards the macula leading to central visual loss in the 4th to 7th decade of life. Other ocular manifestations include myopia with marked astigmatism, early posterior subcapsular cataract, and cystoid macular edema.	NM_000276.3(OCRL):c.2530C>T ; NM_000276.3(OCRL):c.1499G>A ; c.2379dup ; c.2511del ; NM_000276.3(OCRL):c.909_910delAG ; NM_000276.3(OCRL):c.2299C>T ; NM_000276.3(OCRL):c.2530C>T ; NM_000276.3(OCRL):c.1499G>A ; c.2379dup ; c.2511del ; NM_000276.3(OCRL):c.909_910delAG ; NM_000276.3(OCRL):c.2299C>T
OCRL	Oculocerebrorenal syndrome of Lowe	Dent disease type 2 is a type of Dent disease in which patients have the manifestations of Dent disease type 1 associated with extra-renal features.	All of them had hypercalciuria and low-molecular-weight (LMW) proteinuria. In addition, these patients may also have nephrocalcinosis, nephrolithiasis, hematuria, hypophosphatemia and/or renal insufficiency. Only a minority (approximately one fourth) of these patients have been observed to have mild intellectual deficit, hypotonia and sub-clinical cataract. The presence of intellectual impairment and sub-clinical cataract were so mild as to dissuade the clinicians from considering a diagnosis of Lowe syndrome (see this term), which is characterized by congenital cataracts, delayed motor milestones, some degree of intellectual impairment in almost all affected males, growth retardation, rickets and renal proximal tubulopathy. Moreover, the patients with Dent disease type 2 and mild intellectual deficit were adults, who had not, over time, developed more overt features of Lowe syndrome.	NM_000276.3(OCRL):c.2530C>T ; NM_000276.3(OCRL):c.1499G>A ; c.2379dup ; c.2511del ; NM_000276.3(OCRL):c.909_910delAG ; NM_000276.3(OCRL):c.2299C>T ; NM_000276.3(OCRL):c.2530C>T ; NM_000276.3(OCRL):c.1499G>A ; c.2379dup ; c.2511del ; NM_000276.3(OCRL):c.909_910delAG ; NM_000276.3(OCRL):c.2299C>T

OTC	Ornithine transcarbamylase deficiency	A rare multisystem disorder characterized by congenital cataracts, glaucoma, intellectual disabilities, seizures, postnatal growth retardation and renal tubular dysfunction with chronic renal failure.	Oculocerebrorenal syndrome of Lowe (OCRL) is a congenital disorder characterized by ocular abnormalities (bilateral congenital discoid cataracts, glaucoma with or without buphthalmos, strabismus, hypermetropia and corneal and conjunctival cheloids), neurological involvement (developmental delay, seizures, hypotonia present at birth typically with absence of deep tendon reflexes), stereotypic behavior (temper tantrums, aggressiveness and obsessive compulsive behavior), postnatal growth retardation, mild to severe intellectual disability (mean IQ 40-50), stereotypic hand movements, renal dysfunction of the Fanconi type (proximal tubular acidosis; phosphate wasting leading to renal rickets, osteomalacia and pathological fractures) and progressive decline in kidney function leading to end-stage renal failure in adulthood. Subtle cataracts are obligate findings in female carriers after puberty. Other clinical manifestations include facial dysmorphism (frontal bossing, deep-set eyes, chubby cheeks, fair complexion), destructive teno-synovitis in older patients, short stature, mucocutaneous anomalies (eruptive vellus hair cysts, tricoepithiloma, excess skin folds and eruption cysts in oral cavity), dental malformations, cryptorchidism and bleeding tendency due to platelet dysfunction.	NM_000531.5(OTC):c.238A>G ; NM_000531.5(OTC):c.460G>T ; NM_000531.5(OTC):c.275G>A ; NM_000531.5(OTC):c.674C>T ; NM_000531.5(OTC):c.118C>T ; NM_000531.5(OTC):c.259G>A ; NM_000531.5(OTC):c.148G>T ; NM_000531.5(OTC):c.119G>A ; NM_000531.5(OTC):c.245T>G ; NM_000531.5(OTC):c.563G>T ; NM_000531.5(OTC):c.332T>C ; NM_000531.5(OTC):c.617T>G ; NM_000531.5(OTC):c.77G>A ; NM_000531.5(OTC):c.646C>G ; NM_000531.5(OTC):c.134T>C ; NM_000531.5(OTC):c.829C>T ; NM_000531.5(OTC):c.421C>T ; NM_000531.5(OTC):c.717+2T>C ; NM_000531.5(OTC):c.238A>G ; NM_000531.5(OTC):c.460G>T ; NM_000531.5(OTC):c.275G>A ; NM_000531.5(OTC):c.674C>T ; NM_000531.5(OTC):c.118C>T ; NM_000531.5(OTC):c.259G>A ; NM_000531.5(OTC):c.148G>T ; NM_000531.5(OTC):c.119G>A ; NM_000531.5(OTC):c.245T>G ; NM_000531.5(OTC):c.563G>T ; NM_000531.5(OTC):c.332T>C ; NM_000531.5(OTC):c.617T>G ; NM_000531.5(OTC):c.77G>A ; NM_000531.5(OTC):c.646C>G ; NM_000531.5(OTC):c.134T>C ; NM_000531.5(OTC):c.829C>T ; NM_000531.5(OTC):c.421C>T ; NM_000531.5(OTC):c.717+2T>C

PAH	Classic phenylketonuria	A rare, genetic disorder of urea cycle metabolism and ammonia detoxification characterized by either a severe, neonatal-onset disease found mainly in males, or later-onset (partial) forms of the disease. Both present with episodes of hyperammonemia that can be fatal and which can lead to neurological sequelae.	Males with the severe, neonatal-onset type are normal at birth but develop poor sucking, hypotonia and lethargy after a few days, rapidly progressing into somnolence and coma. Seizures and hyperventilation may also be present. If untreated, severe encephalopathy will develop with a high risk for death. Patients with a milder form can present at any age. In infants, symptoms can be induced when switching from breast milk to whole milk. In children and adults, environmental stressors (i.e. fasting, high protein diet, pregnancy and the postpartum period, intercurrent illness, surgery) can trigger episodes of hyperammonemic encephalopathy along with nausea, vomiting, headaches, erratic behavior, delirium and combativeness. These episodes can also result in hyperammonemic coma. Neurological complications of hyperammonemic coma include developmental delay and, sometimes, severe cognitive impairment. Many female carriers are asymptomatic; however, they can be affected to the same extent as males if the degree of X-inactivation of the disease allele is unfavorable. Coagulopathy is a frequent finding during metabolic decompensation and sometimes evolves into acute liver failure.	NM_000277.2(PAH):c.261C>A ; NM_000277.3(PAH):c.1217T>C ; NM_000277.3(PAH):c.442-1G>A ; NM_000642.3:c.1222C>T ; NM_000277.3(PAH):c.745C>T ; NM_000277.1(PAH):c.611A>G ; NM_000277.2(PAH):c.1199+17G>A ; NM_000277.3(PAH):c.734T>C ; NM_000277.3(PAH):c.818C>T ; NM_000277.3(PAH):c.529G>A ; NM_000277.3(PAH):c.311C>A ; NM_000277.3(PAH):c.1238G>C ; NM_000277.1(PAH):c.204A>T ; NM_000277.2(PAH):c.733G>C ; NM_000277.3(PAH):c.1241A>G ; NM_000277.3(PAH):c.721C>T ; NM_000277.3:c.898G>T ; NM_000277.3:c.533A>G ; NM_000277.1(PAH):c.728G>A ; NM_000277.2(PAH):c.320A>G ; NM_000277.2(PAH):c.441+1G>A ; NM_000277.3:c.441+5G>T ; NM_000277.2(PAH):c.806delT ; NM_000277.1(PAH):c.1033G>T ; NM_000277.3(PAH):c.829T>G ; NM_000277.3:c.143T>C ; NM_000277.3:c.722G>A ; NM_000277.2(PAH):c.809G>A ; NM_000277.1(PAH):c.117C>G ; c.450dup ; NM_000277.2(PAH):c.764T>C ; NM_000277.2(PAH):c.357delC ; NM_000277.1(PAH):c.838G>A ; NM_000277.3(PAH):c.472C>T ; NM_000277.3(PAH):c.688G>A ; NM_000277.3(PAH):c.490A>G ; NM_000277.1(PAH):c.896T>G ; NM_000277.2(PAH):c.722delG ; NM_000277.3(PAH):c.823C>T ; NM_000277.3:c.473G>A ; NM_000277.2(PAH):c.1066-3C>T ; NM_000277.3(PAH):c.755G>A ; NM_000277.2(PAH):c.1199+1G>A ; NM_000277.2(PAH):c.926C>A ; NM_000277.3:c.1066-11G>A ; NM_000277.3(PAH):c.912+1G>A ; NM_000277.3(PAH):c.1197A>T ; NM_000277.3:c.754C>T ; NM_000277.3(PAH):c.727C>T ; NM_000277.3:c.165T>G ; NM_000277.1(PAH):c.527G>T ; NM_000277.2(PAH):c.737C>A ; NM_000277.3:c.782G>A ; NM_000277.3:c.1315+1G>A ; NM_000277.2(PAH):c.482T>C ; NM_000277.3(PAH):c.1169A>G ; NM_000277.3:c.1208C>T ; NM_000277.2(PAH):c.503delA ; NM_000277.1(PAH):c.842+5G>A ; NM_000277.1(PAH):c.250G>T ; NM_000277.3(PAH):c.1243G>A ; NM_000277.1(PAH):c.136G>A ; NM_000277.3(PAH):c.1139C>T ; NM_000277.3(PAH):c.1162G>A ; NM_000277.3(PAH):c.508C>G ; NM_000277.3(PAH):c.331C>T ; NM_000277.2(PAH):c.569T>C ; NM_000277.3:c.1045T>C ; NM_000277.3(PAH):c.638T>C ; NM_000277.1(PAH):c.1042C>G ; NM_000277.3(PAH):c.1068C>A ; NM_000277.2(PAH):c.47_48delCT ; NM_000277.2(PAH):c.284_286delTCA ; NM_000277.3(PAH):c.926C>T ; NM_000277.2(PAH):c.955G>T ; NM_000277.2(PAH):c.1166delC ; NM_000277.2(PAH):c.442-5C>G ; NM_000277.3(PAH):c.194T>C ; NM_000277.3(PAH):c.814G>T ; NM_000277.2(PAH):c.261C>A ; NM_000277.3(PAH):c.1217T>C ; NM_000277.3(PAH):c.442-1G>A ; NM_000642.3:c.1222C>T ; NM_000277.3(PAH):c.745C>T ; NM_000277.1(PAH):c.611A>G ; NM_000277.2(PAH):c.1199+17G>A ; NM_000277.3(PAH):c.734T>C ; NM_000277.3(PAH):c.818C>T ; NM_000277.3(PAH):c.529G>A ; NM_000277.3(PAH):c.311C>A ; NM_000277.3(PAH):c.1238G>C ; NM_000277.1(PAH):c.204A>T ; NM_000277.2(PAH):c.733G>C ; NM_000277.3(PAH):c.1241A>G ; NM_000277.3(PAH):c.721C>T ; NM_000277.3:c.898G>T ; NM_000277.3:c.533A>G ; NM_000277.1(PAH):c.728G>A ; NM_000277.2(PAH):c.320A>G ; NM_000277.2(PAH):c.441+1G>A ; NM_000277.3:c.441+5G>T ; NM_000277.2(PAH):c.806delT ; NM_000277.1(PAH):c.1033G>T ; NM_000277.3(PAH):c.829T>G ; NM_000277.3:c.143T>C ; NM_000277.3:c.722G>A ; NM_000277.2(PAH):c.809G>A ; NM_000277.1(PAH):c.117C>G ; c.450dup ; NM_000277.2(PAH):c.764T>C ; NM_000277.2(PAH):c.357delC ; NM_000277.1(PAH):c.838G>A ; NM_000277.3(PAH):c.472C>T ; NM_000277.3(PAH):c.688G>A ; NM_000277.3(PAH):c.490A>G ; NM_000277.1(PAH):c.896T>G ; NM_000277.2(PAH):c.722delG ; NM_000277.3(PAH):c.823C>T ; NM_000277.3:c.473G>A ; NM_000277.2(PAH):c.1066-3C>T ; NM_000277.3(PAH):c.755G>A ; NM_000277.2(PAH):c.1199+1G>A ; NM_000277.2(PAH):c.926C>A ; NM_000277.3:c.1066-11G>A ; NM_000277.3(PAH):c.912+1G>A ; NM_000277.3(PAH):c.1197A>T ; NM_000277.3:c.754C>T ; NM_000277.3(PAH):c.727C>T ; NM_000277.3:c.165T>G ; NM_000277.1(PAH):c.527G>T ; NM_000277.2(PAH):c.737C>A ; NM_000277.3:c.782G>A ; NM_000277.3:c.1315+1G>A ; NM_000277.2(PAH):c.482T>C ; NM_000277.3(PAH):c.1169A>G ; NM_000277.3:c.1208C>T ; NM_000277.2(PAH):c.503delA ; NM_000277.1(PAH):c.842+5G>A ; NM_000277.1(PAH):c.250G>T ; NM_000277.3(PAH):c.1243G>A ; NM_000277.1(PAH):c.136G>A ; NM_000277.3(PAH):c.1139C>T ; NM_000277.3(PAH):c.1162G>A ; NM_000277.3(PAH):c.508C>G ; NM_000277.3(PAH):c.331C>T ; NM_000277.2(PAH):c.569T>C ; NM_000277.3:c.1045T>C ; NM_000277.3(PAH):c.638T>C ; NM_000277.1(PAH):c.1042C>G ; NM_000277.3(PAH):c.1068C>A ; NM_000277.2(PAH):c.47_48delCT ; NM_000277.2(PAH):c.284_286delTCA ; NM_000277.3(PAH):c.926C>T ; NM_000277.2(PAH):c.955G>T ; NM_000277.2(PAH):c.1166delC ; NM_000277.2(PAH):c.442-5C>G ; NM_000277.3(PAH):c.194T>C ; NM_000277.3(PAH):c.814G>T

PAH	Maternal phenylketonuria	Severe form of phenylketonuria (PKU) due to phenylalanine hydroxylase deficiency, an inborn error of amino acid metabolism, characterised in untreated patients by severe intellectual deficit and neuropsychiatric complications.	Late diagnosed patients present mostly with progressive developmental delay associated with severe signs including stunted growth, microcephaly, seizures, tremors, eczema, vomiting, musty odor, and subsequently behavioral (hyperactivity) and motor disorders. Untreated patients develop profound, permanent intellectual impairment and deterioration of cognitive performance and motor skills. Demyelination and decreased dopamine, norepinephrine, and serotonin production have been found in patients who do not pursue dietary restrictions into adulthood. Complications later on include exaggerated deep tendon reflexes, tremor, and paraplegia or hemiplegia. In treated patients, clinical signs vary based on treatment and diet compliance, and may include psychiatric disorders such as attention deficit-hyperactivity disorder and depression.	NM_000277.2(PAH):c.261C>A ; NM_000277.3(PAH):c.1217T>C ; NM_000277.3(PAH):c.442-1G>A ; NM_000642.3:c.1222C>T ; NM_000277.3(PAH):c.745C>T ; NM_000277.1(PAH):c.611A>G ; NM_000277.2(PAH):c.1199+17G>A ; NM_000277.3(PAH):c.734T>C ; NM_000277.3(PAH):c.818C>T ; NM_000277.3(PAH):c.529G>A ; NM_000277.3(PAH):c.311C>A ; NM_000277.3(PAH):c.1238G>C ; NM_000277.1(PAH):c.204A>T ; NM_000277.2(PAH):c.733G>C ; NM_000277.3(PAH):c.1241A>G ; NM_000277.3(PAH):c.721C>T ; NM_000277.3:c.898G>T ; NM_000277.3:c.533A>G ; NM_000277.1(PAH):c.728G>A ; NM_000277.2(PAH):c.320A>G ; NM_000277.2(PAH):c.441+1G>A ; NM_000277.3:c.441+5G>T ; NM_000277.2(PAH):c.806delT ; NM_000277.1(PAH):c.1033G>T ; NM_000277.3(PAH):c.829T>G ; NM_000277.3:c.143T>C ; NM_000277.3:c.722G>A ; NM_000277.2(PAH):c.809G>A ; NM_000277.1(PAH):c.117C>G ; c.450dup ; NM_000277.2(PAH):c.764T>C ; NM_000277.2(PAH):c.357delC ; NM_000277.1(PAH):c.838G>A ; NM_000277.3(PAH):c.472C>T ; NM_000277.3(PAH):c.688G>A ; NM_000277.3(PAH):c.490A>G ; NM_000277.1(PAH):c.896T>G ; NM_000277.2(PAH):c.722delG ; NM_000277.3(PAH):c.823C>T ; NM_000277.3:c.473G>A ; NM_000277.2(PAH):c.1066-3C>T ; NM_000277.3(PAH):c.755G>A ; NM_000277.2(PAH):c.1199+1G>A ; NM_000277.2(PAH):c.926C>A ; NM_000277.3:c.1066-11G>A ; NM_000277.3(PAH):c.912+1G>A ; NM_000277.3(PAH):c.1197A>T ; NM_000277.3:c.754C>T ; NM_000277.3(PAH):c.727C>T ; NM_000277.3:c.165T>G ; NM_000277.1(PAH):c.527G>T ; NM_000277.2(PAH):c.737C>A ; NM_000277.3:c.782G>A ; NM_000277.3:c.1315+1G>A ; NM_000277.2(PAH):c.482T>C ; NM_000277.3(PAH):c.1169A>G ; NM_000277.3:c.1208C>T ; NM_000277.2(PAH):c.503delA ; NM_000277.1(PAH):c.842+5G>A ; NM_000277.1(PAH):c.250G>T ; NM_000277.3(PAH):c.1243G>A ; NM_000277.1(PAH):c.136G>A ; NM_000277.3(PAH):c.1139C>T ; NM_000277.3(PAH):c.1162G>A ; NM_000277.3(PAH):c.508C>G ; NM_000277.3(PAH):c.331C>T ; NM_000277.2(PAH):c.569T>C ; NM_000277.3:c.1045T>C ; NM_000277.3(PAH):c.638T>C ; NM_000277.1(PAH):c.1042C>G ; NM_000277.3(PAH):c.1068C>A ; NM_000277.2(PAH):c.47_48delCT ; NM_000277.2(PAH):c.284_286delTCA ; NM_000277.3(PAH):c.926C>T ; NM_000277.2(PAH):c.955G>T ; NM_000277.2(PAH):c.1166delC ; NM_000277.2(PAH):c.442-5C>G ; NM_000277.3(PAH):c.194T>C ; NM_000277.3(PAH):c.814G>T ; NM_000277.2(PAH):c.261C>A ; NM_000277.3(PAH):c.1217T>C ; NM_000277.3(PAH):c.442-1G>A ; NM_000642.3:c.1222C>T ; NM_000277.3(PAH):c.745C>T ; NM_000277.1(PAH):c.611A>G ; NM_000277.2(PAH):c.1199+17G>A ; NM_000277.3(PAH):c.734T>C ; NM_000277.3(PAH):c.818C>T ; NM_000277.3(PAH):c.529G>A ; NM_000277.3(PAH):c.311C>A ; NM_000277.3(PAH):c.1238G>C ; NM_000277.1(PAH):c.204A>T ; NM_000277.2(PAH):c.733G>C ; NM_000277.3(PAH):c.1241A>G ; NM_000277.3(PAH):c.721C>T ; NM_000277.3:c.898G>T ; NM_000277.3:c.533A>G ; NM_000277.1(PAH):c.728G>A ; NM_000277.2(PAH):c.320A>G ; NM_000277.2(PAH):c.441+1G>A ; NM_000277.3:c.441+5G>T ; NM_000277.2(PAH):c.806delT ; NM_000277.1(PAH):c.1033G>T ; NM_000277.3(PAH):c.829T>G ; NM_000277.3:c.143T>C ; NM_000277.3:c.722G>A ; NM_000277.2(PAH):c.809G>A ; NM_000277.1(PAH):c.117C>G ; c.450dup ; NM_000277.2(PAH):c.764T>C ; NM_000277.2(PAH):c.357delC ; NM_000277.1(PAH):c.838G>A ; NM_000277.3(PAH):c.472C>T ; NM_000277.3(PAH):c.688G>A ; NM_000277.3(PAH):c.490A>G ; NM_000277.1(PAH):c.896T>G ; NM_000277.2(PAH):c.722delG ; NM_000277.3(PAH):c.823C>T ; NM_000277.3:c.473G>A ; NM_000277.2(PAH):c.1066-3C>T ; NM_000277.3(PAH):c.755G>A ; NM_000277.2(PAH):c.1199+1G>A ; NM_000277.2(PAH):c.926C>A ; NM_000277.3:c.1066-11G>A ; NM_000277.3(PAH):c.912+1G>A ; NM_000277.3(PAH):c.1197A>T ; NM_000277.3:c.754C>T ; NM_000277.3(PAH):c.727C>T ; NM_000277.3:c.165T>G ; NM_000277.1(PAH):c.527G>T ; NM_000277.2(PAH):c.737C>A ; NM_000277.3:c.782G>A ; NM_000277.3:c.1315+1G>A ; NM_000277.2(PAH):c.482T>C ; NM_000277.3(PAH):c.1169A>G ; NM_000277.3:c.1208C>T ; NM_000277.2(PAH):c.503delA ; NM_000277.1(PAH):c.842+5G>A ; NM_000277.1(PAH):c.250G>T ; NM_000277.3(PAH):c.1243G>A ; NM_000277.1(PAH):c.136G>A ; NM_000277.3(PAH):c.1139C>T ; NM_000277.3(PAH):c.1162G>A ; NM_000277.3(PAH):c.508C>G ; NM_000277.3(PAH):c.331C>T ; NM_000277.2(PAH):c.569T>C ; NM_000277.3:c.1045T>C ; NM_000277.3(PAH):c.638T>C ; NM_000277.1(PAH):c.1042C>G ; NM_000277.3(PAH):c.1068C>A ; NM_000277.2(PAH):c.47_48delCT ; NM_000277.2(PAH):c.284_286delTCA ; NM_000277.3(PAH):c.926C>T ; NM_000277.2(PAH):c.955G>T ; NM_000277.2(PAH):c.1166delC ; NM_000277.2(PAH):c.442-5C>G ; NM_000277.3(PAH):c.194T>C ; NM_000277.3(PAH):c.814G>T

PAH	Mild hyperphenylalaninemia	A rare disorder of phenylalanine (Phe) metabolism, an inborn error of amino acid metabolism, characterized by the development of microcephaly, growth retardation, congenital heart disease, facial dysmorphism and intellectual disability in non-phenylketonuric offspring of mothers with excess blood Phe concentrations.	Hyperphenylalaninemia is classified by blood Phe concentrations of more than 1,200 micromol/L (classic PKU) or less than 600 micromol/L (mild hyperphenylalaninemia), between 600 and 1,200 micromol/L as mild PKU. Maternal phenylketonuria syndrome has been shown to result in intrauterine and postnatal growth retardation with associated low birth weight, microcephaly, and intellectual disability in the offspring. Congenital heart malformation is also found and may include double-chambered right ventricle, tetralogy of Fallot, and ventricular septal defects. In severe cases, facial dysmorphism may also occur with various features reported including receding forehead, ptosis or fused eyes, strabismus, dysplastic ear helices, high palate, underdeveloped philtrum, anteverted nostrils, broad flat nasal bridge, deviated nasal septum, and micrognathia. Optimal maternal blood Phe concentrations should be strictly maintained throughout pregnancy to reduce the risk of these abnormalities. This can be achieved by minimal dietary Phe intake, along with tyrosine-enriched supplements. Studies have also shown that dietary treatment to control blood Phe concentrations can prevent the disorder if started before conception.	NM_000277.2(PAH):c.261C>A ; NM_000277.3(PAH):c.1217T>C ; NM_000277.3(PAH):c.442-1G>A ; NM_000642.3:c.1222C>T ; NM_000277.3(PAH):c.745C>T ; NM_000277.1(PAH):c.611A>G ; NM_000277.2(PAH):c.1199+17G>A ; NM_000277.3(PAH):c.734T>C ; NM_000277.3(PAH):c.818C>T ; NM_000277.3(PAH):c.529G>A ; NM_000277.3(PAH):c.311C>A ; NM_000277.3(PAH):c.1238G>C ; NM_000277.1(PAH):c.204A>T ; NM_000277.2(PAH):c.733G>C ; NM_000277.3(PAH):c.1241A>G ; NM_000277.3(PAH):c.721C>T ; NM_000277.3:c.898G>T ; NM_000277.3:c.533A>G ; NM_000277.1(PAH):c.728G>A ; NM_000277.2(PAH):c.320A>G ; NM_000277.2(PAH):c.441+1G>A ; NM_000277.3:c.441+5G>T ; NM_000277.2(PAH):c.806delT ; NM_000277.1(PAH):c.1033G>T ; NM_000277.3(PAH):c.829T>G ; NM_000277.3:c.143T>C ; NM_000277.3:c.722G>A ; NM_000277.2(PAH):c.809G>A ; NM_000277.1(PAH):c.117C>G ; c.450dup ; NM_000277.2(PAH):c.764T>C ; NM_000277.2(PAH):c.357delC ; NM_000277.1(PAH):c.838G>A ; NM_000277.3(PAH):c.472C>T ; NM_000277.3(PAH):c.688G>A ; NM_000277.3(PAH):c.490A>G ; NM_000277.1(PAH):c.896T>G ; NM_000277.2(PAH):c.722delG ; NM_000277.3(PAH):c.823C>T ; NM_000277.3:c.473G>A ; NM_000277.2(PAH):c.1066-3C>T ; NM_000277.3(PAH):c.755G>A ; NM_000277.2(PAH):c.1199+1G>A ; NM_000277.2(PAH):c.926C>A ; NM_000277.3:c.1066-11G>A ; NM_000277.3(PAH):c.912+1G>A ; NM_000277.3(PAH):c.1197A>T ; NM_000277.3:c.754C>T ; NM_000277.3(PAH):c.727C>T ; NM_000277.3:c.165T>G ; NM_000277.1(PAH):c.527G>T ; NM_000277.2(PAH):c.737C>A ; NM_000277.3:c.782G>A ; NM_000277.3:c.1315+1G>A ; NM_000277.2(PAH):c.482T>C ; NM_000277.3(PAH):c.1169A>G ; NM_000277.3:c.1208C>T ; NM_000277.2(PAH):c.503delA ; NM_000277.1(PAH):c.842+5G>A ; NM_000277.1(PAH):c.250G>T ; NM_000277.3(PAH):c.1243G>A ; NM_000277.1(PAH):c.136G>A ; NM_000277.3(PAH):c.1139C>T ; NM_000277.3(PAH):c.1162G>A ; NM_000277.3(PAH):c.508C>G ; NM_000277.3(PAH):c.331C>T ; NM_000277.2(PAH):c.569T>C ; NM_000277.3:c.1045T>C ; NM_000277.3(PAH):c.638T>C ; NM_000277.1(PAH):c.1042C>G ; NM_000277.3(PAH):c.1068C>A ; NM_000277.2(PAH):c.47_48delCT ; NM_000277.2(PAH):c.284_286delTCA ; NM_000277.3(PAH):c.926C>T ; NM_000277.2(PAH):c.955G>T ; NM_000277.2(PAH):c.1166delC ; NM_000277.2(PAH):c.442-5C>G ; NM_000277.3(PAH):c.194T>C ; NM_000277.3(PAH):c.814G>T ; NM_000277.2(PAH):c.261C>A ; NM_000277.3(PAH):c.1217T>C ; NM_000277.3(PAH):c.442-1G>A ; NM_000642.3:c.1222C>T ; NM_000277.3(PAH):c.745C>T ; NM_000277.1(PAH):c.611A>G ; NM_000277.2(PAH):c.1199+17G>A ; NM_000277.3(PAH):c.734T>C ; NM_000277.3(PAH):c.818C>T ; NM_000277.3(PAH):c.529G>A ; NM_000277.3(PAH):c.311C>A ; NM_000277.3(PAH):c.1238G>C ; NM_000277.1(PAH):c.204A>T ; NM_000277.2(PAH):c.733G>C ; NM_000277.3(PAH):c.1241A>G ; NM_000277.3(PAH):c.721C>T ; NM_000277.3:c.898G>T ; NM_000277.3:c.533A>G ; NM_000277.1(PAH):c.728G>A ; NM_000277.2(PAH):c.320A>G ; NM_000277.2(PAH):c.441+1G>A ; NM_000277.3:c.441+5G>T ; NM_000277.2(PAH):c.806delT ; NM_000277.1(PAH):c.1033G>T ; NM_000277.3(PAH):c.829T>G ; NM_000277.3:c.143T>C ; NM_000277.3:c.722G>A ; NM_000277.2(PAH):c.809G>A ; NM_000277.1(PAH):c.117C>G ; c.450dup ; NM_000277.2(PAH):c.764T>C ; NM_000277.2(PAH):c.357delC ; NM_000277.1(PAH):c.838G>A ; NM_000277.3(PAH):c.472C>T ; NM_000277.3(PAH):c.688G>A ; NM_000277.3(PAH):c.490A>G ; NM_000277.1(PAH):c.896T>G ; NM_000277.2(PAH):c.722delG ; NM_000277.3(PAH):c.823C>T ; NM_000277.3:c.473G>A ; NM_000277.2(PAH):c.1066-3C>T ; NM_000277.3(PAH):c.755G>A ; NM_000277.2(PAH):c.1199+1G>A ; NM_000277.2(PAH):c.926C>A ; NM_000277.3:c.1066-11G>A ; NM_000277.3(PAH):c.912+1G>A ; NM_000277.3(PAH):c.1197A>T ; NM_000277.3:c.754C>T ; NM_000277.3(PAH):c.727C>T ; NM_000277.3:c.165T>G ; NM_000277.1(PAH):c.527G>T ; NM_000277.2(PAH):c.737C>A ; NM_000277.3:c.782G>A ; NM_000277.3:c.1315+1G>A ; NM_000277.2(PAH):c.482T>C ; NM_000277.3(PAH):c.1169A>G ; NM_000277.3:c.1208C>T ; NM_000277.2(PAH):c.503delA ; NM_000277.1(PAH):c.842+5G>A ; NM_000277.1(PAH):c.250G>T ; NM_000277.3(PAH):c.1243G>A ; NM_000277.1(PAH):c.136G>A ; NM_000277.3(PAH):c.1139C>T ; NM_000277.3(PAH):c.1162G>A ; NM_000277.3(PAH):c.508C>G ; NM_000277.3(PAH):c.331C>T ; NM_000277.2(PAH):c.569T>C ; NM_000277.3:c.1045T>C ; NM_000277.3(PAH):c.638T>C ; NM_000277.1(PAH):c.1042C>G ; NM_000277.3(PAH):c.1068C>A ; NM_000277.2(PAH):c.47_48delCT ; NM_000277.2(PAH):c.284_286delTCA ; NM_000277.3(PAH):c.926C>T ; NM_000277.2(PAH):c.955G>T ; NM_000277.2(PAH):c.1166delC ; NM_000277.2(PAH):c.442-5C>G ; NM_000277.3(PAH):c.194T>C ; NM_000277.3(PAH):c.814G>T

PAH	Mild phenylketonuria	A rare form of phenylketonuria, an inborn error of amino acid metabolism, characterized by blood phenylalanine (Phe) concentrations of 120-600 micromol/L with or without clinical manifestations of impaired cognitive function, and behavioral and developmental disorders.	Phenylketonuria (PKU) is an autosomal recessive inborn error of metabolism resulting from a deficiency of phenylalanine hydroxylase (PAH), an enzyme that catalyzes the hydroxylation of phenylalanine to tyrosine, the rate-limiting step in phenylalanine catabolism. If undiagnosed and untreated, phenylketonuria can result in impaired postnatal cognitive development resulting from a neurotoxic effect of hyperphenylalaninemia.	NM_000277.2(PAH):c.261C>A ; NM_000277.3(PAH):c.1217T>C ; NM_000277.3(PAH):c.442-1G>A ; NM_000642.3:c.1222C>T ; NM_000277.3(PAH):c.745C>T ; NM_000277.1(PAH):c.611A>G ; NM_000277.2(PAH):c.1199+17G>A ; NM_000277.3(PAH):c.734T>C ; NM_000277.3(PAH):c.818C>T ; NM_000277.3(PAH):c.529G>A ; NM_000277.3(PAH):c.311C>A ; NM_000277.3(PAH):c.1238G>C ; NM_000277.1(PAH):c.204A>T ; NM_000277.2(PAH):c.733G>C ; NM_000277.3(PAH):c.1241A>G ; NM_000277.3(PAH):c.721C>T ; NM_000277.3:c.898G>T ; NM_000277.3:c.533A>G ; NM_000277.1(PAH):c.728G>A ; NM_000277.2(PAH):c.320A>G ; NM_000277.2(PAH):c.441+1G>A ; NM_000277.3:c.441+5G>T ; NM_000277.2(PAH):c.806delT ; NM_000277.1(PAH):c.1033G>T ; NM_000277.3(PAH):c.829T>G ; NM_000277.3:c.143T>C ; NM_000277.3:c.722G>A ; NM_000277.2(PAH):c.809G>A ; NM_000277.1(PAH):c.117C>G ; c.450dup ; NM_000277.2(PAH):c.764T>C ; NM_000277.2(PAH):c.357delC ; NM_000277.1(PAH):c.838G>A ; NM_000277.3(PAH):c.472C>T ; NM_000277.3(PAH):c.688G>A ; NM_000277.3(PAH):c.490A>G ; NM_000277.1(PAH):c.896T>G ; NM_000277.2(PAH):c.722delG ; NM_000277.3(PAH):c.823C>T ; NM_000277.3:c.473G>A ; NM_000277.2(PAH):c.1066-3C>T ; NM_000277.3(PAH):c.755G>A ; NM_000277.2(PAH):c.1199+1G>A ; NM_000277.2(PAH):c.926C>A ; NM_000277.3:c.1066-11G>A ; NM_000277.3(PAH):c.912+1G>A ; NM_000277.3(PAH):c.1197A>T ; NM_000277.3:c.754C>T ; NM_000277.3(PAH):c.727C>T ; NM_000277.3:c.165T>G ; NM_000277.1(PAH):c.527G>T ; NM_000277.2(PAH):c.737C>A ; NM_000277.3:c.782G>A ; NM_000277.3:c.1315+1G>A ; NM_000277.2(PAH):c.482T>C ; NM_000277.3(PAH):c.1169A>G ; NM_000277.3:c.1208C>T ; NM_000277.2(PAH):c.503delA ; NM_000277.1(PAH):c.842+5G>A ; NM_000277.1(PAH):c.250G>T ; NM_000277.3(PAH):c.1243G>A ; NM_000277.1(PAH):c.136G>A ; NM_000277.3(PAH):c.1139C>T ; NM_000277.3(PAH):c.1162G>A ; NM_000277.3(PAH):c.508C>G ; NM_000277.3(PAH):c.331C>T ; NM_000277.2(PAH):c.569T>C ; NM_000277.3:c.1045T>C ; NM_000277.3(PAH):c.638T>C ; NM_000277.1(PAH):c.1042C>G ; NM_000277.3(PAH):c.1068C>A ; NM_000277.2(PAH):c.47_48delCT ; NM_000277.2(PAH):c.284_286delTCA ; NM_000277.3(PAH):c.926C>T ; NM_000277.2(PAH):c.955G>T ; NM_000277.2(PAH):c.1166delC ; NM_000277.2(PAH):c.442-5C>G ; NM_000277.3(PAH):c.194T>C ; NM_000277.3(PAH):c.814G>T ; NM_000277.2(PAH):c.261C>A ; NM_000277.3(PAH):c.1217T>C ; NM_000277.3(PAH):c.442-1G>A ; NM_000642.3:c.1222C>T ; NM_000277.3(PAH):c.745C>T ; NM_000277.1(PAH):c.611A>G ; NM_000277.2(PAH):c.1199+17G>A ; NM_000277.3(PAH):c.734T>C ; NM_000277.3(PAH):c.818C>T ; NM_000277.3(PAH):c.529G>A ; NM_000277.3(PAH):c.311C>A ; NM_000277.3(PAH):c.1238G>C ; NM_000277.1(PAH):c.204A>T ; NM_000277.2(PAH):c.733G>C ; NM_000277.3(PAH):c.1241A>G ; NM_000277.3(PAH):c.721C>T ; NM_000277.3:c.898G>T ; NM_000277.3:c.533A>G ; NM_000277.1(PAH):c.728G>A ; NM_000277.2(PAH):c.320A>G ; NM_000277.2(PAH):c.441+1G>A ; NM_000277.3:c.441+5G>T ; NM_000277.2(PAH):c.806delT ; NM_000277.1(PAH):c.1033G>T ; NM_000277.3(PAH):c.829T>G ; NM_000277.3:c.143T>C ; NM_000277.3:c.722G>A ; NM_000277.2(PAH):c.809G>A ; NM_000277.1(PAH):c.117C>G ; c.450dup ; NM_000277.2(PAH):c.764T>C ; NM_000277.2(PAH):c.357delC ; NM_000277.1(PAH):c.838G>A ; NM_000277.3(PAH):c.472C>T ; NM_000277.3(PAH):c.688G>A ; NM_000277.3(PAH):c.490A>G ; NM_000277.1(PAH):c.896T>G ; NM_000277.2(PAH):c.722delG ; NM_000277.3(PAH):c.823C>T ; NM_000277.3:c.473G>A ; NM_000277.2(PAH):c.1066-3C>T ; NM_000277.3(PAH):c.755G>A ; NM_000277.2(PAH):c.1199+1G>A ; NM_000277.2(PAH):c.926C>A ; NM_000277.3:c.1066-11G>A ; NM_000277.3(PAH):c.912+1G>A ; NM_000277.3(PAH):c.1197A>T ; NM_000277.3:c.754C>T ; NM_000277.3(PAH):c.727C>T ; NM_000277.3:c.165T>G ; NM_000277.1(PAH):c.527G>T ; NM_000277.2(PAH):c.737C>A ; NM_000277.3:c.782G>A ; NM_000277.3:c.1315+1G>A ; NM_000277.2(PAH):c.482T>C ; NM_000277.3(PAH):c.1169A>G ; NM_000277.3:c.1208C>T ; NM_000277.2(PAH):c.503delA ; NM_000277.1(PAH):c.842+5G>A ; NM_000277.1(PAH):c.250G>T ; NM_000277.3(PAH):c.1243G>A ; NM_000277.1(PAH):c.136G>A ; NM_000277.3(PAH):c.1139C>T ; NM_000277.3(PAH):c.1162G>A ; NM_000277.3(PAH):c.508C>G ; NM_000277.3(PAH):c.331C>T ; NM_000277.2(PAH):c.569T>C ; NM_000277.3:c.1045T>C ; NM_000277.3(PAH):c.638T>C ; NM_000277.1(PAH):c.1042C>G ; NM_000277.3(PAH):c.1068C>A ; NM_000277.2(PAH):c.47_48delCT ; NM_000277.2(PAH):c.284_286delTCA ; NM_000277.3(PAH):c.926C>T ; NM_000277.2(PAH):c.955G>T ; NM_000277.2(PAH):c.1166delC ; NM_000277.2(PAH):c.442-5C>G ; NM_000277.3(PAH):c.194T>C ; NM_000277.3(PAH):c.814G>T

PAH	Tetrahydrobiopterin-responsive hyperphenylalaninemia/phenylketonuria	A mild to moderate form of phenylketouria (PKU), an inborn error of amino acid metabolism, characterized by blood phenylalanine concentrations of 600-1,200 micromol/L and manifests with reduced cognitive function and behavioral and developmental disorders. Dietary phenylalanine tolerance is 400-600 mg/day.	Phenylketonuria (PKU) is an autosomal recessive inborn error of metabolism resulting from a deficiency of phenylalanine hydroxylase (PAH;Â 612349), an enzyme that catalyzes the hydroxylation of phenylalanine to tyrosine, the rate-limiting step in phenylalanine catabolism. If undiagnosed and untreated, phenylketonuria can result in impaired postnatal cognitive development resulting from a neurotoxic effect of hyperphenylalaninemia.Â	NM_000277.2(PAH):c.261C>A ; NM_000277.3(PAH):c.1217T>C ; NM_000277.3(PAH):c.442-1G>A ; NM_000642.3:c.1222C>T ; NM_000277.3(PAH):c.745C>T ; NM_000277.1(PAH):c.611A>G ; NM_000277.2(PAH):c.1199+17G>A ; NM_000277.3(PAH):c.734T>C ; NM_000277.3(PAH):c.818C>T ; NM_000277.3(PAH):c.529G>A ; NM_000277.3(PAH):c.311C>A ; NM_000277.3(PAH):c.1238G>C ; NM_000277.1(PAH):c.204A>T ; NM_000277.2(PAH):c.733G>C ; NM_000277.3(PAH):c.1241A>G ; NM_000277.3(PAH):c.721C>T ; NM_000277.3:c.898G>T ; NM_000277.3:c.533A>G ; NM_000277.1(PAH):c.728G>A ; NM_000277.2(PAH):c.320A>G ; NM_000277.2(PAH):c.441+1G>A ; NM_000277.3:c.441+5G>T ; NM_000277.2(PAH):c.806delT ; NM_000277.1(PAH):c.1033G>T ; NM_000277.3(PAH):c.829T>G ; NM_000277.3:c.143T>C ; NM_000277.3:c.722G>A ; NM_000277.2(PAH):c.809G>A ; NM_000277.1(PAH):c.117C>G ; c.450dup ; NM_000277.2(PAH):c.764T>C ; NM_000277.2(PAH):c.357delC ; NM_000277.1(PAH):c.838G>A ; NM_000277.3(PAH):c.472C>T ; NM_000277.3(PAH):c.688G>A ; NM_000277.3(PAH):c.490A>G ; NM_000277.1(PAH):c.896T>G ; NM_000277.2(PAH):c.722delG ; NM_000277.3(PAH):c.823C>T ; NM_000277.3:c.473G>A ; NM_000277.2(PAH):c.1066-3C>T ; NM_000277.3(PAH):c.755G>A ; NM_000277.2(PAH):c.1199+1G>A ; NM_000277.2(PAH):c.926C>A ; NM_000277.3:c.1066-11G>A ; NM_000277.3(PAH):c.912+1G>A ; NM_000277.3(PAH):c.1197A>T ; NM_000277.3:c.754C>T ; NM_000277.3(PAH):c.727C>T ; NM_000277.3:c.165T>G ; NM_000277.1(PAH):c.527G>T ; NM_000277.2(PAH):c.737C>A ; NM_000277.3:c.782G>A ; NM_000277.3:c.1315+1G>A ; NM_000277.2(PAH):c.482T>C ; NM_000277.3(PAH):c.1169A>G ; NM_000277.3:c.1208C>T ; NM_000277.2(PAH):c.503delA ; NM_000277.1(PAH):c.842+5G>A ; NM_000277.1(PAH):c.250G>T ; NM_000277.3(PAH):c.1243G>A ; NM_000277.1(PAH):c.136G>A ; NM_000277.3(PAH):c.1139C>T ; NM_000277.3(PAH):c.1162G>A ; NM_000277.3(PAH):c.508C>G ; NM_000277.3(PAH):c.331C>T ; NM_000277.2(PAH):c.569T>C ; NM_000277.3:c.1045T>C ; NM_000277.3(PAH):c.638T>C ; NM_000277.1(PAH):c.1042C>G ; NM_000277.3(PAH):c.1068C>A ; NM_000277.2(PAH):c.47_48delCT ; NM_000277.2(PAH):c.284_286delTCA ; NM_000277.3(PAH):c.926C>T ; NM_000277.2(PAH):c.955G>T ; NM_000277.2(PAH):c.1166delC ; NM_000277.2(PAH):c.442-5C>G ; NM_000277.3(PAH):c.194T>C ; NM_000277.3(PAH):c.814G>T ; NM_000277.2(PAH):c.261C>A ; NM_000277.3(PAH):c.1217T>C ; NM_000277.3(PAH):c.442-1G>A ; NM_000642.3:c.1222C>T ; NM_000277.3(PAH):c.745C>T ; NM_000277.1(PAH):c.611A>G ; NM_000277.2(PAH):c.1199+17G>A ; NM_000277.3(PAH):c.734T>C ; NM_000277.3(PAH):c.818C>T ; NM_000277.3(PAH):c.529G>A ; NM_000277.3(PAH):c.311C>A ; NM_000277.3(PAH):c.1238G>C ; NM_000277.1(PAH):c.204A>T ; NM_000277.2(PAH):c.733G>C ; NM_000277.3(PAH):c.1241A>G ; NM_000277.3(PAH):c.721C>T ; NM_000277.3:c.898G>T ; NM_000277.3:c.533A>G ; NM_000277.1(PAH):c.728G>A ; NM_000277.2(PAH):c.320A>G ; NM_000277.2(PAH):c.441+1G>A ; NM_000277.3:c.441+5G>T ; NM_000277.2(PAH):c.806delT ; NM_000277.1(PAH):c.1033G>T ; NM_000277.3(PAH):c.829T>G ; NM_000277.3:c.143T>C ; NM_000277.3:c.722G>A ; NM_000277.2(PAH):c.809G>A ; NM_000277.1(PAH):c.117C>G ; c.450dup ; NM_000277.2(PAH):c.764T>C ; NM_000277.2(PAH):c.357delC ; NM_000277.1(PAH):c.838G>A ; NM_000277.3(PAH):c.472C>T ; NM_000277.3(PAH):c.688G>A ; NM_000277.3(PAH):c.490A>G ; NM_000277.1(PAH):c.896T>G ; NM_000277.2(PAH):c.722delG ; NM_000277.3(PAH):c.823C>T ; NM_000277.3:c.473G>A ; NM_000277.2(PAH):c.1066-3C>T ; NM_000277.3(PAH):c.755G>A ; NM_000277.2(PAH):c.1199+1G>A ; NM_000277.2(PAH):c.926C>A ; NM_000277.3:c.1066-11G>A ; NM_000277.3(PAH):c.912+1G>A ; NM_000277.3(PAH):c.1197A>T ; NM_000277.3:c.754C>T ; NM_000277.3(PAH):c.727C>T ; NM_000277.3:c.165T>G ; NM_000277.1(PAH):c.527G>T ; NM_000277.2(PAH):c.737C>A ; NM_000277.3:c.782G>A ; NM_000277.3:c.1315+1G>A ; NM_000277.2(PAH):c.482T>C ; NM_000277.3(PAH):c.1169A>G ; NM_000277.3:c.1208C>T ; NM_000277.2(PAH):c.503delA ; NM_000277.1(PAH):c.842+5G>A ; NM_000277.1(PAH):c.250G>T ; NM_000277.3(PAH):c.1243G>A ; NM_000277.1(PAH):c.136G>A ; NM_000277.3(PAH):c.1139C>T ; NM_000277.3(PAH):c.1162G>A ; NM_000277.3(PAH):c.508C>G ; NM_000277.3(PAH):c.331C>T ; NM_000277.2(PAH):c.569T>C ; NM_000277.3:c.1045T>C ; NM_000277.3(PAH):c.638T>C ; NM_000277.1(PAH):c.1042C>G ; NM_000277.3(PAH):c.1068C>A ; NM_000277.2(PAH):c.47_48delCT ; NM_000277.2(PAH):c.284_286delTCA ; NM_000277.3(PAH):c.926C>T ; NM_000277.2(PAH):c.955G>T ; NM_000277.2(PAH):c.1166delC ; NM_000277.2(PAH):c.442-5C>G ; NM_000277.3(PAH):c.194T>C ; NM_000277.3(PAH):c.814G>T
PANK2	Atypical pantothenate kinase-associated neurodegeneration	A form of phenylketonuria (PKU), an inborn error of amino acid metabolism, characterized by mild to moderate symptoms of PKU including impaired cognitive function, seizures, and behavioral and developmental disorders, and a marked reduction of elevated phenylalanine concentrations after oral loading with tetrahydrobiopterin (BH4), an essential cofactor of phenylalanine hydroxylase.	Phenylketonuria (PKU) is an autosomal recessive inborn error of metabolism resulting from a deficiency of phenylalanine hydroxylase (PAH), an enzyme that catalyzes the hydroxylation of phenylalanine to tyrosine, the rate-limiting step in phenylalanine catabolism. If undiagnosed and untreated, phenylketonuria can result in impaired postnatal cognitive development resulting from a neurotoxic effect of hyperphenylalaninemia.	c.823_824del ; NM_153638.3(PANK2):c.790C>T ; NM_153638.3(PANK2):c.1561G>A ; NM_153638.3(PANK2):c.1583C>T ; NC_000020.11:g.3910806A>T ; c.823_824del ; NM_153638.3(PANK2):c.790C>T ; NM_153638.3(PANK2):c.1561G>A ; NM_153638.3(PANK2):c.1583C>T ; NC_000020.11:g.3910806A>T

PANK2	Classic pantothenate kinase-associated neurodegeneration	Pantothenate kinase-associated neurodegeneration (PKAN) is the most common type of neurodegeneration with brain iron accumulation (NBIA; see this term), a rare neurodegenerative disorder characterized by progressive extrapyramidal dysfunction (dystonia, rigidity, choreoathetosis), iron accumulation on the brain and axonal spheroids in the central nervous system.	Classic PKAN (75% of cases) is characterized by early onset, usually before six years of age, and rapid progression. Atypical PKAN (25% of cases) has later onset, between 13 and 14 years of age, and slower progression. Patients present with symptoms anywhere along a continuum between the two. In classic PKAN, patients present with impaired gait and falling, often related to dystonia, rigidity, impaired balance, or spasticity, and usually lose the ability to ambulate by 10-15 years after onset. Episodes of rapid decline, which may include status dystonicus, occur interspersed with longer periods of relative stability. Developmental delay (primarily motor, sometimes global) may occur. Patients frequently develop pigmentary retinal degeneration and dysarthria. Later in disease course common complications include dysphagia, gastro-oesophageal reflux, chronic constipation, aspiration pneumonia and malnutrition. In atypical PKAN, patients present with speech difficulty, mild gait abnormalities, prominent psychiatric symptoms that may include depression, emotional lability, impulsivity, or violent outbursts, pigmentary retinal degeneration (less frequently than in classic PKAN) and both verbal and motor tourettism. Motor involvement is generally less severe and loss of ambulation occurs within 15-40 years of onset. The association of hyperprebetalipoproteinemia, acanthocytes and retinitis pigmentosa (HARP syndrome) is within the PKAN spectrum.	c.823_824del ; NM_153638.3(PANK2):c.790C>T ; NM_153638.3(PANK2):c.1561G>A ; NM_153638.3(PANK2):c.1583C>T ; NC_000020.11:g.3910806A>T ; c.823_824del ; NM_153638.3(PANK2):c.790C>T ; NM_153638.3(PANK2):c.1561G>A ; NM_153638.3(PANK2):c.1583C>T ; NC_000020.11:g.3910806A>T

PC	Pyruvate carboxylase deficiency, benign type	Pantothenate kinase-associated neurodegeneration (PKAN) is the most common type of neurodegeneration with brain iron accumulation (NBIA; see this term), a rare neurodegenerative disorder characterized by progressive extrapyramidal dysfunction (dystonia, rigidity, choreoathetosis), iron accumulation on the brain and axonal spheroids in the central nervous system.	Classic PKAN (75% of cases) is characterized by early onset, usually before six years of age, and rapid progression. Atypical PKAN (25% of cases) has later onset, between 13 and 14 years of age, and slower progression. Patients present with symptoms anywhere along a continuum between the two. In classic PKAN, patients present with impaired gait and falling, often related to dystonia, rigidity, impaired balance, or spasticity, and usually lose the ability to ambulate by 10-15 years after onset. Episodes of rapid decline, which may include status dystonicus, occur interspersed with longer periods of relative stability. Developmental delay (primarily motor, sometimes global) may occur. Patients frequently develop pigmentary retinal degeneration and dysarthria. Later in disease course common complications include dysphagia, gastro-oesophageal reflux, chronic constipation, aspiration pneumonia and malnutrition. In atypical PKAN, patients present with speech difficulty, mild gait abnormalities, prominent psychiatric symptoms that may include depression, emotional lability, impulsivity, or violent outbursts, pigmentary retinal degeneration (less frequently than in classic PKAN) and both verbal and motor tourettism. Motor involvement is generally less severe and loss of ambulation occurs within 15-40 years of onset. The association of hyperprebetalipoproteinemia, acanthocytes and retinitis pigmentosa (HARP syndrome) is within the PKAN spectrum.	NM_001040716.1(PC):c.1748G>T ; NM_000920.3(PC):c.434T>C ; NM_001040716.1(PC):c.1748G>T ; NM_000920.3(PC):c.434T>C
PC	Pyruvate carboxylase deficiency, infantile type	Benign pyruvate carboxylase (PC) deficiency (Type C) is a rare, very mild form of PC deficiency characterized by episodic metabolic acidosis and normal or mildly delayed neurological development.	Onset typically occurs during the first year of life with episodic metabolic acidosis associated with lactic acidemia and occasionally with ketoacidosis during metabolic stress. Neurological development is normal or mildly impaired. Other signs include dystonia, episodic ataxia, dysarthria, transitory hemiparesis and seizures.	NM_001040716.1(PC):c.1748G>T ; NM_000920.3(PC):c.434T>C ; NM_001040716.1(PC):c.1748G>T ; NM_000920.3(PC):c.434T>C

PC	Pyruvate carboxylase deficiency, severe neonatal type	Infantile pyruvate carboxylase (PC) deficiency (Type A) is a rare, severe form of PC deficiency characterized by infantile-onset, mild to moderate lactic acidemia, and a generally severe course.	Patients with Type A PC deficiency usually first present with symptoms at the age of two to five months, often after normal early development. Clinical manifestations include mild to moderate metabolic acidosis with acute vomiting and tachypnea, failure to thrive, apathy, delayed intellectual and motor development, hypotonia, pyramidal dysfunction, ataxia, nystagmus and seizures. Renal tubular acidosis has also been reported.	NM_001040716.1(PC):c.1748G>T ; NM_000920.3(PC):c.434T>C ; NM_001040716.1(PC):c.1748G>T ; NM_000920.3(PC):c.434T>C
PCCA	Propionic acidemia	Severe neonatal pyruvate carboxylase (PC) deficiency (Type B) is a rare, extremely severe form of PC deficiency characterized by severe, early-onset metabolic acidosis, and a generally fatal outcome in early infancy.	Patients develop clinical manifestations during the first 72 hours of life with severe truncal hypotonia and tachypnea. Subsequent clinical signs include anorexia, failure to thrive, hepatomegaly, myoclonic or generalized tonic-clonic seizures, stupor, pyramidal dysfunction, abnormal movements (high-amplitude tremor and dyskinesia), abnormal limb and ocular movements and severe impairment of mental and motor development. Renal tubular acidosis has been reported.	NM_000282.3(PCCA):c.1891G>C ; NM_000282.3(PCCA):c.1118T>A ; NM_000282.3(PCCA):c.1023dupT ; c.261dup ; NM_000282.3(PCCA):c.862A>T ; c.1226_1227del ; NM_000282.3(PCCA):c.412G>A ; c.600+1G>A ; c.1598_1601del ; NM_000282.3(PCCA):c.229C>T ; NM_000282.3(PCCA):c.1284+1G>A ; NM_000282.3(PCCA):c.1899+4_1899+7delAGTA ; NM_000282.3(PCCA):c.1891G>C ; NM_000282.3(PCCA):c.1118T>A ; NM_000282.3(PCCA):c.1023dupT ; c.261dup ; NM_000282.3(PCCA):c.862A>T ; c.1226_1227del ; NM_000282.3(PCCA):c.412G>A ; c.600+1G>A ; c.1598_1601del ; NM_000282.3(PCCA):c.229C>T ; NM_000282.3(PCCA):c.1284+1G>A ; NM_000282.3(PCCA):c.1899+4_1899+7delAGTA

PCCB	Propionic acidemia	Propionic acidemia (PA) is an organic aciduria caused by the deficient activity of the propionyl Coenzyme A carboxylase and is characterized by life threatening episodes of metabolic decompensation, neurological dysfunction and that may be complicated by cardiomyopathy.	Propionic acidemia can present in one of the following forms: severe neonatal onset, intermittent late onset or a chronic progressive form. In the severe neonatal onset form, the affected infants present with symptoms of metabolic intoxication (poor feeding, vomiting, altered sensorium) and pancytopenia within several hours to weeks after birth. In the intermittent late onset form, the disease presents after a year or even later in life with episodes of metabolic decompensation provoked by periods of catabolic stress like fever, vomiting and trauma. Patients may also present with acute neurological crisis characterized by dystonia, rigidity, choreoathetosis and dementia (due to infarction of basal ganglia). In the chronic progressive form, the disease presents as failure to thrive, chronic vomiting, psychomotor delay, hypotonia, seizures and movement disorders. Intellectual disability, optic neuropathy, cardiomyopathy, long QT syndrome, pancreatitis, dermatitis, and immune dysfunction are known complications.	NM_000532.4(PCCB):c.562G>A ; c.1219_1224delinsAA ; NM_000532.4(PCCB):c.337C>T ; NM_000532.4(PCCB):c.502G>A ; NM_000532.4(PCCB):c.990dupT ; NM_000532.4:c.1229_1230insT ; NM_000532.4(PCCB):c.1534C>T ; NM_000532.4(PCCB):c.1606A>G ; c.1223_1226del ; NM_000532.4(PCCB):c.1228C>T ; NM_000532.4(PCCB):c.1283C>T ; NM_000532.4(PCCB):c.1218_1231delGGGCATCATCCGGCinsTAGAGCACAGGA ; NM_000532.4(PCCB):c.1304A>G ; NM_000532.4(PCCB):c.683C>T ; NM_000532.4(PCCB):c.331C>T ; NM_000532.4(PCCB):c.1539_1540insCCC ; NM_000532.4(PCCB):c.1173dupT ; NM_000532.4(PCCB):c.562G>A ; c.1219_1224delinsAA ; NM_000532.4(PCCB):c.337C>T ; NM_000532.4(PCCB):c.502G>A ; NM_000532.4(PCCB):c.990dupT ; NM_000532.4:c.1229_1230insT ; NM_000532.4(PCCB):c.1534C>T ; NM_000532.4(PCCB):c.1606A>G ; c.1223_1226del ; NM_000532.4(PCCB):c.1228C>T ; NM_000532.4(PCCB):c.1283C>T ; NM_000532.4(PCCB):c.1218_1231delGGGCATCATCCGGCinsTAGAGCACAGGA ; NM_000532.4(PCCB):c.1304A>G ; NM_000532.4(PCCB):c.683C>T ; NM_000532.4(PCCB):c.331C>T ; NM_000532.4(PCCB):c.1539_1540insCCC ; NM_000532.4(PCCB):c.1173dupT

PCDH15	Autosomal recessive non-syndromic sensorineural deafness type DFNB	Propionic acidemia (PA) is an organic aciduria caused by the deficient activity of the propionyl Coenzyme A carboxylase and is characterized by life threatening episodes of metabolic decompensation, neurological dysfunction and that may be complicated by cardiomyopathy.	Propionic acidemia can present in one of the following forms: severe neonatal onset, intermittent late onset or a chronic progressive form. In the severe neonatal onset form, the affected infants present with symptoms of metabolic intoxication (poor feeding, vomiting, altered sensorium) and pancytopenia within several hours to weeks after birth. In the intermittent late onset form, the disease presents after a year or even later in life with episodes of metabolic decompensation provoked by periods of catabolic stress like fever, vomiting and trauma. Patients may also present with acute neurological crisis characterized by dystonia, rigidity, choreoathetosis and dementia (due to infarction of basal ganglia). In the chronic progressive form, the disease presents as failure to thrive, chronic vomiting, psychomotor delay, hypotonia, seizures and movement disorders. Intellectual disability, optic neuropathy, cardiomyopathy, long QT syndrome, pancreatitis, dermatitis, and immune dysfunction are known complications.	NM_033056.3(PCDH15):c.1086delT ; NM_001142772.1(PCDH15):c.400C>T ; c.4548_4551dup ; NM_033056.3:c.4961_4962insTGAT ; NM_033056.3(PCDH15):c.1737C>G ; c.4864del ; NM_033056.3(PCDH15):c.7C>T ; c.5659A>T ; c.2645_2646del ; NM_033056.3(PCDH15):c.785G>A ; c.5724_5755del ; NM_033056.3(PCDH15):c.400C>G ; c.4937_4940dup ; NM_033056.3(PCDH15):c.1006C>T ; c.3718-2A>G ; NM_033056.3(PCDH15):c.1583T>A ; NM_033056.3(PCDH15):c.1940C>G ; NM_033056.3(PCDH15):c.1086delT ; NM_001142772.1(PCDH15):c.400C>T ; c.4548_4551dup ; NM_033056.3:c.4961_4962insTGAT ; NM_033056.3(PCDH15):c.1737C>G ; c.4864del ; NM_033056.3(PCDH15):c.7C>T ; c.5659A>T ; c.2645_2646del ; NM_033056.3(PCDH15):c.785G>A ; c.5724_5755del ; NM_033056.3(PCDH15):c.400C>G ; c.4937_4940dup ; NM_033056.3(PCDH15):c.1006C>T ; c.3718-2A>G ; NM_033056.3(PCDH15):c.1583T>A ; NM_033056.3(PCDH15):c.1940C>G

PCDH15	Usher syndrome type 1	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	NM_033056.3(PCDH15):c.1086delT ; NM_001142772.1(PCDH15):c.400C>T ; c.4548_4551dup ; NM_033056.3:c.4961_4962insTGAT ; NM_033056.3(PCDH15):c.1737C>G ; c.4864del ; NM_033056.3(PCDH15):c.7C>T ; c.5659A>T ; c.2645_2646del ; NM_033056.3(PCDH15):c.785G>A ; c.5724_5755del ; NM_033056.3(PCDH15):c.400C>G ; c.4937_4940dup ; NM_033056.3(PCDH15):c.1006C>T ; c.3718-2A>G ; NM_033056.3(PCDH15):c.1583T>A ; NM_033056.3(PCDH15):c.1940C>G ; NM_033056.3(PCDH15):c.1086delT ; NM_001142772.1(PCDH15):c.400C>T ; c.4548_4551dup ; NM_033056.3:c.4961_4962insTGAT ; NM_033056.3(PCDH15):c.1737C>G ; c.4864del ; NM_033056.3(PCDH15):c.7C>T ; c.5659A>T ; c.2645_2646del ; NM_033056.3(PCDH15):c.785G>A ; c.5724_5755del ; NM_033056.3(PCDH15):c.400C>G ; c.4937_4940dup ; NM_033056.3(PCDH15):c.1006C>T ; c.3718-2A>G ; NM_033056.3(PCDH15):c.1583T>A ; NM_033056.3(PCDH15):c.1940C>G

PDHA1	Leigh syndrome with leukodystrophy	Usher syndrome type I is an autosomal recessive condition characterized by profound congenital hearing impairment with unintelligible speech, early retinitis pigmentosa (usually evident within the first decade), and constant vestibular dysfunction. Type I is distinguished from type II on the basis of severity of hearing loss and the extent of vestibular involvement. Type I patients are profoundly deaf, whereas type II patients are 'hard of hearing.' Vestibular function is defective in type I patients, whereas type II patients have normal vestibular function. Patients with type III (USH3) have progressive hearing loss.	A rare ciliopathy characterized by profound congenital deafness, retinitis pigmentosa and vestibular dysfunction. Retinitis pigmentosa results in visual loss and generally manifests as night blindness, progressively constricted visual fields, and impaired visual acuity. Vestibular dysfunction a defining feature of this form, manifests as delayed motor development with affected infants taking longer to sit independently and to walk. Later on, vestibular dysfunction results in difficulty with activities requiring balance.	NM_000284.3(PDHA1):c.773A>C ; NM_000284.3(PDHA1):c.787C>G ; NM_000284.3(PDHA1):c.773A>C ; NM_000284.3(PDHA1):c.787C>G

PDHA1	Pyruvate dehydrogenase E1-alpha deficiency	LeighÂ syndromeÂ is a clinically and genetically heterogeneous disorder resulting from defective mitochondrial energy generation. It most commonly presents as a progressive and severe neurodegenerative disorderÂ withÂ onset within the first months or years of life, and may result in early death. Affected individuals usually show global developmental delay or developmental regression, hypotonia, ataxia, dystonia, and ophthalmologic abnormalities, such as nystagmus or optic atrophy. The neurologic features are associatedÂ withÂ the classic findings of T2-weighted hyperintensities in the basal ganglia and/or brainstem on brain imaging.Â LeighÂ syndromeÂ can also have detrimental multisystemic affects on the cardiac, hepatic, gastrointestinal, and renal organs. Biochemical studies in patientsÂ withÂ LeighÂ syndromeÂ tend to show increased lactate and abnormalities of mitochondrial oxidative phosphorylation.		NM_000284.3(PDHA1):c.773A>C ; NM_000284.3(PDHA1):c.787C>G ; NM_000284.3(PDHA1):c.773A>C ; NM_000284.3(PDHA1):c.787C>G

PEX1	Deafness-enamel hypoplasia-nail defects syndrome	A disorder that is the most frequent form of pyruvate dehydrogenase deficiency (PDHD) characterized by variable lactic acidosis, impaired psychomotor development, hypotonia and neurological dysfunction.	Patients present with a range of classic signs and symptoms of PDHD, including lactic acidosis, poor feeding, lethargy, tachypnea, developmental delay, growth retardation, poor acquisition or loss of motor milestones, hypotonia, seizures, ataxia and dystonia. Structural brain lesions including cortical atrophy, dilated ventricles, and incomplete corpus callosum, absence of the medullary pyramids and ectopia of the olivary nuclei are commonly observed, especially in female patients heterozygous for the disease-causing mutations that result in complete deficiency of E1-alpha subunit protein in cells expressing the gene mutation.	NM_000466.2(PEX1):c.2916delA ; NM_000466.2(PEX1):c.1842delA ; NM_000466.2(PEX1):c.2528G>A ; NM_000466.2(PEX1):c.2097dupT ; NM_000466.2(PEX1):c.1952_1960dupCAGTGTGGA ; NM_000466.2(PEX1):c.3505_3517delCAGTTGTTTTCAC ; NM_000466.2(PEX1):c.1991T>C ; c.877C>T ; NM_000466.2(PEX1):c.1239+1G>T ; NM_000466.2(PEX1):c.2916delA ; NM_000466.2(PEX1):c.1842delA ; NM_000466.2(PEX1):c.2528G>A ; NM_000466.2(PEX1):c.2097dupT ; NM_000466.2(PEX1):c.1952_1960dupCAGTGTGGA ; NM_000466.2(PEX1):c.3505_3517delCAGTTGTTTTCAC ; NM_000466.2(PEX1):c.1991T>C ; c.877C>T ; NM_000466.2(PEX1):c.1239+1G>T
PEX1	Infantile Refsum disease	Heimler syndrome-1 (HMLR1), which represents the mildest end of the peroxisomal biogenesis disorder spectrum (PBD1A), is a rare autosomal recessive disorder characterized by sensorineural hearing loss, enamel hyoplasia of the secondary dentition, and nail abnormalities.	A rare genetic disease characterized by sensorineural hearing loss, abnormalities in the secondary dentition (such as enamel hypoplasia, taurodontism, or dental overcrowding), and nail abnormalities (including leukonychia and presence of transverse ridges). Association with macular dystrophy has also been reported.	NM_000466.2(PEX1):c.2916delA ; NM_000466.2(PEX1):c.1842delA ; NM_000466.2(PEX1):c.2528G>A ; NM_000466.2(PEX1):c.2097dupT ; NM_000466.2(PEX1):c.1952_1960dupCAGTGTGGA ; NM_000466.2(PEX1):c.3505_3517delCAGTTGTTTTCAC ; NM_000466.2(PEX1):c.1991T>C ; c.877C>T ; NM_000466.2(PEX1):c.1239+1G>T ; NM_000466.2(PEX1):c.2916delA ; NM_000466.2(PEX1):c.1842delA ; NM_000466.2(PEX1):c.2528G>A ; NM_000466.2(PEX1):c.2097dupT ; NM_000466.2(PEX1):c.1952_1960dupCAGTGTGGA ; NM_000466.2(PEX1):c.3505_3517delCAGTTGTTTTCAC ; NM_000466.2(PEX1):c.1991T>C ; c.877C>T ; NM_000466.2(PEX1):c.1239+1G>T

PEX1	Neonatal adrenoleukodystrophy	Infantile Refsum disease (IRD) is the mildest variant of the peroxisome biogenesis disorders, Zellweger syndrome spectrum (PBD- ZSS; see this term), characterized by hypotonia, retinitis pigmentosa, developmental delay, sensorineural hearing loss and liver dysfunction. Phenotypic overlap is seen between IRD and neonatal adrenoleukodystrophy (NALD) (see this term).	IRD has an onset at birth or early infancy but manifestations may be subtle enough that diagnosis is not until adulthood. In infancy, symptoms may include nystagmus, hypotonia, sensorineural hearing loss, growth retardation, mild facial dysmorphism, and hepatomegaly. Hepatic dysfunction is first displayed in infants with jaundice and later in some with episodes of intracranial bleeding due to coagulopathy. In childhood, progressive retinitis pigmentosa, developmental deficits and hypotonia are seen. Most achieve motor milestones, though delayed, and communicate in a few words or signs. Osteoporosis and fractures can occur in the less mobile. Adrenal insufficiency and renal calcium oxalate stones can present in older children. Leukodystrophy with loss of previously acquired skills can occur at any age and may stabilize, or progress and be fatal. Atypical presentations (visual and hearing loss with preservation of intellect and cerebellar ataxia with/without peripheral neuropathy) have been described.	NM_000466.2(PEX1):c.2916delA ; NM_000466.2(PEX1):c.1842delA ; NM_000466.2(PEX1):c.2528G>A ; NM_000466.2(PEX1):c.2097dupT ; NM_000466.2(PEX1):c.1952_1960dupCAGTGTGGA ; NM_000466.2(PEX1):c.3505_3517delCAGTTGTTTTCAC ; NM_000466.2(PEX1):c.1991T>C ; c.877C>T ; NM_000466.2(PEX1):c.1239+1G>T ; NM_000466.2(PEX1):c.2916delA ; NM_000466.2(PEX1):c.1842delA ; NM_000466.2(PEX1):c.2528G>A ; NM_000466.2(PEX1):c.2097dupT ; NM_000466.2(PEX1):c.1952_1960dupCAGTGTGGA ; NM_000466.2(PEX1):c.3505_3517delCAGTTGTTTTCAC ; NM_000466.2(PEX1):c.1991T>C ; c.877C>T ; NM_000466.2(PEX1):c.1239+1G>T

PEX1	Zellweger syndrome	A variant of intermediate severity of the PBD-Zellweger syndrome spectrum (PBD-ZSS) charcterized by hypotonia, leukodystrophy, and vision and sensorineural hearing deficiencies. Phenotypic overlap is seen between NALD and infantile Refsum disease (IRD).	NALD has an onset at birth or early infancy, but manifestations may be subtle enough that it is not diagnosed until late infancy or early childhood (or when a leukodystrophy develops). It is characterized by hypotonia, seizures, diffuse encephalopathy, sensorineural hearing loss, peripheral neuropathy, mild facial dysmorphism (hypertelorism and a flat midface), failure to thrive and severely delayed psychomotor development. Eye findings include chorioretinopathy, optic nerve dysplasia and cataracts. Hepatic dysfunction is first displayed in infants with jaundice and later in some with episodes of intracranial bleeding due to vitamin K-responsive coagulopathy. Adrenal insufficiency and renal calcium oxalate stones can present in older children. Vision and hearing dysfunction are progressive and result in blindness and deafness. Osteoporosis and fractures can occur in patients who are less mobile. Neurological regression reflects a leukodystrophy, leading to the loss of previously acquired skills, dementia and ultimately death.	NM_000466.2(PEX1):c.2916delA ; NM_000466.2(PEX1):c.1842delA ; NM_000466.2(PEX1):c.2528G>A ; NM_000466.2(PEX1):c.2097dupT ; NM_000466.2(PEX1):c.1952_1960dupCAGTGTGGA ; NM_000466.2(PEX1):c.3505_3517delCAGTTGTTTTCAC ; NM_000466.2(PEX1):c.1991T>C ; c.877C>T ; NM_000466.2(PEX1):c.1239+1G>T ; NM_000466.2(PEX1):c.2916delA ; NM_000466.2(PEX1):c.1842delA ; NM_000466.2(PEX1):c.2528G>A ; NM_000466.2(PEX1):c.2097dupT ; NM_000466.2(PEX1):c.1952_1960dupCAGTGTGGA ; NM_000466.2(PEX1):c.3505_3517delCAGTTGTTTTCAC ; NM_000466.2(PEX1):c.1991T>C ; c.877C>T ; NM_000466.2(PEX1):c.1239+1G>T

PEX12	Infantile Refsum disease	A rare peroxisome biogenesis disorder (the most severe variant of Peroxisome biogenesis disorder spectrum) characterized by neuronal migration defects in the brain, dysmorphic craniofacial features, profound hypotonia, neonatal seizures, and liver dysfunction.	Onset is in the neonatal period, reflecting both organ malformations that occurred in utero and progressive disease due to ongoing peroxisome dysfunction. Infants present with characteristic dysmorphic craniofacial features (flattened facies, large anterior fontanel, split sutures, prominent high forehead, flattened occiput, upslanting palpebral fissures, epicanthal folds, and broad nasal bridge), profound hypotonia and seizures. Macrocephaly or microcephaly, high arched palate, micrognathia and redundant neck skin folds may be present. Skeletal abnormalities (chondrodysplasia punctata, most often in the patella and hips) and subcortical renal cysts are frequent. There is often failure to thrive, hepatomegaly, jaundice, and coagulopathy. Eye findings include cataracts, glaucoma, pigmentary retinopathy, nystagmus, corneal clouding and optic nerve atrophy. Visual changes and loss are progressive. Sensorineural hearing loss may be present. Cryptorchidism and hypospadias (male) and clitoromegaly (female) may occur. CNS function is severely affected and infants have profound psychomotor delay.	NM_000286.2(PEX12):c.771delC ; NM_000286.2(PEX12):c.894delC ; c.455_459dup ; NM_000286.2(PEX12):c.538C>T ; NM_000286.2(PEX12):c.888_889delCT ; NM_000286.2(PEX12):c.771delC ; NM_000286.2(PEX12):c.894delC ; c.455_459dup ; NM_000286.2(PEX12):c.538C>T ; NM_000286.2(PEX12):c.888_889delCT

PEX12	Neonatal adrenoleukodystrophy	Infantile Refsum disease (IRD) is the mildest variant of the peroxisome biogenesis disorders, Zellweger syndrome spectrum (PBD- ZSS; see this term), characterized by hypotonia, retinitis pigmentosa, developmental delay, sensorineural hearing loss and liver dysfunction. Phenotypic overlap is seen between IRD and neonatal adrenoleukodystrophy (NALD) (see this term).	IRD has an onset at birth or early infancy but manifestations may be subtle enough that diagnosis is not until adulthood. In infancy, symptoms may include nystagmus, hypotonia, sensorineural hearing loss, growth retardation, mild facial dysmorphism, and hepatomegaly. Hepatic dysfunction is first displayed in infants with jaundice and later in some with episodes of intracranial bleeding due to coagulopathy. In childhood, progressive retinitis pigmentosa, developmental deficits and hypotonia are seen. Most achieve motor milestones, though delayed, and communicate in a few words or signs. Osteoporosis and fractures can occur in the less mobile. Adrenal insufficiency and renal calcium oxalate stones can present in older children. Leukodystrophy with loss of previously acquired skills can occur at any age and may stabilize, or progress and be fatal. Atypical presentations (visual and hearing loss with preservation of intellect and cerebellar ataxia with/without peripheral neuropathy) have been described.	NM_000286.2(PEX12):c.771delC ; NM_000286.2(PEX12):c.894delC ; c.455_459dup ; NM_000286.2(PEX12):c.538C>T ; NM_000286.2(PEX12):c.888_889delCT ; NM_000286.2(PEX12):c.771delC ; NM_000286.2(PEX12):c.894delC ; c.455_459dup ; NM_000286.2(PEX12):c.538C>T ; NM_000286.2(PEX12):c.888_889delCT

PEX12	Zellweger syndrome	A variant of intermediate severity of the PBD-Zellweger syndrome spectrum (PBD-ZSS) charcterized by hypotonia, leukodystrophy, and vision and sensorineural hearing deficiencies. Phenotypic overlap is seen between NALD and infantile Refsum disease (IRD).	NALD has an onset at birth or early infancy, but manifestations may be subtle enough that it is not diagnosed until late infancy or early childhood (or when a leukodystrophy develops). It is characterized by hypotonia, seizures, diffuse encephalopathy, sensorineural hearing loss, peripheral neuropathy, mild facial dysmorphism (hypertelorism and a flat midface), failure to thrive and severely delayed psychomotor development. Eye findings include chorioretinopathy, optic nerve dysplasia and cataracts. Hepatic dysfunction is first displayed in infants with jaundice and later in some with episodes of intracranial bleeding due to vitamin K-responsive coagulopathy. Adrenal insufficiency and renal calcium oxalate stones can present in older children. Vision and hearing dysfunction are progressive and result in blindness and deafness. Osteoporosis and fractures can occur in patients who are less mobile. Neurological regression reflects a leukodystrophy, leading to the loss of previously acquired skills, dementia and ultimately death.	NM_000286.2(PEX12):c.771delC ; NM_000286.2(PEX12):c.894delC ; c.455_459dup ; NM_000286.2(PEX12):c.538C>T ; NM_000286.2(PEX12):c.888_889delCT ; NM_000286.2(PEX12):c.771delC ; NM_000286.2(PEX12):c.894delC ; c.455_459dup ; NM_000286.2(PEX12):c.538C>T ; NM_000286.2(PEX12):c.888_889delCT

PEX2	Infantile Refsum disease	A rare peroxisome biogenesis disorder (the most severe variant of Peroxisome biogenesis disorder spectrum) characterized by neuronal migration defects in the brain, dysmorphic craniofacial features, profound hypotonia, neonatal seizures, and liver dysfunction.	Onset is in the neonatal period, reflecting both organ malformations that occurred in utero and progressive disease due to ongoing peroxisome dysfunction. Infants present with characteristic dysmorphic craniofacial features (flattened facies, large anterior fontanel, split sutures, prominent high forehead, flattened occiput, upslanting palpebral fissures, epicanthal folds, and broad nasal bridge), profound hypotonia and seizures. Macrocephaly or microcephaly, high arched palate, micrognathia and redundant neck skin folds may be present. Skeletal abnormalities (chondrodysplasia punctata, most often in the patella and hips) and subcortical renal cysts are frequent. There is often failure to thrive, hepatomegaly, jaundice, and coagulopathy. Eye findings include cataracts, glaucoma, pigmentary retinopathy, nystagmus, corneal clouding and optic nerve atrophy. Visual changes and loss are progressive. Sensorineural hearing loss may be present. Cryptorchidism and hypospadias (male) and clitoromegaly (female) may occur. CNS function is severely affected and infants have profound psychomotor delay.	c.789_790del ; NM_001079867.1(PEX2):c.163G>A ; c.789_790del ; NM_001079867.1(PEX2):c.163G>A

PEX2	Neonatal adrenoleukodystrophy	Infantile Refsum disease (IRD) is the mildest variant of the peroxisome biogenesis disorders, Zellweger syndrome spectrum (PBD- ZSS; see this term), characterized by hypotonia, retinitis pigmentosa, developmental delay, sensorineural hearing loss and liver dysfunction. Phenotypic overlap is seen between IRD and neonatal adrenoleukodystrophy (NALD) (see this term).	IRD has an onset at birth or early infancy but manifestations may be subtle enough that diagnosis is not until adulthood. In infancy, symptoms may include nystagmus, hypotonia, sensorineural hearing loss, growth retardation, mild facial dysmorphism, and hepatomegaly. Hepatic dysfunction is first displayed in infants with jaundice and later in some with episodes of intracranial bleeding due to coagulopathy. In childhood, progressive retinitis pigmentosa, developmental deficits and hypotonia are seen. Most achieve motor milestones, though delayed, and communicate in a few words or signs. Osteoporosis and fractures can occur in the less mobile. Adrenal insufficiency and renal calcium oxalate stones can present in older children. Leukodystrophy with loss of previously acquired skills can occur at any age and may stabilize, or progress and be fatal. Atypical presentations (visual and hearing loss with preservation of intellect and cerebellar ataxia with/without peripheral neuropathy) have been described.	c.789_790del ; NM_001079867.1(PEX2):c.163G>A ; c.789_790del ; NM_001079867.1(PEX2):c.163G>A

PEX2	Zellweger syndrome	A variant of intermediate severity of the PBD-Zellweger syndrome spectrum (PBD-ZSS) charcterized by hypotonia, leukodystrophy, and vision and sensorineural hearing deficiencies. Phenotypic overlap is seen between NALD and infantile Refsum disease (IRD).	NALD has an onset at birth or early infancy, but manifestations may be subtle enough that it is not diagnosed until late infancy or early childhood (or when a leukodystrophy develops). It is characterized by hypotonia, seizures, diffuse encephalopathy, sensorineural hearing loss, peripheral neuropathy, mild facial dysmorphism (hypertelorism and a flat midface), failure to thrive and severely delayed psychomotor development. Eye findings include chorioretinopathy, optic nerve dysplasia and cataracts. Hepatic dysfunction is first displayed in infants with jaundice and later in some with episodes of intracranial bleeding due to vitamin K-responsive coagulopathy. Adrenal insufficiency and renal calcium oxalate stones can present in older children. Vision and hearing dysfunction are progressive and result in blindness and deafness. Osteoporosis and fractures can occur in patients who are less mobile. Neurological regression reflects a leukodystrophy, leading to the loss of previously acquired skills, dementia and ultimately death.	c.789_790del ; NM_001079867.1(PEX2):c.163G>A ; c.789_790del ; NM_001079867.1(PEX2):c.163G>A

PEX7	Refsum disease	A rare peroxisome biogenesis disorder (the most severe variant of Peroxisome biogenesis disorder spectrum) characterized by neuronal migration defects in the brain, dysmorphic craniofacial features, profound hypotonia, neonatal seizures, and liver dysfunction.	Onset is in the neonatal period, reflecting both organ malformations that occurred in utero and progressive disease due to ongoing peroxisome dysfunction. Infants present with characteristic dysmorphic craniofacial features (flattened facies, large anterior fontanel, split sutures, prominent high forehead, flattened occiput, upslanting palpebral fissures, epicanthal folds, and broad nasal bridge), profound hypotonia and seizures. Macrocephaly or microcephaly, high arched palate, micrognathia and redundant neck skin folds may be present. Skeletal abnormalities (chondrodysplasia punctata, most often in the patella and hips) and subcortical renal cysts are frequent. There is often failure to thrive, hepatomegaly, jaundice, and coagulopathy. Eye findings include cataracts, glaucoma, pigmentary retinopathy, nystagmus, corneal clouding and optic nerve atrophy. Visual changes and loss are progressive. Sensorineural hearing loss may be present. Cryptorchidism and hypospadias (male) and clitoromegaly (female) may occur. CNS function is severely affected and infants have profound psychomotor delay.	NM_000288.3(PEX7):c.618G>A ; NM_000288.3(PEX7):c.854A>G ; NM_000288.3(PEX7):c.694C>T ; c.532C>T ; NM_000288.3(PEX7):c.903+1G>C ; NM_000288.3(PEX7):c.653C>T ; NM_000288.3(PEX7):c.875T>A ; NM_000288.3(PEX7):c.649G>A ; NM_000288.3(PEX7):c.618G>A ; NM_000288.3(PEX7):c.854A>G ; NM_000288.3(PEX7):c.694C>T ; c.532C>T ; NM_000288.3(PEX7):c.903+1G>C ; NM_000288.3(PEX7):c.653C>T ; NM_000288.3(PEX7):c.875T>A ; NM_000288.3(PEX7):c.649G>A

PEX7	Rhizomelic chondrodysplasia punctata type 1	A metabolic disease characterized by anosmia, cataract, early-onset retinitis pigmentosa and possible neurological manifestations, including peripheral neuropathy and cerebellar ataxia. Other features can be deafness, ichthyosis, skeletal abnormalities, and cardiac arrhythmia. It is characterized biochemically by accumulation of phytanic acid in plasma and tissues.	Age of onset ranges is childhood to over 50 years of age but may be difficult to determine. Retinitis pigmentosa is often the first sign and is found in almost all patients. Onset of night blindness in childhood is common. Cataract and nystagmus may be found later on. Anosmia is a universal clinical manifestation. Symmetric mild-to-profound sensorineural hearing loss, ataxia of late onset causing an unsteady gait, and more rarely mild generalized ichthyosis may develop subsequently. Mixed motor and sensory neuropathy may also be found, causing muscular atrophy, weakness, and peripheral sensory disturbances. Autism spectrum disorder and attention deficit-hyperactivity disorder (AD-HD) are also reported. Short metacarpals and metatarsals at birth are found in about 1/3 of cases. Cardiac arrhythmia and cardiomyopathy causing heart failure are also reported.	NM_000288.3(PEX7):c.618G>A ; NM_000288.3(PEX7):c.854A>G ; NM_000288.3(PEX7):c.694C>T ; c.532C>T ; NM_000288.3(PEX7):c.903+1G>C ; NM_000288.3(PEX7):c.653C>T ; NM_000288.3(PEX7):c.875T>A ; NM_000288.3(PEX7):c.649G>A ; NM_000288.3(PEX7):c.618G>A ; NM_000288.3(PEX7):c.854A>G ; NM_000288.3(PEX7):c.694C>T ; c.532C>T ; NM_000288.3(PEX7):c.903+1G>C ; NM_000288.3(PEX7):c.653C>T ; NM_000288.3(PEX7):c.875T>A ; NM_000288.3(PEX7):c.649G>A
PKHD1	Autosomal recessive polycystic kidney disease	A rare, primary bone dysplasia characterized by rhizomelic limb shortening, punctate calcifications in cartilage with epiphyseal and metaphyseal abnormalities (chondrodysplasia punctata) and coronal cleft vertebrae associated with profound postnatal growth deficiency, early-onset cataracts, severe intellectual disability and seizures.	Presentation is at birth with severe joint contractures; cataracts may be present or appear in the first few months of life. Respiratory distress nd feeding difficulties are commonly observed after birth. Whilst birth parameters (weight, length, and head circumference) are in the lower range from normal, profound postnatal growth retardation ensues. Rhizomelic limb shortening is typically greater in the humerus than the femur. Other skeletal abnormalities include punctate calcifications in cartilage with epiphyseal and metaphyseal abnormalities (chondrodysplasia punctata) and coronal cleft vertebrae. Intellectual disability is severe, and the majority of children develop seizures.	NM_138694.3(PKHD1):c.9689delA ; NM_138694.3(PKHD1):c.982C>T ; NM_138694.4:c.3761_3762delCCinsG ; NM_138694.3(PKHD1):c.682A>G ; c.11363_11372del ; NM_138694.3(PKHD1):c.353delG ; NM_138694.3(PKHD1):c.10452dupT ; NM_138694.3(PKHD1):c.8824C>T ; NM_138694.3(PKHD1):c.8870T>C ; NM_138694.3(PKHD1):c.2827_2828delGA ; NM_138694.3(PKHD1):c.3229-2A>C ; NM_138694.3(PKHD1):c.85G>T ; NM_138694.3(PKHD1):c.10219C>T ; NM_138694.3(PKHD1):c.3367G>A ; NM_138694.3(PKHD1):c.370C>T ; NM_138694.3(PKHD1):c.2854G>A ; NM_138694.3(PKHD1):c.664A>G ; NM_138694.3(PKHD1):c.6499C>T ; NM_138694.3(PKHD1):c.5325_5326delAG ; NM_138694.3(PKHD1):c.2452C>T ; NM_138694.3(PKHD1):c.1486C>T ; NM_138694.3(PKHD1):c.8407T>C ; NM_138694.3(PKHD1):c.3940delA ; NM_138694.3(PKHD1):c.5895dupA ; NM_138694.3(PKHD1):c.9719G>A ; NC_000006.12:g.51775844G>A ; NM_138694.3(PKHD1):c.10412T>G ; NM_138694.3(PKHD1):c.930delC ; NM_138694.3(PKHD1):c.8408G>A ; NM_138694.3(PKHD1):c.107C>T ; NM_138694.3(PKHD1):c.2341C>T ; NM_138694.3(PKHD1):c.9370C>T ; NM_138694.3(PKHD1):c.9689delA ; NM_138694.3(PKHD1):c.982C>T ; NM_138694.4:c.3761_3762delCCinsG ; NM_138694.3(PKHD1):c.682A>G ; c.11363_11372del ; NM_138694.3(PKHD1):c.353delG ; NM_138694.3(PKHD1):c.10452dupT ; NM_138694.3(PKHD1):c.8824C>T ; NM_138694.3(PKHD1):c.8870T>C ; NM_138694.3(PKHD1):c.2827_2828delGA ; NM_138694.3(PKHD1):c.3229-2A>C ; NM_138694.3(PKHD1):c.85G>T ; NM_138694.3(PKHD1):c.10219C>T ; NM_138694.3(PKHD1):c.3367G>A ; NM_138694.3(PKHD1):c.370C>T ; NM_138694.3(PKHD1):c.2854G>A ; NM_138694.3(PKHD1):c.664A>G ; NM_138694.3(PKHD1):c.6499C>T ; NM_138694.3(PKHD1):c.5325_5326delAG ; NM_138694.3(PKHD1):c.2452C>T ; NM_138694.3(PKHD1):c.1486C>T ; NM_138694.3(PKHD1):c.8407T>C ; NM_138694.3(PKHD1):c.3940delA ; NM_138694.3(PKHD1):c.5895dupA ; NM_138694.3(PKHD1):c.9719G>A ; NC_000006.12:g.51775844G>A ; NM_138694.3(PKHD1):c.10412T>G ; NM_138694.3(PKHD1):c.930delC ; NM_138694.3(PKHD1):c.8408G>A ; NM_138694.3(PKHD1):c.107C>T ; NM_138694.3(PKHD1):c.2341C>T ; NM_138694.3(PKHD1):c.9370C>T

PKHD1	Caroli disease	A rare, genetic hepatorenal fibrocystic syndrome characterized by cystic dilatation and ectasia of renal collecting tubules, and a ductal plate malformation of the liver resulting in congenital hepatic fibrosis. Clinical presentation, whilst typically in utero or at birth, is variable and in the most severe cases includes Potter-sequence, oligohydramnios, pulmonary hypoplasia, and massively enlarged echogenic kidneys.	The clinical spectrum is broad and may include variable degrees of renal insufficiency, mild to severe life-threating neonatal respiratory distress/failure due to pulmonary hypoplasia, hyponatremia, hypertension and predisposition to urinary tract infections. Patients can progress to end-stage renal disease (ESRD) at varying ages. Congenital hepatic fibrosis (CHF) is invariably presents at birth, although may be clinically undetectable. The progressive manifestations of CHF typically include portal hypertension (pHTN), gastrointestinal varices and associated bleeding, bile duct disease (Caroli syndrome and cholangitis) and hepatosplenomegaly.	NM_138694.3(PKHD1):c.9689delA ; NM_138694.3(PKHD1):c.982C>T ; NM_138694.4:c.3761_3762delCCinsG ; NM_138694.3(PKHD1):c.682A>G ; c.11363_11372del ; NM_138694.3(PKHD1):c.353delG ; NM_138694.3(PKHD1):c.10452dupT ; NM_138694.3(PKHD1):c.8824C>T ; NM_138694.3(PKHD1):c.8870T>C ; NM_138694.3(PKHD1):c.2827_2828delGA ; NM_138694.3(PKHD1):c.3229-2A>C ; NM_138694.3(PKHD1):c.85G>T ; NM_138694.3(PKHD1):c.10219C>T ; NM_138694.3(PKHD1):c.3367G>A ; NM_138694.3(PKHD1):c.370C>T ; NM_138694.3(PKHD1):c.2854G>A ; NM_138694.3(PKHD1):c.664A>G ; NM_138694.3(PKHD1):c.6499C>T ; NM_138694.3(PKHD1):c.5325_5326delAG ; NM_138694.3(PKHD1):c.2452C>T ; NM_138694.3(PKHD1):c.1486C>T ; NM_138694.3(PKHD1):c.8407T>C ; NM_138694.3(PKHD1):c.3940delA ; NM_138694.3(PKHD1):c.5895dupA ; NM_138694.3(PKHD1):c.9719G>A ; NC_000006.12:g.51775844G>A ; NM_138694.3(PKHD1):c.10412T>G ; NM_138694.3(PKHD1):c.930delC ; NM_138694.3(PKHD1):c.8408G>A ; NM_138694.3(PKHD1):c.107C>T ; NM_138694.3(PKHD1):c.2341C>T ; NM_138694.3(PKHD1):c.9370C>T ; NM_138694.3(PKHD1):c.9689delA ; NM_138694.3(PKHD1):c.982C>T ; NM_138694.4:c.3761_3762delCCinsG ; NM_138694.3(PKHD1):c.682A>G ; c.11363_11372del ; NM_138694.3(PKHD1):c.353delG ; NM_138694.3(PKHD1):c.10452dupT ; NM_138694.3(PKHD1):c.8824C>T ; NM_138694.3(PKHD1):c.8870T>C ; NM_138694.3(PKHD1):c.2827_2828delGA ; NM_138694.3(PKHD1):c.3229-2A>C ; NM_138694.3(PKHD1):c.85G>T ; NM_138694.3(PKHD1):c.10219C>T ; NM_138694.3(PKHD1):c.3367G>A ; NM_138694.3(PKHD1):c.370C>T ; NM_138694.3(PKHD1):c.2854G>A ; NM_138694.3(PKHD1):c.664A>G ; NM_138694.3(PKHD1):c.6499C>T ; NM_138694.3(PKHD1):c.5325_5326delAG ; NM_138694.3(PKHD1):c.2452C>T ; NM_138694.3(PKHD1):c.1486C>T ; NM_138694.3(PKHD1):c.8407T>C ; NM_138694.3(PKHD1):c.3940delA ; NM_138694.3(PKHD1):c.5895dupA ; NM_138694.3(PKHD1):c.9719G>A ; NC_000006.12:g.51775844G>A ; NM_138694.3(PKHD1):c.10412T>G ; NM_138694.3(PKHD1):c.930delC ; NM_138694.3(PKHD1):c.8408G>A ; NM_138694.3(PKHD1):c.107C>T ; NM_138694.3(PKHD1):c.2341C>T ; NM_138694.3(PKHD1):c.9370C>T
PLA2G6	Adult-onset dystonia-parkinsonism	Caroli disease (CD) is a rare congenital liver disease characterized by non-obstructive cystic dilatations of the intra-hepatic and rarely extra-hepatic bile ducts.	Caroli disease can present at any age. CD ranges from simple ectasias of the larger intra-hepatic bile ducts (in this less common form the name Caroli disease is used) to a syndromic form (Caroli syndrome) that is more common and includes congenital hepatic fibrosis. Some patients remain asymptomatic throughout the disease course. Some develop intra- or extra-hepatic calculi, leading to recurrent cholangitis (with bacteremia and sepsis), and acute pancreatitis. Manifestations are those of complications, mostly bacterial cholangitis, and include abdominal pain and biliary colic, fever with chills, and jaundice. Hepatomegaly, cirrhosis and portal hypertension (with splenomegaly) are also frequently reported to develop. Besides bacterial cholangitis, complications include liver abscess, biliary infection, and in late stages, cholangiocarcinoma. CS is often associated with recessive polycystic kidney disease (see these terms). The course is largely dependent on the associated disorders.	NM_003560.3(PLA2G6):c.1894C>T ; NM_003560.3(PLA2G6):c.929T>A ; NM_003560.3(PLA2G6):c.1612C>T ; NM_003560.3(PLA2G6):c.2370T>G ; NM_003560.3(PLA2G6):c.2239C>T ; NM_003560.3(PLA2G6):c.1903C>T ; NM_003560.3(PLA2G6):c.109C>T ; NM_003560.3(PLA2G6):c.1634A>C ; NM_003560.3(PLA2G6):c.1894C>T ; NM_003560.3(PLA2G6):c.929T>A ; NM_003560.3(PLA2G6):c.1612C>T ; NM_003560.3(PLA2G6):c.2370T>G ; NM_003560.3(PLA2G6):c.2239C>T ; NM_003560.3(PLA2G6):c.1903C>T ; NM_003560.3(PLA2G6):c.109C>T ; NM_003560.3(PLA2G6):c.1634A>C

PLA2G6	Infantile neuroaxonal dystrophy	A rare neurodegenerative disease usually presenting before the age of 30 and which is characterized by dystonia, L-dopa-responsive parkinsonism, pyramidal signs and rapid cognitive decline.	Disease onset occurs in late adolescence or early adulthood (usually before the age of 30) and usually presents with parkinsonism (tremor, rigidity, bradykinesia), dystonia and rapid cognitive decline. Eye movement abnormalities (supranuclear vertical gaze palsy, eyelid opening apraxia), pyramidal tract signs, and psychiatric features such as depression and personality changes have also been reported in some patients. Dopaminergic treatment is initially successful with regard to parkinsonism, but the development of prominent dyskinesias often follows.	NM_003560.3(PLA2G6):c.1894C>T ; NM_003560.3(PLA2G6):c.929T>A ; NM_003560.3(PLA2G6):c.1612C>T ; NM_003560.3(PLA2G6):c.2370T>G ; NM_003560.3(PLA2G6):c.2239C>T ; NM_003560.3(PLA2G6):c.1903C>T ; NM_003560.3(PLA2G6):c.109C>T ; NM_003560.3(PLA2G6):c.1634A>C ; NM_003560.3(PLA2G6):c.1894C>T ; NM_003560.3(PLA2G6):c.929T>A ; NM_003560.3(PLA2G6):c.1612C>T ; NM_003560.3(PLA2G6):c.2370T>G ; NM_003560.3(PLA2G6):c.2239C>T ; NM_003560.3(PLA2G6):c.1903C>T ; NM_003560.3(PLA2G6):c.109C>T ; NM_003560.3(PLA2G6):c.1634A>C
PMM2	PMM2-CDG	Infantile neuroaxonal dystrophy/atypical neuroaxonal dystrophy (INAD/atypical NAD) is a type of neurodegeneration with brain iron accumulation (NBIA; see this term) characterized by psychomotor delay and regression, increasing neurological involvement with symmetrical pyramidal tract signs and spastic tetraplegia. INAD may be classic or atypical and patients present with symptoms anywhere along a continuum between the two.	Classic INAD usually presents between ages six months and three years with psychomotor delay and regression, delayed walking or gait disturbance. It is characterized by early truncal hypotonia progressing to tetraparesis (usually spastic but can be areflexic) and dementia. Visual signs, including strabismus, pendular nystagmus, uncoordinated eye movements, optic atrophy and failing vision are generally early and prominent. Seizures occur in a minority. Onset of atypical NAD is usually in early childhood but can be as late as the late teens and progression is slower. As a result of slower progression patients may present with speech delay and neurobehavioral disturbances including impulsivity, poor attention span and emotional lability. Tetraparesis occurs late in the disease and is not necessarily preceded by truncal hypotonia and patients are more likely to have progressive dystonia and dysarthria. Optic atrophy, nystagmus and seizures occur as in classic INAD.	NM_000303.2(PMM2):c.710C>G ; NM_000303.2(PMM2):c.647A>T ; NM_000303.2(PMM2):c.669C>G ; NM_000303.2(PMM2):c.256-1G>C ; NM_000303.2(PMM2):c.620T>C ; NM_000303.2(PMM2):c.691G>A ; NM_000303.2(PMM2):c.563A>G ; NM_000303.2(PMM2):c.349G>C ; NM_000303.2(PMM2):c.26G>A ; NM_000303.2(PMM2):c.190delT ; NM_000303.2(PMM2):c.53C>G ; NM_000303.2(PMM2):c.484C>T ; NM_000303.2(PMM2):c.415G>A ; NM_000303.2(PMM2):c.95T>G ; NM_000303.2(PMM2):c.323C>T ; c.97C>T ; NM_000303.2(PMM2):c.255+2T>C ; NM_000303.2(PMM2):c.395T>C ; NM_000303.2(PMM2):c.338C>T ; NM_000303.3(PMM2):c.109C>T ; NM_000303.2(PMM2):c.442G>A ; NM_000303.2(PMM2):c.710C>T ; NM_000303.2(PMM2):c.357C>A ; NM_000303.2(PMM2):c.131T>C ; NM_000303.2(PMM2):c.623G>C ; NM_000303.2(PMM2):c.193G>T ; NM_000303.2(PMM2):c.652C>G ; NM_000303.2(PMM2):c.95_96delTAinsGC ; NM_000303.2(PMM2):c.422G>A ; NM_000303.2(PMM2):c.385G>A ; NM_000303.2(PMM2):c.677C>G ; NM_000303.2(PMM2):c.470T>C ; NM_000303.2(PMM2):c.710C>G ; NM_000303.2(PMM2):c.647A>T ; NM_000303.2(PMM2):c.669C>G ; NM_000303.2(PMM2):c.256-1G>C ; NM_000303.2(PMM2):c.620T>C ; NM_000303.2(PMM2):c.691G>A ; NM_000303.2(PMM2):c.563A>G ; NM_000303.2(PMM2):c.349G>C ; NM_000303.2(PMM2):c.26G>A ; NM_000303.2(PMM2):c.190delT ; NM_000303.2(PMM2):c.53C>G ; NM_000303.2(PMM2):c.484C>T ; NM_000303.2(PMM2):c.415G>A ; NM_000303.2(PMM2):c.95T>G ; NM_000303.2(PMM2):c.323C>T ; c.97C>T ; NM_000303.2(PMM2):c.255+2T>C ; NM_000303.2(PMM2):c.395T>C ; NM_000303.2(PMM2):c.338C>T ; NM_000303.2(PMM2):c.623G>C ; NM_000303.2(PMM2):c.193G>T ; NM_000303.2(PMM2):c.652C>G ; NM_000303.2(PMM2):c.95_96delTAinsGC ; NM_000303.2(PMM2):c.422G>A ; NM_000303.2(PMM2):c.385G>A ; NM_000303.2(PMM2):c.677C>G ; NM_000303.2(PMM2):c.470T>C

PNPO	Pyridoxal phosphate-responsive seizures	PMM2-CDG is the most frequent form of congenital disorder of N-glycosylation and is characterized by cerebellar dysfunction, abnormal fat distribution, inverted nipples, strabismus and hypotonia. 3 forms of PMM2-CDG can be distinguished: the infantile multisystem type, late-infantile and childhood ataxia-intellectual disability type (3-10 yrs old), and the adult stable disability type. Infants usually develop ataxia, psychomotor delay and extraneurological manifestations including failure to thrive, enteropathy, hepatic dysfunction, coagulation abnormalities and cardiac and renal involvement. The phenotype is however highly variable and ranges from infants who die in the first year of life to mildly involved adults.	Congenital disorders of glycosylation (CDGs) are a genetically heterogeneous group of autosomal recessive disorders caused by enzymatic defects in the synthesis and processing of asparagine (N)-linked glycans or oligosaccharides on glycoproteins. These glycoconjugates play critical roles in metabolism, cell recognition and adhesion, cell migration, protease resistance, host defense, and antigenicity, among others. CDGs are divided into 2 main groups: type I CDGs comprise defects in the assembly of the dolichol lipid-linked oligosaccharide (LLO) chain and its transfer to the nascent protein, whereas type II CDGs (see, e.g., CDG2A,Â 212066) refer to defects in the trimming and processing of the protein-bound glycans either late in the endoplasmic reticulum or the Golgi compartments. CDG1A is the most common form of CDG and was the first to be characterized at the molecular level (reviews byÂ Marquardt and Denecke, 2003;Â Grunewald et al., 2002).	NM_018129.3(PNPO):c.674G>A ; NM_018129.3(PNPO):c.685C>T ; NM_018129.3(PNPO):c.674G>A ; NM_018129.3(PNPO):c.685C>T
POLG	Alpers-Huttenlocher syndrome	Pyridoxal phosphate-responsive seizures is a very rare neonatal epileptic encephalopathy disorder characterized clinically by onset of severe seizures within hours of birth that are not responsive to anticonvulsants, but are responsive to treatment with pyridoxal phosphate.	PNPOD is an autosomal recessive inborn error of metabolism resulting in vitamin B6 deficiency that manifests as neonatal-onset severe seizures and subsequent encephalopathy. Patients with PNPO mutations tend to respond better to treatment with pyridoxal 5-prime phosphate (PLP) than with pyridoxine.	NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T ; NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T

POLG	Autosomal dominant progressive external ophthalmoplegia	A cerebrohepatopathy and a rare and severe form of mitochondrial DNA (mtDNA) depletion syndrome characterized by the triad of progressive developmental regression, intractable seizures, and hepatic failure.	Development is usually normal until disease onset and presentations are highly variable. The most common age of onset is between 2-4 years (ranges from 3 months to 36 years). Seizures (mainly partial, secondary generalized tonic-clonic, or myoclonic) are often the presenting feature, evolving into focal status epilepticus, epilepsia partialis continua, and/or multifocal myoclonic epilepsy. Seizures may respond to treatment initially but usually become intractable. Headaches, visual disturbances and movement disorders (e.g. myoclonus and choreoathetosis) are also common. Cerebellar ataxia develops in most patients. Peripheral neuropathy develops in many and becomes increasingly common in older children and young adults. Loss of cognitive function progresses with varying rates (rapid regression seen during infectious diseases) with manifestations including somnolence, irritability, loss of concentration, loss of language skills and memory deficits, ending in dementia and visual loss. Gastrointestinal involvement (i.e. swallowing dysfunction, intestinal dysmotility) is also noted. Liver disease may be indolent for years before the first acute exacerbation, but may be the first presenting symptom in some children. The clinical course of both brain and liver abnormalities is often episodic with acute exacerbations followed by periods of partial recovery.	NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T ; NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T

POLG	Autosomal recessive progressive external ophthalmoplegia	A rare genetic, neuro-ophthalmological disease characterized by progressive weakness of the external eye muscles, resulting in bilateral ptosis and diffuse symmetric ophthalmoparesis. Additional signs may include skeletal muscle weakness, cataracts, hearing loss, sensory axonal neuropathy, ataxia, parkinsonism, cardiomyopathy, hypogonadism and depression. It is usually less severe than autosomal recessive form.	Progressive external ophthalmoplegia is characterized by multiple mitochondrial DNA deletions in skeletal muscle. The most common clinical features include adult onset of weakness of the external eye muscles and exercise intolerance. Additional symptoms are variable, and may include cataracts, hearing loss, sensory axonal neuropathy, ataxia, depression, hypogonadism, and parkinsonism. Both autosomal dominant and autosomal recessive inheritance can occur; autosomal recessive inheritance is usually more severe.	NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T ; NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T
POLG	Mitochondrial neurogastrointestinal encephalomyopathy	A rare genetic, neuro-ophthalmological disease characterized by progressive weakness of the external eye muscles, resulting in bilateral ptosis and diffuse, symmetric ophthalmoparesis. Additional signs may include generalized skeletal muscle weakness, muscle atrophy, sensory axonal neuropathy, ataxia, cardiomyopathy, and psychiatric symptoms. It is usually more severe than autosomal dominant form.	Progressive external ophthalmoplegia (PEO) is characterized by multiple mitochondrial DNA (mtDNA) deletions in skeletal muscle. The most common clinical features include adult-onset of weakness of the external eye muscles and exercise intolerance. Additional symptoms are variable, and may include cataracts, hearing loss, sensory axonal neuropathy, ataxia, depression, hypogonadism, and parkinsonism. Less common features include mitral valve prolapse, cardiomyopathy, and gastrointestinal dysmotility. Both autosomal dominant and autosomal recessive inheritance can occur; autosomal recessive inheritance is usually more severe	NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T ; NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T

POLG	Progressive myoclonic epilepsy type 5	Mitochondrial NeuroGastroIntestinal Encephalomyopathy (MNGIE) syndrome is characterized by the association of gastrointestinal dysmotility, peripheral neuropathy, chronic progressive external ophthalmoplegia and leukoencephalopathy.	The first clinical manifestations generally appear between the ages of 10 and 40 (most often before 20 years of age). The symptoms are progressive and the clinical picture is dominated by severe gastrointestinal disorders (cramping, vomiting, diarrhea, intestinal pseudo-obstruction, dysphagia and gastroparesis) due to abnormal bowel motility. Gastrointestinal disorders gradually progress to chronic pseudo-obstruction leading to cachexia. Neurological involvement includes chronic progressive ophthalmoplegia with or without ptosis, and sensorimotor peripheral neuropathy. Cerebral imaging often reveals subclinical leukodystrophy. Deafness, pigmentary retinopathy, and cerebellar involvement are less frequent findings and are not defining features of the syndrome. Patients are usually thin with short stature. Morphological studies of the muscles reveal the presence of a low proportion of muscle fibers with mitochondrial proliferation (ragged-red fibers) or cytochrome c oxidase deficiency.	NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T ; NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T
POLG	Recessive mitochondrial ataxia syndrome	A rare, genetic neurological disorder characterized by early-onset progressive ataxia associated with myoclonic seizures, generalized tonic-clonic seizures (which are often sleep-related), and normal to mild intellectual disability. Dysarthria, upward gaze palsy, sensory neuropathy, developmental delay and autistic disorder have also been associated.	SANDO is an autosomal recessive systemic disorder characterized mainly by adult onset of sensory ataxic neuropathy, dysarthria, and ophthalmoparesis (SANDO) resulting from mitochondrial dysfunction and associated with mtDNA depletion in skeletal muscle and peripheral nerve tissue. The phenotype varies widely, even within the same family, and can include myopathy, seizures, and hearing loss, but the common clinical feature appears to be sensory ataxia.	NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T ; NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T

POLG	Sensory ataxic neuropathy-dysarthria-ophthalmoparesis syndrome	Recessive mitochondrial ataxia syndrome is a rare, mitochondrial DNA maintenance syndrome characterized by early-onset cerebellar ataxia, and variable combination of epilepsy, headache, dysarthria, ophthalmoplegia, peripheral neuropathy, intellectual disability, psychiatric symptoms and movement disorders.	SANDO is an autosomal recessive systemic disorder characterized mainly by adult onset of sensory ataxic neuropathy, dysarthria, and ophthalmoparesis (SANDO) resulting from mitochondrial dysfunction and associated with mtDNA depletion in skeletal muscle and peripheral nerve tissue. The phenotype varies widely, even within the same family, and can include myopathy, seizures, and hearing loss, but the common clinical feature appears to be sensory ataxia.	NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T ; NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T
POLG	Spinocerebellar ataxia with epilepsy	A rare mitochondrial disease characterized by adult onset of the triad of sensory ataxic neuropathy, dysarthria, and ophthalmoparesis. Additional signs and symptoms are highly variable and include myopathy, seizures, and hearing loss, among others. Brain imaging may show cerebellar white matter abnormalities and/or bilateral thalamic lesions.	SANDO is an autosomal recessive systemic disorder characterized mainly by adult onset of sensory ataxic neuropathy, dysarthria, and ophthalmoparesis (SANDO) resulting from mitochondrial dysfunction and associated with mtDNA depletion in skeletal muscle and peripheral nerve tissue. The phenotype varies widely, even within the same family, and can include myopathy, seizures, and hearing loss, but the common clinical feature appears to be sensory ataxia.	NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T ; NM_002693.2(POLG):c.2794C>T ; c.1437C>G ; NM_002693.2(POLG):c.2542G>A ; NM_002693.2(POLG):c.2605C>T ; c.1754G>A ; NM_002693.2(POLG):c.3218C>T ; c.3644-1G>A ; NM_002693.2(POLG):c.3286C>T ; NM_002693.2(POLG):c.2617G>T ; NM_002693.2(POLG):c.1879C>T ; NM_002693.2(POLG):c.2591A>G ; NM_002693.2(POLG):c.3630dupC ; NM_002693.2(POLG):c.1399G>A ; NM_002693.2(POLG):c.2209G>C ; NM_002693.2(POLG):c.911T>G ; NM_002693.2(POLG):c.1120C>T

POMGNT1	Congenital muscular dystrophy with cerebellar involvement	Spinocerebellar ataxia with epilepsy is a rare, mitochondrial DNA maintenance syndrome characterized by cerebellar ataxia, sensory peripheral neuropathy, myoclonus, epilepsy, progressive cognitive impairment, late-onset ptosis and external ophthalmoplegia. Liver failure may also occur, most often in association with the use of antiepileptic drug sodium valproate.	SANDO is an autosomal recessive systemic disorder characterized mainly by adult onset of sensory ataxic neuropathy, dysarthria, and ophthalmoparesis (SANDO) resulting from mitochondrial dysfunction and associated with mtDNA depletion in skeletal muscle and peripheral nerve tissue. The phenotype varies widely, even within the same family, and can include myopathy, seizures, and hearing loss, but the common clinical feature appears to be sensory ataxia.	NM_017739.3(POMGNT1):c.932G>A ; NM_017739.3(POMGNT1):c.652+1G>A ; c.1411A>T ; NM_017739.3(POMGNT1):c.1814G>C ; NM_001243766.1(POMGNT1):c.92dupA ; NM_017739.3(POMGNT1):c.880-1G>A ; NM_001243766.1(POMGNT1):c.187C>T ; NM_017739.3:c.1864delC ; c.1545del ; NM_017739.3(POMGNT1):c.636C>T ; NM_001243766.1(POMGNT1):c.1425G>A ; NM_017739.3(POMGNT1):c.1469G>A ; NM_017739.3(POMGNT1):c.1274G>C ; NM_017739.3(POMGNT1):c.1539+1G>A ; NM_017739.3(POMGNT1):c.1539+1G>T ; NM_017739.3(POMGNT1):c.931C>T ; NM_017739.3(POMGNT1):c.932G>A ; NM_017739.3(POMGNT1):c.652+1G>A ; c.1411A>T ; NM_017739.3(POMGNT1):c.1814G>C ; NM_001243766.1(POMGNT1):c.92dupA ; NM_017739.3(POMGNT1):c.880-1G>A ; NM_001243766.1(POMGNT1):c.187C>T ; NM_017739.3:c.1864delC ; c.1545del ; NM_017739.3(POMGNT1):c.636C>T ; NM_001243766.1(POMGNT1):c.1425G>A ; NM_017739.3(POMGNT1):c.1469G>A ; NM_017739.3(POMGNT1):c.1274G>C ; NM_017739.3(POMGNT1):c.1539+1G>A ; NM_017739.3(POMGNT1):c.1539+1G>T ; NM_017739.3(POMGNT1):c.931C>T
POMGNT1	Muscle-eye-brain disease	Congenital muscular dystrophy with cerebellar involvement is a rare, congenital muscular dystrophy due to dystroglycanopathy characterized by proximal muscule weakness with a tendency for muscle hypertrophy and pseudohypertrophy, variable cognitive impairment, microcephaly, cerebellar hypoplasia with or without cysts, and other structural brain anomalies.	Congenital muscular dystrophy-dystroglycanopathy with brain and eye anomalies (type A), which includes both the more severe Walker-Warburg syndrome (WWS) and the slightly less severe muscle-eye-brain disease (MEB), is an autosomal recessive disorder with characteristic brain and eye malformations, profound mental retardation, congenital muscular dystrophy, and death usually in the first years of life. It represents the most severe end of a phenotypic spectrum of similar disorders resulting from defective glycosylation of DAG1 (128239), collectively known as 'dystroglycanopathies'.	NM_017739.3(POMGNT1):c.932G>A ; NM_017739.3(POMGNT1):c.652+1G>A ; c.1411A>T ; NM_017739.3(POMGNT1):c.1814G>C ; NM_001243766.1(POMGNT1):c.92dupA ; NM_017739.3(POMGNT1):c.880-1G>A ; NM_001243766.1(POMGNT1):c.187C>T ; NM_017739.3:c.1864delC ; c.1545del ; NM_017739.3(POMGNT1):c.636C>T ; NM_001243766.1(POMGNT1):c.1425G>A ; NM_017739.3(POMGNT1):c.1469G>A ; NM_017739.3(POMGNT1):c.1274G>C ; NM_017739.3(POMGNT1):c.1539+1G>A ; NM_017739.3(POMGNT1):c.1539+1G>T ; NM_017739.3(POMGNT1):c.931C>T

POMGNT1	POMGNT1-related limb-girdle muscular dystrophy R15	A rare, congenital muscular dystrophy due to dystroglycanopathy characterized by early onset muscular dystrophy, severe muscular hypotonia, severe mental retardation and typical brain and eye malformations, including pachygyria, polymicrogyria, agyria, brainstem and cerebellar structural anomalies, severe myopia, glaucoma, optic nerve and retinal hypoplasia. Patients may present with seizures, macrocephaly or microcephaly, microphthalmia, and congenital contractures. Depending on the severity, limited motor function is acquired. Less severe cases have been reported.	Congenital muscular dystrophy-dystroglycanopathy with brain and eye anomalies (type A), which includes both the more severe Walker-Warburg syndrome (WWS) and the slightly less severe muscle-eye-brain disease (MEB), is an autosomal recessive disorder with characteristic brain and eye malformations, profound mental retardation, congenital muscular dystrophy, and death usually in the first years of life. It represents the most severe end of a phenotypic spectrum of similar disorders resulting from defective glycosylation of DAG1, collectively known as 'dystroglycanopathies'.	NM_017739.3(POMGNT1):c.932G>A ; NM_017739.3(POMGNT1):c.652+1G>A ; c.1411A>T ; NM_017739.3(POMGNT1):c.1814G>C ; NM_001243766.1(POMGNT1):c.92dupA ; NM_017739.3(POMGNT1):c.880-1G>A ; NM_001243766.1(POMGNT1):c.187C>T ; NM_017739.3:c.1864delC ; c.1545del ; NM_017739.3(POMGNT1):c.636C>T ; NM_001243766.1(POMGNT1):c.1425G>A ; NM_017739.3(POMGNT1):c.1469G>A ; NM_017739.3(POMGNT1):c.1274G>C ; NM_017739.3(POMGNT1):c.1539+1G>A ; NM_017739.3(POMGNT1):c.1539+1G>T ; NM_017739.3(POMGNT1):c.931C>T ; NM_017739.3(POMGNT1):c.932G>A ; NM_017739.3(POMGNT1):c.652+1G>A ; c.1411A>T ; NM_017739.3(POMGNT1):c.1814G>C ; NM_001243766.1(POMGNT1):c.92dupA ; NM_017739.3(POMGNT1):c.880-1G>A ; NM_001243766.1(POMGNT1):c.187C>T ; NM_017739.3:c.1864delC ; c.1545del ; NM_017739.3(POMGNT1):c.636C>T ; NM_001243766.1(POMGNT1):c.1425G>A ; NM_017739.3(POMGNT1):c.1469G>A ; NM_017739.3(POMGNT1):c.1274G>C ; NM_017739.3(POMGNT1):c.1539+1G>A ; NM_017739.3(POMGNT1):c.1539+1G>T ; NM_017739.3(POMGNT1):c.931C>T
POMGNT1	Retinitis pigmentosa	A form of limb-girdle muscular dystrophy characterized by an onset in childhood or adolescence of rapidly progressive proximal limb muscle weakness (particularly affecting the neck, hip girdle, and shoulder abductors), hypertrophy in the calves and quadriceps, ankle contractures, and myopia.	MDDGC3 is a rare form of autosomal recessive limb-girdle muscular dystrophy with normal cognition.	NM_017739.3(POMGNT1):c.932G>A ; NM_017739.3(POMGNT1):c.652+1G>A ; c.1411A>T ; NM_017739.3(POMGNT1):c.1814G>C ; NM_001243766.1(POMGNT1):c.92dupA ; NM_017739.3(POMGNT1):c.880-1G>A ; NM_001243766.1(POMGNT1):c.187C>T ; NM_017739.3:c.1864delC ; c.1545del ; NM_017739.3(POMGNT1):c.636C>T ; NM_001243766.1(POMGNT1):c.1425G>A ; NM_017739.3(POMGNT1):c.1469G>A ; NM_017739.3(POMGNT1):c.1274G>C ; NM_017739.3(POMGNT1):c.1539+1G>A ; NM_017739.3(POMGNT1):c.1539+1G>T ; NM_017739.3(POMGNT1):c.931C>T ; NM_017739.3(POMGNT1):c.932G>A ; NM_017739.3(POMGNT1):c.652+1G>A ; c.1411A>T ; NM_017739.3(POMGNT1):c.1814G>C ; NM_001243766.1(POMGNT1):c.92dupA ; NM_017739.3(POMGNT1):c.880-1G>A ; NM_001243766.1(POMGNT1):c.187C>T ; NM_017739.3:c.1864delC ; c.1545del ; NM_017739.3(POMGNT1):c.636C>T ; NM_001243766.1(POMGNT1):c.1425G>A ; NM_017739.3(POMGNT1):c.1469G>A ; NM_017739.3(POMGNT1):c.1274G>C ; NM_017739.3(POMGNT1):c.1539+1G>A ; NM_017739.3(POMGNT1):c.1539+1G>T ; NM_017739.3(POMGNT1):c.931C>T

POMGNT1	Walker-Warburg syndrome	Retinitis pigmentosa (RP) is an inherited retinal dystrophy leading to progressive loss of the photoreceptors and retinal pigment epithelium and resulting in blindness usually after several decades.	Retinitis pigmentosa is slowly progressive but relentless. There is however broad variability in age of onset, rate of progression and secondary clinical manifestations. Affected individuals generally first develop night blindness (nyctalopia) due to loss of rod function, often in adolescence or earlier. They then develop peripheral visual field impairment, and over time loss of central vision, usually at late stages, often around midlife. Central visual acuity loss may occur at any age as a result of cystoid macular edema or photoreceptor loss. Posterior subcapsular cataracts are common and severity is age dependent. Reduced color vision may also be found. Fundus examination reveals bone spicule pigment deposits, attenuated retinal vessels, retinal atrophy and waxy optic nerve pallor. Severity is partly correlated with the pattern of inheritance with X-linked cases having the most severe course, autosomal recessive and single occurrence cases having intermediate severity, and autosomal dominant the most favorable course.	NM_017739.3(POMGNT1):c.932G>A ; NM_017739.3(POMGNT1):c.652+1G>A ; c.1411A>T ; NM_017739.3(POMGNT1):c.1814G>C ; NM_001243766.1(POMGNT1):c.92dupA ; NM_017739.3(POMGNT1):c.880-1G>A ; NM_001243766.1(POMGNT1):c.187C>T ; NM_017739.3:c.1864delC ; c.1545del ; NM_017739.3(POMGNT1):c.636C>T ; NM_001243766.1(POMGNT1):c.1425G>A ; NM_017739.3(POMGNT1):c.1469G>A ; NM_017739.3(POMGNT1):c.1274G>C ; NM_017739.3(POMGNT1):c.1539+1G>A ; NM_017739.3(POMGNT1):c.1539+1G>T ; NM_017739.3(POMGNT1):c.931C>T ; NM_017739.3(POMGNT1):c.932G>A ; NM_017739.3(POMGNT1):c.652+1G>A ; c.1411A>T ; NM_017739.3(POMGNT1):c.1814G>C ; NM_001243766.1(POMGNT1):c.92dupA ; NM_017739.3(POMGNT1):c.880-1G>A ; NM_001243766.1(POMGNT1):c.187C>T ; NM_017739.3:c.1864delC ; c.1545del ; NM_017739.3(POMGNT1):c.636C>T ; NM_001243766.1(POMGNT1):c.1425G>A ; NM_017739.3(POMGNT1):c.1469G>A ; NM_017739.3(POMGNT1):c.1274G>C ; NM_017739.3(POMGNT1):c.1539+1G>A ; NM_017739.3(POMGNT1):c.1539+1G>T ; NM_017739.3(POMGNT1):c.931C>T
PPT1	CLN1 disease	Walker-Warburg Syndrome (WWS) is a rare form of congenital muscular dystrophy associated with brain and eye abnormalities.	Patients present at birth with generalized severe hypotonia, muscle weakness, absent or very poor psychomotor development, eye involvement and seizures. Brain MRI shows type II cobblestone lissencephaly, hydrocephalus (see these terms), severe brainstem and cerebellar hypoplasia (Dandy-Walker malformation is possible, see this term). White matter abnormalities are also observed.	c.768dup ; NM_000310.3(PPT1):c.29T>A ; NM_000310.3(PPT1):c.451C>T ; NM_000310.3(PPT1):c.541G>T ; NM_000310.3(PPT1):c.223A>C ; NM_000310.3(PPT1):c.627+1G>T ; c.768dup ; NM_000310.3(PPT1):c.29T>A ; NM_000310.3(PPT1):c.451C>T ; NM_000310.3(PPT1):c.541G>T ; NM_000310.3(PPT1):c.223A>C ; NM_000310.3(PPT1):c.627+1G>T

PROP1	Combined pituitary hormone deficiencies, genetic forms	Neuronal ceroid lipofuscinoses (NCLs) are a group of inherited progressive degenerative brain diseases characterized clinically by a decline of mental and other capacities, epilepsy, and vision loss through retinal degeneration, and histopathologically by intracellular accumulation of an autofluorescent material, ceroid lipofuscin, in the neuronal cells in the brain and in the retina.	The clinical presentation varies widely between forms but the clinical hallmark is a combination of dementia, visual loss, and epilepsy. Manifestations may begin between the neonatal period and young adult age depending on the form, leading to the original classification of NCLs by age at onset into congenital, infantile, late infantile, juvenile and adult NCL subgroups (see these terms). A Northern epilepsy variant (progressive epilepsy-intellectual deficit, Finnish type; see this term), in which the visual problems may be absent or be mild and go unrecognized, has also been described.	NM_006261.4(PROP1):c.263T>C ; c.247C>T ; NM_006261.4(PROP1):c.295C>T ; NM_006261.4(PROP1):c.310delC ; NM_006261.4(PROP1):c.217C>T ; NM_006261.4(PROP1):c.218G>A ; c.157del ; NM_006261.4(PROP1):c.301_302delAG ; NM_006261.4(PROP1):c.112_124del13 ; NM_006261.4(PROP1):c.349T>A ; c.4del ; c.469dup ; NM_006261.4(PROP1):c.150delA ; NM_006261.4(PROP1):c.358C>T ; NM_006261.4(PROP1):c.2T>C ; NM_006261.4(PROP1):c.263T>C ; c.247C>T ; NM_006261.4(PROP1):c.295C>T ; NM_006261.4(PROP1):c.310delC ; NM_006261.4(PROP1):c.217C>T ; NM_006261.4(PROP1):c.218G>A ; c.157del ; NM_006261.4(PROP1):c.301_302delAG ; NM_006261.4(PROP1):c.112_124del13 ; NM_006261.4(PROP1):c.349T>A ; c.4del ; c.469dup ; NM_006261.4(PROP1):c.150delA ; NM_006261.4(PROP1):c.358C>T ; NM_006261.4(PROP1):c.2T>C
PROP1	Hypothyroidism due to deficient transcription factors involved in pituitary development or function	Congenital hypopituitarism is characterized by multiple pituitary hormone deficiency, including somatotroph, thyrotroph, lactotroph, corticotroph or gonadotroph deficiencies, due to mutations of pituitary transcription factors involved in pituitary ontogenesis. Congenital hypopituitarism is rare compared with the high incidence of hypopituitarism induced by pituitary adenomas, transsphenoidal surgery or radiotherapy.	Clinical presentation is variable, depending on the type and severity of deficiencies and on the age at diagnosis. If untreated, main symptoms include short stature, cognitive alterations or delayed puberty.	NM_006261.4(PROP1):c.263T>C ; c.247C>T ; NM_006261.4(PROP1):c.295C>T ; NM_006261.4(PROP1):c.310delC ; NM_006261.4(PROP1):c.217C>T ; NM_006261.4(PROP1):c.218G>A ; c.157del ; NM_006261.4(PROP1):c.301_302delAG ; NM_006261.4(PROP1):c.112_124del13 ; NM_006261.4(PROP1):c.349T>A ; c.4del ; c.469dup ; NM_006261.4(PROP1):c.150delA ; NM_006261.4(PROP1):c.358C>T ; NM_006261.4(PROP1):c.2T>C ; NM_006261.4(PROP1):c.263T>C ; c.247C>T ; NM_006261.4(PROP1):c.295C>T ; NM_006261.4(PROP1):c.310delC ; NM_006261.4(PROP1):c.217C>T ; NM_006261.4(PROP1):c.218G>A ; c.157del ; NM_006261.4(PROP1):c.301_302delAG ; NM_006261.4(PROP1):c.112_124del13 ; NM_006261.4(PROP1):c.349T>A ; c.4del ; c.469dup ; NM_006261.4(PROP1):c.150delA ; NM_006261.4(PROP1):c.358C>T ; NM_006261.4(PROP1):c.2T>C

PROP1	Non-acquired panhypopituitarism	Hypothyroidism due to mutations in transcription factors involved in pituitary development or function is a type of central congenital hypothyroidism (see this term), a permanent thyroid deficiency that is present from birth, characterized by low levels of thyroid hormones caused by disorders in the development or function of the pituitary.	The clinical manifestations can be subtle, probably as a result of trans-placental passage of some maternal thyroid hormone or due to the fact that many infants have some thyroid production of their own. More specific symptoms and signs often do not develop until several months of age. Common clinical features and signs include decreased activity and increased sleep, feeding difficulty and constipation, prolonged jaundice, myxedematous facies, large fontanels (especially posterior), macroglossia, a distended abdomen with umbilical hernia, and hypotonia. Goiter is always absent. Slow linear growth and developmental delay are usually apparent by 4-6 months of age. Without treatment hypothyroidism results in severe intellectual deficit and short stature. Clinical manifestations may often include signs of hypopituitarism including septo-optic dysplasia or cleft lip and/or palate among others.	NM_006261.4(PROP1):c.263T>C ; c.247C>T ; NM_006261.4(PROP1):c.295C>T ; NM_006261.4(PROP1):c.310delC ; NM_006261.4(PROP1):c.217C>T ; NM_006261.4(PROP1):c.218G>A ; c.157del ; NM_006261.4(PROP1):c.301_302delAG ; NM_006261.4(PROP1):c.112_124del13 ; NM_006261.4(PROP1):c.349T>A ; c.4del ; c.469dup ; NM_006261.4(PROP1):c.150delA ; NM_006261.4(PROP1):c.358C>T ; NM_006261.4(PROP1):c.2T>C ; NM_006261.4(PROP1):c.263T>C ; c.247C>T ; NM_006261.4(PROP1):c.295C>T ; NM_006261.4(PROP1):c.310delC ; NM_006261.4(PROP1):c.217C>T ; NM_006261.4(PROP1):c.218G>A ; c.157del ; NM_006261.4(PROP1):c.301_302delAG ; NM_006261.4(PROP1):c.112_124del13 ; NM_006261.4(PROP1):c.349T>A ; c.4del ; c.469dup ; NM_006261.4(PROP1):c.150delA ; NM_006261.4(PROP1):c.358C>T ; NM_006261.4(PROP1):c.2T>C
PRPS1	Lethal ataxia with deafness and optic atrophy	A rare genetic pituitary disease characterized by variable deficiency of all hormones produced in the anterior lobe of the pituitary gland. Clinical manifestations include hypothyroidism, hypogonadism, growth retardation and short stature, and secondary adrenal insufficiency. Age of onset is variable. Signs and symptoms usually develop gradually, and loss of the different hormones is often sequential.	Patients showed sequential loss of anterior pituitary tropic hormones, a developed deficiency of growth hormone (GH) and gonadotropin in the first decade of life, with subsequent loss of thyroid-stimulating hormone (TSH) function, and finally development of ACTH deficiency in the third decade.	NM_002764.3(PRPS1):c.193G>A ; NM_002764.3(PRPS1):c.344T>C ; NM_002764.3(PRPS1):c.916G>A ; NM_002764.3(PRPS1):c.398A>C ; NM_002764.3(PRPS1):c.869T>C ; NM_002764.3(PRPS1):c.193G>A ; NM_002764.3(PRPS1):c.344T>C ; NM_002764.3(PRPS1):c.916G>A ; NM_002764.3(PRPS1):c.398A>C ; NM_002764.3(PRPS1):c.869T>C

PRPS1	Severe phosphoribosylpyrophosphate synthetase superactivity	Lethal ataxia with deafness and optic atrophy (also known as Arts syndrome) is characterized by intellectual deficit, early-onset hypotonia, ataxia, delayed motor development, hearing impairment and loss of vision due to optic atrophy.	Other manifestations included floppiness, susceptibility to infections, and later, flaccid tetraplegia and areflexia.	NM_002764.3(PRPS1):c.193G>A ; NM_002764.3(PRPS1):c.344T>C ; NM_002764.3(PRPS1):c.916G>A ; NM_002764.3(PRPS1):c.398A>C ; NM_002764.3(PRPS1):c.869T>C ; NM_002764.3(PRPS1):c.193G>A ; NM_002764.3(PRPS1):c.344T>C ; NM_002764.3(PRPS1):c.916G>A ; NM_002764.3(PRPS1):c.398A>C ; NM_002764.3(PRPS1):c.869T>C
PRPS1	X-linked Charcot-Marie-Tooth disease type 5	A severe form of phosphoribosylpyrophosphate (PRPP) synthetase superactivity, an X-linked disorder of purine metabolism, characterized by early onset hyperuricemia and hyperuricosuria, and clinically manifesting with urolithiasis, gout and neurodevelopmental anomalies consisting of variable combinations of sensorineural hearing loss, hypotonia, and ataxia.	The phenotype varies greatly among patients. The severe form manifests in infancy or early childhood (but may occur earlier) usually with uric acid crystalluria and urinary stones (kidney and/or bladder), followed by the development of gouty arthritis and eventually renal failure as a result of obstructive uropathy from uric acid crystal deposition. This form also shows neurologic impairment, mainly sensorineural hearing loss, hypotonia, ataxia, developmental delay, and /or intellectual disability. Axonal neuropathy with demyelination is also possible (reported in one family).	NM_002764.3(PRPS1):c.193G>A ; NM_002764.3(PRPS1):c.344T>C ; NM_002764.3(PRPS1):c.916G>A ; NM_002764.3(PRPS1):c.398A>C ; NM_002764.3(PRPS1):c.869T>C ; NM_002764.3(PRPS1):c.193G>A ; NM_002764.3(PRPS1):c.344T>C ; NM_002764.3(PRPS1):c.916G>A ; NM_002764.3(PRPS1):c.398A>C ; NM_002764.3(PRPS1):c.869T>C
PRPS1	X-linked intellectual disability-limb spasticity-retinal dystrophy-diabetes insipidus syndrome	The phenotype of X-linked Charcot-Marie-Tooth disease-5 typically comprises the triad of optic atrophy, deafness, and polyneuropathy.	X-linked Charcot-Marie-Tooth disease type 5 is a rare, genetic, peripheral sensorimotor neuropathy characterized by an X-linked recessive inheritance pattern and the infancy- to childhood-onset of: 1) progressive distal muscle weakness and atrophy (first appearing and more prominent in the lower extremities than the upper) which usually manifests with foot drop and gait disturbance, 2) bilateral, profound, prelingual sensorineural hearing loss and 3) progressive optic neuropathy. Females are asymptomatic and do not display the phenotype.	NM_002764.3(PRPS1):c.193G>A ; NM_002764.3(PRPS1):c.344T>C ; NM_002764.3(PRPS1):c.916G>A ; NM_002764.3(PRPS1):c.398A>C ; NM_002764.3(PRPS1):c.869T>C ; NM_002764.3(PRPS1):c.193G>A ; NM_002764.3(PRPS1):c.344T>C ; NM_002764.3(PRPS1):c.916G>A ; NM_002764.3(PRPS1):c.398A>C ; NM_002764.3(PRPS1):c.869T>C

PRPS1	X-linked non-syndromic sensorineural deafness type DFN	X-linked intellectual disability-limb spasticity-retinal dystrophy-diabetes insipidus syndrome is a rare genetic neurometabolic disease characterized by severe intellectual disability, spastic quadraparesis, Leber's congenital amaurosis and diabetes insipidus. Additional manifestations include facial dysmorphy (dolichocephalic skull, hypertelorism, deep-set eyes, hypoplastic nares, low-set ears), short stature, truncal hypotonia and axial hypertonia. Brain anomalies (e.g. thin corpus callosum with lack of isthmus and tapered splenium, hypoplasia or atrophy of the optic chiasm, prominent lateral ventricles, diminished white matter), described on magnetic resonance imaging, have been reported. High prenatal Î±-fetoprotein and intrauterine growth restriction is observed in routine pregnancy examination.		NM_002764.3(PRPS1):c.193G>A ; NM_002764.3(PRPS1):c.344T>C ; NM_002764.3(PRPS1):c.916G>A ; NM_002764.3(PRPS1):c.398A>C ; NM_002764.3(PRPS1):c.869T>C ; NM_002764.3(PRPS1):c.193G>A ; NM_002764.3(PRPS1):c.344T>C ; NM_002764.3(PRPS1):c.916G>A ; NM_002764.3(PRPS1):c.398A>C ; NM_002764.3(PRPS1):c.869T>C

PSAP	Atypical Gaucher disease due to saposin C deficiency	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	NM_002778.2(PSAP):c.607C>T ; NM_001042465.2(PSAP):c.1A>T ; NM_001042465.2(PSAP):c.1055T>C ; NM_001042465.2(PSAP):c.1297C>T ; NM_001042465.2(PSAP):c.643A>C ; NM_002778.2(PSAP):c.607C>T ; NM_001042465.2(PSAP):c.1A>T ; NM_001042465.2(PSAP):c.1055T>C ; NM_001042465.2(PSAP):c.1297C>T ; NM_001042465.2(PSAP):c.643A>C

PSAP	Encephalopathy due to prosaposin deficiency	Gaucher disease (GD) is a lysosomal storage disorder encompassing three main forms (types 1, 2 and 3), a fetal form and a variant with cardiac involvement (Gaucher disease - ophthalmoplegia - cardiovascular calcification or Gaucher-like disease).	The clinical manifestations of this disease are highly variable. GD type 1 (90% of cases) is the chronic and non-neurological form associated with organomegaly (spleen, liver), bone anomalies (pain, osteonecrosis, pathological fractures) and cytopenia. Type 2, the acute neurological form, is characterized by early onset, rapidly progressing brainstem dysfunction, associated with organomegaly and leading to death before the age of 2. Type 3, the subacute neurological form, affects children or adolescents and is characterized by progressive encephalopathy (oculomotor apraxia, epilepsy and ataxia) with the systemic manifestations seen in type 1. The fetal form manifests with a decrease or absence of fetal movements or anasarca. Gaucher-like disease presents with progressive calcification of the aorta and the aortic and/ or mitral valves as its main feature.	NM_002778.2(PSAP):c.607C>T ; NM_001042465.2(PSAP):c.1A>T ; NM_001042465.2(PSAP):c.1055T>C ; NM_001042465.2(PSAP):c.1297C>T ; NM_001042465.2(PSAP):c.643A>C ; NM_002778.2(PSAP):c.607C>T ; NM_001042465.2(PSAP):c.1A>T ; NM_001042465.2(PSAP):c.1055T>C ; NM_001042465.2(PSAP):c.1297C>T ; NM_001042465.2(PSAP):c.643A>C
PSAP	Infantile Krabbe disease	A lysosomal storage disease belonging to the group of sphingolipidoses.	Clinically, it is a severe neurovisceral disease manifesting immediately after birth and following a rapidly progressive fatal course (death between 1 and 4 months in the cases documented so far). The neurological signs and symptoms include hypotonia, massive myoclonic bursts, abnormal ocular movements and dystonia. Grand mal seizures and seizures triggered by tactile stimuli have been described. Patients also develop hepatosplenomegaly. Death usually occurs from respiratory failure following repeated pulmonary infections.	NM_002778.2(PSAP):c.607C>T ; NM_001042465.2(PSAP):c.1A>T ; NM_001042465.2(PSAP):c.1055T>C ; NM_001042465.2(PSAP):c.1297C>T ; NM_001042465.2(PSAP):c.643A>C ; NM_002778.2(PSAP):c.607C>T ; NM_001042465.2(PSAP):c.1A>T ; NM_001042465.2(PSAP):c.1055T>C ; NM_001042465.2(PSAP):c.1297C>T ; NM_001042465.2(PSAP):c.643A>C

PSAP	Metachromatic leukodystrophy, adult form	A rare lysosomal disorder that affects the white matter of the central and peripheral nervous systems characterized by neurodegeneration with severity depending on the age of onset (infantile, late-infantile, juvenile, adolescent and adulthood).	The infantile form has an onset at 2-6 months of age and is divided into 3 stages. In the first stage, symptoms include irritability, stiffness, poor head control, feeding difficulties, intermittent thumb clasp, episodes of increased temperature, and developmental delay. In the second stage, hypertonic episodes occur with opisthotonus, myoclonic seizures, developmental regression, fisting and vision deficits. In the third stage, hypotonia, blindness and deafness occur. Patients progress into a vegetative state and usually die before the age of 2-3 years, generally due to respiratory infections. In the late infantile/juvenile (1-16 years) and adult (>16 years) forms, the presenting symptoms vary greatly and progression is variable (generally slower in older patients). Patients with late infantile /juvenile onset most resemble infantile patients, while the first signs in adult forms are often weakness, gait disturbances (spastic paraparesis or ataxia), burning paresthesias, hemiplegia, and/or vision loss, with or without peripheral neuropathy. Cognitive regression is variable and often absent in adult forms. In the later-onset forms the disease progresses at a slower rate than infantile patients with some adults living until the sixth decade with mild symptoms.	NM_002778.2(PSAP):c.607C>T ; NM_001042465.2(PSAP):c.1A>T ; NM_001042465.2(PSAP):c.1055T>C ; NM_001042465.2(PSAP):c.1297C>T ; NM_001042465.2(PSAP):c.643A>C ; NM_002778.2(PSAP):c.607C>T ; NM_001042465.2(PSAP):c.1A>T ; NM_001042465.2(PSAP):c.1055T>C ; NM_001042465.2(PSAP):c.1297C>T ; NM_001042465.2(PSAP):c.643A>C

PSAP	Metachromatic leukodystrophy, juvenile form	The metachromatic leukodystrophies comprise several allelic disorders.Â 7 forms are recognized: 5 allelic forms of MLD: late infantile, juvenile, and adult forms, partial cerebroside sulfate deficiency, and pseudoarylsulfatase A deficiency; and 2 nonallelic forms: metachromatic leukodystrophy due to saposin B deficiency and multiple sulfatase deficiency or juvenile sulfatidosis, a disorder that combines features of a mucopolysaccharidosis with those of metachromatic leukodystrophy.	A subtype of Metachromatic leukodystrophy characterized by progressive psychomotor regression with an insidious onset after the age of 16 years, most often beginning with intellectual and behavioral changes, such as memory deficits or emotional instability. The clinical picture is dominated by gradual cognitive, later also motor, decline, taking a protracted course with periods of waxing and waning. Decerebration and death occur within decades after disease onset.	NM_002778.2(PSAP):c.607C>T ; NM_001042465.2(PSAP):c.1A>T ; NM_001042465.2(PSAP):c.1055T>C ; NM_001042465.2(PSAP):c.1297C>T ; NM_001042465.2(PSAP):c.643A>C ; NM_002778.2(PSAP):c.607C>T ; NM_001042465.2(PSAP):c.1A>T ; NM_001042465.2(PSAP):c.1055T>C ; NM_001042465.2(PSAP):c.1297C>T ; NM_001042465.2(PSAP):c.643A>C
PSAP	Metachromatic leukodystrophy, late infantile form	The metachromatic leukodystrophies comprise several allelic disorders.Â 7 forms are recognized: 5 allelic forms of MLD: late infantile, juvenile, and adult forms, partial cerebroside sulfate deficiency, and pseudoarylsulfatase A deficiency; and 2 nonallelic forms: metachromatic leukodystrophy due to saposin B deficiency and multiple sulfatase deficiency or juvenile sulfatidosis, a disorder that combines features of a mucopolysaccharidosis with those of metachromatic leukodystrophy.	A subtype of Metachromatic leukodystrophy characterized by progressive psychomotor regression with an onset between 30 months and 16 years of age, often beginning with behavioral abnormalities or deterioration of school performance. Further manifestations are ataxia, gait disturbances, reduced deep tendon reflexes, spasticity, seizures, paralysis, dementia, and loss of speech, vision, and hearing, eventually resulting in complete loss of motor and cognitive skills, and decerebration. The rate of deterioration is variable with possible survival up to the third decade of life.	NM_002778.2(PSAP):c.607C>T ; NM_001042465.2(PSAP):c.1A>T ; NM_001042465.2(PSAP):c.1055T>C ; NM_001042465.2(PSAP):c.1297C>T ; NM_001042465.2(PSAP):c.643A>C ; NM_002778.2(PSAP):c.607C>T ; NM_001042465.2(PSAP):c.1A>T ; NM_001042465.2(PSAP):c.1055T>C ; NM_001042465.2(PSAP):c.1297C>T ; NM_001042465.2(PSAP):c.643A>C

PYGM	Glycogen storage disease due to muscle glycogen phosphorylase deficiency	The metachromatic leukodystrophies comprise several allelic disorders.Â 7 forms are recognized: 5 allelic forms of MLD: late infantile, juvenile, and adult forms, partial cerebroside sulfate deficiency, and pseudoarylsulfatase A deficiency; and 2 nonallelic forms: metachromatic leukodystrophy due to saposin B deficiency and multiple sulfatase deficiency or juvenile sulfatidosis, a disorder that combines features of a mucopolysaccharidosis with those of metachromatic leukodystrophy.	A subtype of Metachromatic leukodystrophy characterized by rapidly progressive psychomotor regression with an onset before 30 months of age after a period of apparently normal development. Manifestations developing during the course of the disease are impaired feeding and swallowing due to pseudobulbar palsies, seizures, painful spasms, muscle weakness, ataxia, paralysis, dementia, and loss of speech, vision, and hearing, quickly resulting in complete loss of motor and cognitive skills, and decerebration. Death occurs within the first decade of life.	NM_005609.3(PYGM):c.1A>G ; NM_005609.2(PYGM):c.1726C>T ; NM_005609.3(PYGM):c.148C>T ; NM_005609.3(PYGM):c.13_14delCT ; NM_005609.3(PYGM):c.1827G>A ; NM_005609.3(PYGM):c.1628A>C ; NM_005609.3(PYGM):c.255C>A ; c.393del ; NM_005609.2(PYGM):c.1768+1G>A ; NM_005609.3(PYGM):c.1963G>A ; NM_005609.2(PYGM):c.1466C>G ; NM_005609.3(PYGM):c.613G>A ; NM_005609.3(PYGM):c.2262delA ; NM_005609.3(PYGM):c.2128_2130delTTC ; NM_005609.3(PYGM):c.1722T>G ; NM_005609.3(PYGM):c.280C>T ; NM_005609.3(PYGM):c.2392T>C ; NM_005609.3(PYGM):c.1621G>T ; NM_005609.3(PYGM):c.501dup ; NM_005609.3(PYGM):c.1A>G ; NM_005609.2(PYGM):c.1726C>T ; NM_005609.3(PYGM):c.148C>T ; NM_005609.3(PYGM):c.13_14delCT ; NM_005609.3(PYGM):c.1827G>A ; NM_005609.3(PYGM):c.1628A>C ; NM_005609.3(PYGM):c.255C>A ; c.393del ; NM_005609.2(PYGM):c.1768+1G>A ; NM_005609.3(PYGM):c.1963G>A ; NM_005609.2(PYGM):c.1466C>G ; NM_005609.3(PYGM):c.613G>A ; NM_005609.3(PYGM):c.2262delA ; NM_005609.3(PYGM):c.2128_2130delTTC ; NM_005609.3(PYGM):c.1722T>G ; NM_005609.3(PYGM):c.280C>T ; NM_005609.3(PYGM):c.2392T>C ; NM_005609.3(PYGM):c.1621G>T ; NM_005609.3(PYGM):c.501dup
RAB23	Carpenter syndrome	Myophosphorylase deficiency (McArdle's disease), or glycogen storage disease type 5 (GSD5) , is a severe form of glycogen storage disease characterized by exercise intolerance.	Onset occurs in childhood. Patients present with a syndrome of muscular exercise intolerance with myalgia, cramps, fatigue, and muscle weakness. Massive elevation of creatine-kinase and rhabdomyolysis with myoglobinuria (dark urine) after exercise is noted in around 50% of patients, potentially leading to acute kidney failure. A 'second wind' phenomenon with relief of myalgia and fatigue after a few minutes of rest is observed in many patients. The clinical presentation is usually very classical, but some patients may have very moderate forms. In a few cases, onset very early in life with hypotonia, generalized muscle weakness and progressive respiratory failure has been described.	c.407dup ; NM_183227.2(RAB23):c.434T>A ; c.407dup ; NM_183227.2(RAB23):c.434T>A

RAG1	Combined immunodeficiency due to partial RAG1 deficiency	A rare syndromic craniosynostosis with variable phenotypic expression characterized by craniosynostosis, intellectual disability, distinctive facies, abnormalities of the fingers and toes (brachydactyly, polydactyly and syndactyly), short stature, congenital heart disease, skeletal defects, obesity, genital abnormalities and umbilical hernia.	Presentation at birth is with macrosomia, umbilical hernia and craniosynostosis which ranges from cloverleaf configuration to predominant involvement of the metopic ridge to craniofacial asymmetry. Cranial anomalies may lead to raised intercranial pressure, difficulty in articulation, frequent otitis media and resultant hearing loss. Typical abnormalities of the digits include brachydactyly, cutaneous syndactyly, preaxial polydactyly in the toes and postaxial polydactlyly in the hands with broad thumbs and absent middle phalanges. Characteristic facial features may include flat nasal bridge with epicanthal folds, down-slanting palpebral fissures, corneal anomalies, low-set, posteriorly rotated malformed ears, and an underdeveloped maxilla and mandible. Congenital cardiac malformations are frequent and may include ventricular septal defect, patent ductus arteriosus, pulmonic stenosis, tetralogy of Fallot, and transposition of great vessels. Intellectual disability is common (affecting 63-75% of cases). Males often have genital abnormalities such as hypogonadism and cryptorchidism. Small primary dentition is usual, teeth are short, undersized and widely spaced, appearing as small buds worn to the gingival margins and often there is prolonged retention of primary teeth. Growth is either slightly delayed or normal and many individuals have short stature. Persistent obesity, particularly truncal obesity, beginning in childhood is common. Additional skeletal abnormalities such as deformed hips, kyphoscoliosis, and genu valgum frequently occur. Situs inversus, dextrocardia, and polysplenia has been observed in a few patients.	NM_000448.2(RAG1):c.256_257delAA ; NM_000448.2(RAG1):c.1682G>A ; NM_000448.2(RAG1):c.940C>T ; NM_000448.2(RAG1):c.2326C>T ; NM_000448.2(RAG1):c.983G>A ; NM_000448.2(RAG1):c.2320G>T ; NM_000448.2(RAG1):c.2814T>G ; NM_000448.2(RAG1):c.2164G>A ; NM_000448.2(RAG1):c.2333G>A ; NM_000448.2(RAG1):c.1681C>T ; NM_000448.2(RAG1):c.256_257delAA ; NM_000448.2(RAG1):c.1682G>A ; NM_000448.2(RAG1):c.940C>T ; NM_000448.2(RAG1):c.2326C>T ; NM_000448.2(RAG1):c.983G>A ; NM_000448.2(RAG1):c.2320G>T ; NM_000448.2(RAG1):c.2814T>G ; NM_000448.2(RAG1):c.2164G>A ; NM_000448.2(RAG1):c.2333G>A ; NM_000448.2(RAG1):c.1681C>T

RAG1	Combined immunodeficiency with granulomatosis	Combined immunodeficiency due to partial RAG1 deficiency is a form of combined T and B cell immunodeficiency (CID; see this term) characterized by severe and persistent cytomegalovirus (CMV) infection and autoimmune cytopenia.	Patients present before the age of one year with severe disseminated CMV infection, which can manifest with fever and splenomegaly, and recurrent and severe co-infections including sepsis and pneumonitis. Autoimmune cytopenia also occurs and can include autoimmune hemolytic anemia (see these terms) or neutropenia.	NM_000448.2(RAG1):c.256_257delAA ; NM_000448.2(RAG1):c.1682G>A ; NM_000448.2(RAG1):c.940C>T ; NM_000448.2(RAG1):c.2326C>T ; NM_000448.2(RAG1):c.983G>A ; NM_000448.2(RAG1):c.2320G>T ; NM_000448.2(RAG1):c.2814T>G ; NM_000448.2(RAG1):c.2164G>A ; NM_000448.2(RAG1):c.2333G>A ; NM_000448.2(RAG1):c.1681C>T ; NM_000448.2(RAG1):c.256_257delAA ; NM_000448.2(RAG1):c.1682G>A ; NM_000448.2(RAG1):c.940C>T ; NM_000448.2(RAG1):c.2326C>T ; NM_000448.2(RAG1):c.983G>A ; NM_000448.2(RAG1):c.2320G>T ; NM_000448.2(RAG1):c.2814T>G ; NM_000448.2(RAG1):c.2164G>A ; NM_000448.2(RAG1):c.2333G>A ; NM_000448.2(RAG1):c.1681C>T
RAG1	Omenn syndrome	A rare, genetic, non-severe combined immunodeficiency disease characterized by immunodeficiency (manifested by recurrent and/or severe bacterial and viral infections), destructive noninfectious granulomas involving skin, mucosa and internal organs, and various autoimmune manifestations (including cytopenias, vitiligo, psoriasis, myasthenia gravis, enteropathy). Immunophenotypically, T-cell and B-cell lymphopenia, hypogammaglobulinemia , abnormal specific antibody production and impaired T-cell function are observed.	The first patient presented at age 2.5 years with multiple facial papulonodular lesions composed of epithelioid cells with a strong lymphocytic infiltrate. She was originally diagnosed with a T-cell lymphoma, but there was a poor response to chemotherapy. Extensive laboratory evaluation showed profound hypogammaglobulinemia, decreased T cells, and defective T-cell function. Bone marrow transplant was successful. The second patient developed severe infections in infancy and later developed skin, tongue, and lung lesions consistent with noninfectious granulomas. Immunophenotyping showed low numbers of B and T cells. Bone marrow transplant was successful. The third patient presented at age 10 years with a history of severe infections and massive splenomegaly. She was found to have hypogammaglobulinemia and defective T-cell function. Noninfectious granulomas were present in the spleen and lungs. None of the patients had a thymus visible on ultrasonography.	NM_000448.2(RAG1):c.256_257delAA ; NM_000448.2(RAG1):c.1682G>A ; NM_000448.2(RAG1):c.940C>T ; NM_000448.2(RAG1):c.2326C>T ; NM_000448.2(RAG1):c.983G>A ; NM_000448.2(RAG1):c.2320G>T ; NM_000448.2(RAG1):c.2814T>G ; NM_000448.2(RAG1):c.2164G>A ; NM_000448.2(RAG1):c.2333G>A ; NM_000448.2(RAG1):c.1681C>T ; NM_000448.2(RAG1):c.256_257delAA ; NM_000448.2(RAG1):c.1682G>A ; NM_000448.2(RAG1):c.940C>T ; NM_000448.2(RAG1):c.2326C>T ; NM_000448.2(RAG1):c.983G>A ; NM_000448.2(RAG1):c.2320G>T ; NM_000448.2(RAG1):c.2814T>G ; NM_000448.2(RAG1):c.2164G>A ; NM_000448.2(RAG1):c.2333G>A ; NM_000448.2(RAG1):c.1681C>T

RAG1	Severe combined immunodeficiency due to complete RAG1/2 deficiency	Omenn syndrome (OS) is an inflammatory condition characterized by erythroderma, desquamation, alopecia, chronic diarrhea, failure to thrive, lymphadenopathy, and hepatosplenomegaly, associated with severe combined immunodeficiency (SCID; see this term).	OS presents during the first year of life with features of SCID including chronic diarrhea, pneumonitis and failure to thrive. In addition, patients present with inflammatory symptoms including lymphadenopathy, hepatosplenomegaly and generalized erythroderma, which may often cause alopecia and loss of eyebrows and eyelashes; protein loss may lead to generalized edema and metabolic disturbances. The signs and symptoms of OS can evolve over time and may not appear simultaneously. Some patients present with some but not all of these symptoms and may be described as having atypical Omenn syndrome. OS may also be associated with syndromic disorders including cartilage-hair hypoplasia (CHH), adenosine deaminase (ADA) deficiency, monosomy 22q11, coloboma of the eye, CHARGE syndrome and ligase 4 deficiency (see these terms).	NM_000448.2(RAG1):c.256_257delAA ; NM_000448.2(RAG1):c.1682G>A ; NM_000448.2(RAG1):c.940C>T ; NM_000448.2(RAG1):c.2326C>T ; NM_000448.2(RAG1):c.983G>A ; NM_000448.2(RAG1):c.2320G>T ; NM_000448.2(RAG1):c.2814T>G ; NM_000448.2(RAG1):c.2164G>A ; NM_000448.2(RAG1):c.2333G>A ; NM_000448.2(RAG1):c.1681C>T ; NM_000448.2(RAG1):c.256_257delAA ; NM_000448.2(RAG1):c.1682G>A ; NM_000448.2(RAG1):c.940C>T ; NM_000448.2(RAG1):c.2326C>T ; NM_000448.2(RAG1):c.983G>A ; NM_000448.2(RAG1):c.2320G>T ; NM_000448.2(RAG1):c.2814T>G ; NM_000448.2(RAG1):c.2164G>A ; NM_000448.2(RAG1):c.2333G>A ; NM_000448.2(RAG1):c.1681C>T

RAG2	Combined immunodeficiency with granulomatosis	Severe combined immunodeficiency due to complete RAG1/2 deficiency is a rare, genetic T-B- severe combined immunodeficiency disorder due to null mutations in recombination activating gene (RAG) 1 and/or RAG2 resulting in less than 1% of wild type V(D)J recombination activity. Patients present with neonatal onset of life-threatening, severe, recurrent infections by opportunistic fungal, viral and bacterial micro-organisms, as well as skin rashes, chronic diarrhea, failure to thrive and fever. Immunologic observations include profound T- and B-cell lymphopenia, normal NK counts and low or absent serum immunoglobulins; some patients may have eosinophilia.	Severe combined immunodeficiency refers to a genetically and clinically heterogeneous group of disorders with defective cellular and humoral immune function. Patients with SCID present in infancy with recurrent, persistent infections by opportunistic organisms, including Candida albicans, Pneumocystis carinii, and cytomegalovirus, among many others. Laboratory analysis shows profound lymphopenia with diminished or absent immunoglobulins. The common characteristic of all types of SCID is absence of T cell-mediated cellular immunity due to a defect in T-cell development. Without treatment, patients usually die within the first year of life. The overall prevalence of all types of SCID is approximately 1 in 75,000 births.	NM_000536.3(RAG2):c.230C>A ; c.601C>T ; NM_000536.3(RAG2):c.115A>G ; NM_001243785.1(RAG2):c.283G>A ; NM_000536.3(RAG2):c.230C>A ; c.601C>T ; NM_000536.3(RAG2):c.115A>G ; NM_001243785.1(RAG2):c.283G>A

RAG2	Omenn syndrome	A rare, genetic, non-severe combined immunodeficiency disease characterized by immunodeficiency (manifested by recurrent and/or severe bacterial and viral infections), destructive noninfectious granulomas involving skin, mucosa and internal organs, and various autoimmune manifestations (including cytopenias, vitiligo, psoriasis, myasthenia gravis, enteropathy). Immunophenotypically, T-cell and B-cell lymphopenia, hypogammaglobulinemia , abnormal specific antibody production and impaired T-cell function are observed.	The first patient presented at age 2.5 years with multiple facial papulonodular lesions composed of epithelioid cells with a strong lymphocytic infiltrate. She was originally diagnosed with a T-cell lymphoma, but there was a poor response to chemotherapy. Extensive laboratory evaluation showed profound hypogammaglobulinemia, decreased T cells, and defective T-cell function. Bone marrow transplant was successful. The second patient developed severe infections in infancy and later developed skin, tongue, and lung lesions consistent with noninfectious granulomas. Immunophenotyping showed low numbers of B and T cells. Bone marrow transplant was successful. The third patient presented at age 10 years with a history of severe infections and massive splenomegaly. She was found to have hypogammaglobulinemia and defective T-cell function. Noninfectious granulomas were present in the spleen and lungs. None of the patients had a thymus visible on ultrasonography.	NM_000536.3(RAG2):c.230C>A ; c.601C>T ; NM_000536.3(RAG2):c.115A>G ; NM_001243785.1(RAG2):c.283G>A ; NM_000536.3(RAG2):c.230C>A ; c.601C>T ; NM_000536.3(RAG2):c.115A>G ; NM_001243785.1(RAG2):c.283G>A
RAG2	Severe combined immunodeficiency due to complete RAG1/2 deficiency	Omenn syndrome (OS) is an inflammatory condition characterized by erythroderma, desquamation, alopecia, chronic diarrhea, failure to thrive, lymphadenopathy, and hepatosplenomegaly, associated with severe combined immunodeficiency (SCID; see this term).	OS presents during the first year of life with features of SCID including chronic diarrhea, pneumonitis and failure to thrive. In addition, patients present with inflammatory symptoms including lymphadenopathy, hepatosplenomegaly and generalized erythroderma, which may often cause alopecia and loss of eyebrows and eyelashes; protein loss may lead to generalized edema and metabolic disturbances. The signs and symptoms of OS can evolve over time and may not appear simultaneously. Some patients present with some but not all of these symptoms and may be described as having atypical Omenn syndrome. OS may also be associated with syndromic disorders including cartilage-hair hypoplasia (CHH), adenosine deaminase (ADA) deficiency, monosomy 22q11, coloboma of the eye, CHARGE syndrome and ligase 4 deficiency (see these terms).	NM_000536.3(RAG2):c.230C>A ; c.601C>T ; NM_000536.3(RAG2):c.115A>G ; NM_001243785.1(RAG2):c.283G>A ; NM_000536.3(RAG2):c.230C>A ; c.601C>T ; NM_000536.3(RAG2):c.115A>G ; NM_001243785.1(RAG2):c.283G>A

RAPSN	Fetal akinesia deformation sequence	Severe combined immunodeficiency due to complete RAG1/2 deficiency is a rare, genetic T-B- severe combined immunodeficiency disorder due to null mutations in recombination activating gene (RAG) 1 and/or RAG2 resulting in less than 1% of wild type V(D)J recombination activity. Patients present with neonatal onset of life-threatening, severe, recurrent infections by opportunistic fungal, viral and bacterial micro-organisms, as well as skin rashes, chronic diarrhea, failure to thrive and fever. Immunologic observations include profound T- and B-cell lymphopenia, normal NK counts and low or absent serum immunoglobulins; some patients may have eosinophilia.	Severe combined immunodeficiency refers to a genetically and clinically heterogeneous group of disorders with defective cellular and humoral immune function. Patients with SCID present in infancy with recurrent, persistent infections by opportunistic organisms, including Candida albicans, Pneumocystis carinii, and cytomegalovirus, among many others. Laboratory analysis shows profound lymphopenia with diminished or absent immunoglobulins. The common characteristic of all types of SCID is absence of T cell-mediated cellular immunity due to a defect in T-cell development. Without treatment, patients usually die within the first year of life. The overall prevalence of all types of SCID is approximately 1 in 75,000 births.	NM_005055.4(RAPSN):c.416T>C ; NM_005055.4(RAPSN):c.484G>A ; NM_005055.4(RAPSN):c.490C>T ; NM_005055.4(RAPSN):c.807C>A ; NM_005055.4(RAPSN):c.566C>T ; NM_005055.4(RAPSN):c.848T>C ; NM_005055.4(RAPSN):c.416T>C ; NM_005055.4(RAPSN):c.484G>A ; NM_005055.4(RAPSN):c.490C>T ; NM_005055.4(RAPSN):c.807C>A ; NM_005055.4(RAPSN):c.566C>T ; NM_005055.4(RAPSN):c.848T>C

RAPSN	Lethal multiple pterygium syndrome	The fetal akinesia/hypokinesia sequence (or Pena-Shokeir syndrome type I) is characterized by multiple joint contractures, facial anomalies and pulmonary hypoplasia. Whatever the cause, the common feature of this sequence is decreased foetal activity.	Failure of normal deglutition results in polyhydramnios, and a lack of movement of the diaphragm and intercostal muscles leads to pulmonary hypoplasia. The lack of normal fetal movement also results in a short umbilical cord and multiple joint contractures. Ulnar deviation of the hands, rocker-bottom feet, camptodactyly, sparse dermal ridges and absence of palmar flexion creases are the other components of the fetal akinesia sequence. The face is expressionless, with hypertelorism, telecanthus and poorly folded, small, and posteriorly angulated ears, and the mouth is small with micrognathia and high-arched palate. Cleft palate and cardiac defects may occur occasionally. Many of these babies are born prematurely, and even when born at term their growth is delayed, they have a short neck and cryptorchidism. If they survive, they are likely to develop short-gut syndrome with malabsorption.	NM_005055.4(RAPSN):c.416T>C ; NM_005055.4(RAPSN):c.484G>A ; NM_005055.4(RAPSN):c.490C>T ; NM_005055.4(RAPSN):c.807C>A ; NM_005055.4(RAPSN):c.566C>T ; NM_005055.4(RAPSN):c.848T>C ; NM_005055.4(RAPSN):c.416T>C ; NM_005055.4(RAPSN):c.484G>A ; NM_005055.4(RAPSN):c.490C>T ; NM_005055.4(RAPSN):c.807C>A ; NM_005055.4(RAPSN):c.566C>T ; NM_005055.4(RAPSN):c.848T>C

RAPSN	Postsynaptic congenital myasthenic syndromes	A rare genetic multiple pterygium syndrome characterized by intrauterine growth retardation, fetal akinesia, multiple joint contractures causing severe arthrogryposis and pterygia (webbing) across multiple joints. Cystic hygroma and/or fetal hydrops are almost invariably present.	Lethal multiple pterygium syndrome (LMPS) is characterized by growth deficiency of prenatal onset, pterygia present in multiple areas (chin to sternum, cervical, axillary, humero-ulnar, crural, popliteal and the ankles) and flexion contractures giving rise to severe arthrogryposis. Subcutaneous edema varies from mildly edematous skin to fetal hydrops with cystic hygroma, lung hypoplasia, and oligo or polyhydramnios. Facial anomalies include hypertelorism, down-slanting palpebral fissures, epicanthic folds, flat nasal root, microretrognathism, microstomia, low-set malformed ears and cleft palate. Other anomalies include a small chest, reduced muscle bulk, cryptorchidism, central nervous system abnormalities (in particular cerebellar hypoplasia, ventricular dilatation and polymicrogyria), hypoplastic dermal ridges and creases, and less frequently a mid-forehead hemangioma, intestinal malrotation, cardiac hypoplasia, diaphragmatic hernia, obstructive uropathy, rocker bottom feet, microcephaly and/or cerebellar and pontine hypoplasia.	NM_005055.4(RAPSN):c.416T>C ; NM_005055.4(RAPSN):c.484G>A ; NM_005055.4(RAPSN):c.490C>T ; NM_005055.4(RAPSN):c.807C>A ; NM_005055.4(RAPSN):c.566C>T ; NM_005055.4(RAPSN):c.848T>C ; NM_005055.4(RAPSN):c.416T>C ; NM_005055.4(RAPSN):c.484G>A ; NM_005055.4(RAPSN):c.490C>T ; NM_005055.4(RAPSN):c.807C>A ; NM_005055.4(RAPSN):c.566C>T ; NM_005055.4(RAPSN):c.848T>C
RDH12	Leber congenital amaurosis	Congenital myasthenic syndrome (CMS) is a group of genetic disorders of impaired neuromuscular transmission at the motor endplate characterized by fatigable muscle weakness.	Congenital myasthenic syndrome associated with AChR deficiency is a disorder of the postsynaptic neuromuscular junction (NMJ) clinically characterized by early-onset muscle weakness with variable severity. Electrophysiologic studies show low amplitude of the miniature endplate potential (MEPP) and current (MEPC) resulting from deficiency of AChR at the endplate. Treatment with cholinesterase inhibitors or amifampridine may be helpful.	NM_152443.2(RDH12):c.146C>T ; NM_152443.2(RDH12):c.565C>T ; NM_152443.2(RDH12):c.379G>T ; NM_152443.2(RDH12):c.184C>T ; NM_152443.2:c.210dupC ; NM_152443.2(RDH12):c.377C>T ; NM_152443.2(RDH12):c.464C>T ; c.448+4_448+7del ; NM_152443.2(RDH12):c.295C>A ; NM_152443.2(RDH12):c.152T>A ; NM_152443.2(RDH12):c.806_810delCCCTG ; NM_152443.2(RDH12):c.451C>A ; NM_152443.2(RDH12):c.451C>G ; NM_152443.2(RDH12):c.523T>C ; NM_152443.2(RDH12):c.677A>G ; NM_152443.2(RDH12):c.146C>T ; NM_152443.2(RDH12):c.565C>T ; NM_152443.2(RDH12):c.379G>T ; NM_152443.2(RDH12):c.184C>T ; NM_152443.2:c.210dupC ; NM_152443.2(RDH12):c.377C>T ; NM_152443.2(RDH12):c.464C>T ; c.448+4_448+7del ; NM_152443.2(RDH12):c.295C>A ; NM_152443.2(RDH12):c.152T>A ; NM_152443.2(RDH12):c.806_810delCCCTG ; NM_152443.2(RDH12):c.451C>A ; NM_152443.2(RDH12):c.451C>G ; NM_152443.2(RDH12):c.523T>C ; NM_152443.2(RDH12):c.677A>G

RDH12	Retinitis pigmentosa	Leber congenital amaurosis (LCA) is a retinal dystrophy defined by blindness and responses to electrophysiological stimulation (Ganzfeld electroretinogram (ERG)) below threshold, associated with severe visual impairment within the first year of life.	LCA is characterized by severely reduced visual acuity (less or equal 20/400) or blindness within in the first year of life. Sluggish pupillary responses, roving eye movement, photophobia, high hyperopia, nystagmus, convergent strabismus, or keratoconus may occur depending on the genetic cause. The Franceschetti's oculo-digital sign, comprising eye poking, pressing, and rubbing is pathognomonic. LCA may be associated with mutations in genes linked to syndromes presenting with neurodevelopmental delay, intellectual disability, oculomotor apraxia-type behavior (difficulty moving the eye) and renal dysfunction.	NM_152443.2(RDH12):c.146C>T ; NM_152443.2(RDH12):c.565C>T ; NM_152443.2(RDH12):c.379G>T ; NM_152443.2(RDH12):c.184C>T ; NM_152443.2:c.210dupC ; NM_152443.2(RDH12):c.377C>T ; NM_152443.2(RDH12):c.464C>T ; c.448+4_448+7del ; NM_152443.2(RDH12):c.295C>A ; NM_152443.2(RDH12):c.152T>A ; NM_152443.2(RDH12):c.806_810delCCCTG ; NM_152443.2(RDH12):c.451C>A ; NM_152443.2(RDH12):c.451C>G ; NM_152443.2(RDH12):c.523T>C ; NM_152443.2(RDH12):c.677A>G ; NM_152443.2(RDH12):c.146C>T ; NM_152443.2(RDH12):c.565C>T ; NM_152443.2(RDH12):c.379G>T ; NM_152443.2(RDH12):c.184C>T ; NM_152443.2:c.210dupC ; NM_152443.2(RDH12):c.377C>T ; NM_152443.2(RDH12):c.464C>T ; c.448+4_448+7del ; NM_152443.2(RDH12):c.295C>A ; NM_152443.2(RDH12):c.152T>A ; NM_152443.2(RDH12):c.806_810delCCCTG ; NM_152443.2(RDH12):c.451C>A ; NM_152443.2(RDH12):c.451C>G ; NM_152443.2(RDH12):c.523T>C ; NM_152443.2(RDH12):c.677A>G
RLBP1	Bothnia retinal dystrophy	Retinitis pigmentosa (RP) is an inherited retinal dystrophy leading to progressive loss of the photoreceptors and retinal pigment epithelium and resulting in blindness usually after several decades.	Retinitis pigmentosa is slowly progressive but relentless. There is however broad variability in age of onset, rate of progression and secondary clinical manifestations. Affected individuals generally first develop night blindness (nyctalopia) due to loss of rod function, often in adolescence or earlier. They then develop peripheral visual field impairment, and over time loss of central vision, usually at late stages, often around midlife. Central visual acuity loss may occur at any age as a result of cystoid macular edema or photoreceptor loss. Posterior subcapsular cataracts are common and severity is age dependent. Reduced color vision may also be found. Fundus examination reveals bone spicule pigment deposits, attenuated retinal vessels, retinal atrophy and waxy optic nerve pallor. Severity is partly correlated with the pattern of inheritance with X-linked cases having the most severe course, autosomal recessive and single occurrence cases having intermediate severity, and autosomal dominant the most favorable course.	c.333T>G ; NM_000326.4(RLBP1):c.700C>T ; NM_000326.4(RLBP1):c.452G>A ; c.333T>G ; NM_000326.4(RLBP1):c.700C>T ; NM_000326.4(RLBP1):c.452G>A

RLBP1	Fundus albipunctatus	Bothnia retinal dystrophy is a rare form of retinal dystrophy, seen mostly in Northern Sweden, presenting in early childhood with night blindness and progressive maculopathy with a decrease in visual acuity, eventually leading to blindness by adulthood. Retinal degeneration, without obvious bone spicule formation, accompanied by affected visual fields and the typical presence of retinitis punctata albescens (see this term) in the posterior pole are also noted.	Patients typically show night blindness from early childhood. In young adults, retinitis punctata albescens is observed, followed by macular degeneration and a decrease in visual acuity that leads to legal blindness in early adulthood. Dark adaptometry and electrophysiologic testing showed an initial loss of rod function followed by progressive reduction of the cone responses in older ages.	c.333T>G ; NM_000326.4(RLBP1):c.700C>T ; NM_000326.4(RLBP1):c.452G>A ; c.333T>G ; NM_000326.4(RLBP1):c.700C>T ; NM_000326.4(RLBP1):c.452G>A
RLBP1	Retinitis pigmentosa	This form of fleck retina disease is characterized by discrete uniform white dots over the entire fundus with greatest density in the midperiphery and no macular involvement. Night blindness occurs.	Fundus albipunctatus is a rare, genetic retinal dystrophy disorder characterized by the presence of numerous small, round, yellowish-white retinal lesions that are distributed throughout the retina but spare the fovea. Patients present in childhood with non-progressive night blindness with prolonged cone and rod adaptation times. The macula may or may not be involved, which may result in a decrease of central visual acuity with age.	c.333T>G ; NM_000326.4(RLBP1):c.700C>T ; NM_000326.4(RLBP1):c.452G>A ; c.333T>G ; NM_000326.4(RLBP1):c.700C>T ; NM_000326.4(RLBP1):c.452G>A

RLBP1	Retinitis punctata albescens	Retinitis pigmentosa (RP) is an inherited retinal dystrophy leading to progressive loss of the photoreceptors and retinal pigment epithelium and resulting in blindness usually after several decades.	Retinitis pigmentosa is slowly progressive but relentless. There is however broad variability in age of onset, rate of progression and secondary clinical manifestations. Affected individuals generally first develop night blindness (nyctalopia) due to loss of rod function, often in adolescence or earlier. They then develop peripheral visual field impairment, and over time loss of central vision, usually at late stages, often around midlife. Central visual acuity loss may occur at any age as a result of cystoid macular edema or photoreceptor loss. Posterior subcapsular cataracts are common and severity is age dependent. Reduced color vision may also be found. Fundus examination reveals bone spicule pigment deposits, attenuated retinal vessels, retinal atrophy and waxy optic nerve pallor. Severity is partly correlated with the pattern of inheritance with X-linked cases having the most severe course, autosomal recessive and single occurrence cases having intermediate severity, and autosomal dominant the most favorable course.	c.333T>G ; NM_000326.4(RLBP1):c.700C>T ; NM_000326.4(RLBP1):c.452G>A ; c.333T>G ; NM_000326.4(RLBP1):c.700C>T ; NM_000326.4(RLBP1):c.452G>A
RPE65	Leber congenital amaurosis	A progressive form of familial flecked retinopathy characterized by white punctata throughout the fundus (but sparing the macula in the early stages). Patients present with nightblindness in childhood and may also experience a loss of visual acuity. Significant loss of vision is reported in the 5th and 6th decades of life.		NM_000329.2(RPE65):c.1087C>A ; NM_000329.2(RPE65):c.907A>T ; NM_000329.2(RPE65):c.271C>T ; NM_000329.2(RPE65):c.1355T>G ; NM_000329.2(RPE65):c.1543C>T ; NM_000329.2(RPE65):c.1292A>G ; c.514_515del ; NM_000329.2(RPE65):c.1022T>C ; NM_000329.2(RPE65):c.1102T>C ; NM_000329.2(RPE65):c.1087C>A ; NM_000329.2(RPE65):c.907A>T ; NM_000329.2(RPE65):c.271C>T ; NM_000329.2(RPE65):c.1355T>G ; NM_000329.2(RPE65):c.1543C>T ; NM_000329.2(RPE65):c.1292A>G ; c.514_515del ; NM_000329.2(RPE65):c.1022T>C ; NM_000329.2(RPE65):c.1102T>C

RPE65	Retinitis pigmentosa	Leber congenital amaurosis (LCA) is a retinal dystrophy defined by blindness and responses to electrophysiological stimulation (Ganzfeld electroretinogram (ERG)) below threshold, associated with severe visual impairment within the first year of life.	LCA is characterized by severely reduced visual acuity (less or equal 20/400) or blindness within in the first year of life. Sluggish pupillary responses, roving eye movement, photophobia, high hyperopia, nystagmus, convergent strabismus, or keratoconus may occur depending on the genetic cause. The Franceschetti's oculo-digital sign, comprising eye poking, pressing, and rubbing is pathognomonic. LCA may be associated with mutations in genes linked to syndromes presenting with neurodevelopmental delay, intellectual disability, oculomotor apraxia-type behavior (difficulty moving the eye) and renal dysfunction.	NM_000329.2(RPE65):c.1087C>A ; NM_000329.2(RPE65):c.907A>T ; NM_000329.2(RPE65):c.271C>T ; NM_000329.2(RPE65):c.1355T>G ; NM_000329.2(RPE65):c.1543C>T ; NM_000329.2(RPE65):c.1292A>G ; c.514_515del ; NM_000329.2(RPE65):c.1022T>C ; NM_000329.2(RPE65):c.1102T>C ; NM_000329.2(RPE65):c.1087C>A ; NM_000329.2(RPE65):c.907A>T ; NM_000329.2(RPE65):c.271C>T ; NM_000329.2(RPE65):c.1355T>G ; NM_000329.2(RPE65):c.1543C>T ; NM_000329.2(RPE65):c.1292A>G ; c.514_515del ; NM_000329.2(RPE65):c.1022T>C ; NM_000329.2(RPE65):c.1102T>C
RPE65	Severe early-childhood-onset retinal dystrophy	Retinitis pigmentosa (RP) is an inherited retinal dystrophy leading to progressive loss of the photoreceptors and retinal pigment epithelium and resulting in blindness usually after several decades.	Retinitis pigmentosa is slowly progressive but relentless. There is however broad variability in age of onset, rate of progression and secondary clinical manifestations. Affected individuals generally first develop night blindness (nyctalopia) due to loss of rod function, often in adolescence or earlier. They then develop peripheral visual field impairment, and over time loss of central vision, usually at late stages, often around midlife. Central visual acuity loss may occur at any age as a result of cystoid macular edema or photoreceptor loss. Posterior subcapsular cataracts are common and severity is age dependent. Reduced color vision may also be found. Fundus examination reveals bone spicule pigment deposits, attenuated retinal vessels, retinal atrophy and waxy optic nerve pallor. Severity is partly correlated with the pattern of inheritance with X-linked cases having the most severe course, autosomal recessive and single occurrence cases having intermediate severity, and autosomal dominant the most favorable course.	NM_000329.2(RPE65):c.1087C>A ; NM_000329.2(RPE65):c.907A>T ; NM_000329.2(RPE65):c.271C>T ; NM_000329.2(RPE65):c.1355T>G ; NM_000329.2(RPE65):c.1543C>T ; NM_000329.2(RPE65):c.1292A>G ; c.514_515del ; NM_000329.2(RPE65):c.1022T>C ; NM_000329.2(RPE65):c.1102T>C ; NM_000329.2(RPE65):c.1087C>A ; NM_000329.2(RPE65):c.907A>T ; NM_000329.2(RPE65):c.271C>T ; NM_000329.2(RPE65):c.1355T>G ; NM_000329.2(RPE65):c.1543C>T ; NM_000329.2(RPE65):c.1292A>G ; c.514_515del ; NM_000329.2(RPE65):c.1022T>C ; NM_000329.2(RPE65):c.1102T>C

RPGRIP1L	Joubert syndrome with hepatic defect	Severe early childhood onset retinal dystrophy (SECORD) is an inherited retinal dystrophy characterized by a severe congenital night blindness, progressive retinal dystrophy and nystagmus. Best corrected visual acuity can reach 0.3 in the first decade of life and can pertain well into the second decade of life. Blindness is often complete by the age of 30 years.	SECORD occurs during childhood and covers patients with severe congenital night blindness, nystagmus, a significantly reduced visual acuity (less or equal than 0.3) along with a progressive panretinal dystrophy of diverse extent and affection of the macula. The first symptoms can be recognized in the first year of life. Color vision is impaired in saturated and desaturated tests. An overlap with Leber congenital amaurosis (LCA) occurs when patients are characterized by their visual acuity and panretinal dystrophy. However, compared to LCA, the visual function in SECORD is much better, despite the progressive loss of visual function early in the disease that can lead to blindness in the second to third decade of life, depending on the underlying gene and mutation.	c.1326_1329del ; NM_015272.4(RPGRIP1L):c.1329dup ; NM_001127897.3(RPGRIP1L):c.394A>T ; NM_015272.4(RPGRIP1L):c.1975T>C ; c.776+1G>A ; NM_001127897.3(RPGRIP1L):c.757C>T ; NM_015272.2(RPGRIP1L):c.1843A>C ; NM_015272.4(RPGRIP1L):c.2050C>T ; c.3394_3397del ; NM_015272.4(RPGRIP1L):c.2794_2795delTT ; NM_015272.4(RPGRIP1L):c.2413C>T ; c.1326_1329del ; NM_015272.4(RPGRIP1L):c.1329dup ; NM_001127897.3(RPGRIP1L):c.394A>T ; NM_015272.4(RPGRIP1L):c.1975T>C ; c.776+1G>A ; NM_001127897.3(RPGRIP1L):c.757C>T ; NM_015272.2(RPGRIP1L):c.1843A>C ; NM_015272.4(RPGRIP1L):c.2050C>T ; c.3394_3397del ; NM_015272.4(RPGRIP1L):c.2794_2795delTT ; NM_015272.4(RPGRIP1L):c.2413C>T
RPGRIP1L	Joubert syndrome with renal defect	Joubert syndrome with hepatic defect is a very rare subtype of Joubert syndrome and related disorders (JSRD, see this term) characterized by the neurological features of JS associated with congenital hepatic fibrosis (CHF).	The age of onset and severity of hepatic manifestations are variable. Some patients may also present chorioretinal or optic nerve colobomas and nephronophthisis (NPH), but these are not mandatory features.	c.1326_1329del ; NM_015272.4(RPGRIP1L):c.1329dup ; NM_001127897.3(RPGRIP1L):c.394A>T ; NM_015272.4(RPGRIP1L):c.1975T>C ; c.776+1G>A ; NM_001127897.3(RPGRIP1L):c.757C>T ; NM_015272.2(RPGRIP1L):c.1843A>C ; NM_015272.4(RPGRIP1L):c.2050C>T ; c.3394_3397del ; NM_015272.4(RPGRIP1L):c.2794_2795delTT ; NM_015272.4(RPGRIP1L):c.2413C>T ; c.1326_1329del ; NM_015272.4(RPGRIP1L):c.1329dup ; NM_001127897.3(RPGRIP1L):c.394A>T ; NM_015272.4(RPGRIP1L):c.1975T>C ; c.776+1G>A ; NM_001127897.3(RPGRIP1L):c.757C>T ; NM_015272.2(RPGRIP1L):c.1843A>C ; NM_015272.4(RPGRIP1L):c.2050C>T ; c.3394_3397del ; NM_015272.4(RPGRIP1L):c.2794_2795delTT ; NM_015272.4(RPGRIP1L):c.2413C>T
RPGRIP1L	Meckel syndrome	Joubert syndrome with renal defect is a rare subtype of Joubert syndrome and related disorders (JSRD, see this term) characterized by the neurological features of JS associated with renal disease, in the absence of retinopathy.	In most cases, renal disease manifests as juvenile nephronophthisis, with onset of clinical symptoms in the late first/early second decade of life, although in rare cases there may be infantile NPH, with onset in the first years of life.	c.1326_1329del ; NM_015272.4(RPGRIP1L):c.1329dup ; NM_001127897.3(RPGRIP1L):c.394A>T ; NM_015272.4(RPGRIP1L):c.1975T>C ; c.776+1G>A ; NM_001127897.3(RPGRIP1L):c.757C>T ; NM_015272.2(RPGRIP1L):c.1843A>C ; NM_015272.4(RPGRIP1L):c.2050C>T ; c.3394_3397del ; NM_015272.4(RPGRIP1L):c.2794_2795delTT ; NM_015272.4(RPGRIP1L):c.2413C>T ; c.1326_1329del ; NM_015272.4(RPGRIP1L):c.1329dup ; NM_001127897.3(RPGRIP1L):c.394A>T ; NM_015272.4(RPGRIP1L):c.1975T>C ; c.776+1G>A ; NM_001127897.3(RPGRIP1L):c.757C>T ; NM_015272.2(RPGRIP1L):c.1843A>C ; NM_015272.4(RPGRIP1L):c.2050C>T ; c.3394_3397del ; NM_015272.4(RPGRIP1L):c.2794_2795delTT ; NM_015272.4(RPGRIP1L):c.2413C>T

SACS	Autosomal recessive spastic ataxia of Charlevoix-Saguenay	A rare, lethal, genetic, multiple congenital anomaly disorder characterized by the triad of brain malformation (mainly occipital encephalocele), large polycystic kidneys, and polydactyly, as well as associated abnormalities that may include cleft lip/palate, cardiac and genital anomalies, central nervous system (CNS) malformations, liver fibrosis, and bone dysplasia.	Fetuses affected by Meckel syndrome (MKS) survive only a few days to a few weeks at the most, or dieÃ in utero. The main CNS features include occipital encephalocele, hydrocephalus, anencephaly, holoprosencephaly, as well as Dandy-Walker. Large polycystic kidneys with cystic dysplasia are a constant feature of Meckel syndrome. Hepatic dysgenesis and liver fibrosis are frequent. Polydactyly may affect all four extremities and is typically postaxial (80%) or very rarely preaxial. Affected individuals have pulmonary hypoplasia secondary to oligohydramnios. Cleft lip and palate, microphthalmia and micrognathia may be observed. Cardiac malformations may include atrial septal defect, aorta coarctation, patent arterial duct, and valvular pulmonary stenosis. Incomplete development of internal and external genitalia, and cryptorchidism in males are common.	c.994A>T ; c.13237C>T ; NM_014363.5(SACS):c.8844delT ; c.6563T>A ; NM_014363.5(SACS):c.7504C>T ; NM_014363.5(SACS):c.6355C>T ; c.4933C>T ; NM_014363.5(SACS):c.5618_5619del ; NM_014363.5(SACS):c.12160C>T ; NC_000013.11:g.23358422G>A ; c.3198T>A ; c.994A>T ; c.13237C>T ; NM_014363.5(SACS):c.8844delT ; c.6563T>A ; NM_014363.5(SACS):c.7504C>T ; NM_014363.5(SACS):c.6355C>T ; c.4933C>T ; NM_014363.5(SACS):c.5618_5619del ; NM_014363.5(SACS):c.12160C>T ; NC_000013.11:g.23358422G>A ; c.3198T>A

SBDS	Idiopathic aplastic anemia	Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) is a neurodegenerative disorder characterised by early-onset cerebellar ataxia with spasticity, a pyramidal syndrome and peripheral neuropathy.	The age of onset in non-Quebec patients is variable (ranging from late infantile, juvenile to early-adult onset) but in individuals from Quebec, onset occurs between 12 and 18 months of age with gait disturbance and walking difficulties. Other early signs of cerebellar ataxia include dysarthria and nystagmus. The spasticity is progressive and eventually dominates the clinical picture. The pyramidal syndrome is characterised by brisk patellar tendon reflexes and the Babinski sign. Onset of the peripheral neuropathy generally occurs later and leads to absence of the Achilles tendon reflex, distal amyotrophy and deep sensory disturbances (impaired vibration sense). Retinal hypermyelination (without vision loss) is a constant feature in ARSACS patients from Quebec but may be absent in patients from other countries. Lack of leg spasticity has been reported in some Japanese families and intellectual deficit may be a feature in some non-Quebec patients. Other manifestations may include mitral valve prolapse,Â pes cavus, and bladder dysfunction.	NM_016038.2(SBDS):c.184A>T ; NM_016038.3(SBDS):c.120del ; NM_016038.2(SBDS):c.183_184delTAinsCT ; NM_016038.2(SBDS):c.258+2T>C ; NM_016038.3(SBDS):c.377G>C ; NM_016038.3(SBDS):c.652C>T ; NM_016038.2(SBDS):c.184A>T ; NM_016038.3(SBDS):c.120del ; NM_016038.2(SBDS):c.183_184delTAinsCT ; NM_016038.2(SBDS):c.258+2T>C ; NM_016038.3(SBDS):c.377G>C ; NM_016038.3(SBDS):c.652C>T
SBDS	Shwachman-Diamond syndrome	0	Aplastic anemia is a serious disorder of the bone marrow that affects between 2 and 5 persons per million per year. About 75% of these cases are classified as idiopathic. In about 15% of cases a drug or infection can be identified that precipitates the aplasia, although why only some individuals are susceptible is unclear. In about 5 to 10% of patients, the aplastic anemia is constitutional--i.e., is familial or presents with one or more associated somatic abnormalities.	NM_016038.2(SBDS):c.184A>T ; NM_016038.3(SBDS):c.120del ; NM_016038.2(SBDS):c.183_184delTAinsCT ; NM_016038.2(SBDS):c.258+2T>C ; NM_016038.3(SBDS):c.377G>C ; NM_016038.3(SBDS):c.652C>T ; NM_016038.2(SBDS):c.184A>T ; NM_016038.3(SBDS):c.120del ; NM_016038.2(SBDS):c.183_184delTAinsCT ; NM_016038.2(SBDS):c.258+2T>C ; NM_016038.3(SBDS):c.377G>C ; NM_016038.3(SBDS):c.652C>T

SERPINA1	Alpha-1-antitrypsin deficiency	Shwachman-Diamond syndrome (SDS) is a rare multisystemic syndrome characterized by chronic and usually mild neutropenia, pancreatic exocrine insufficiency associated with steatorrhea and growth failure, skeletal dysplasia with short stature, and an increased risk of bone marrow aplasia or leukemic transformation.	SDS shows a variable clinical picture, even within families. It generally manifests during infancy or early childhood. The most common anomaly is usually intermittent and moderate neutropenia that is associated with recurrent infections. Mild anemia and thrombocytopenia may also occur. Exocrine pancreatic insufficiency results in failure to thrive, growth retardation, and chronic steatorrhea. Bone involvement is characterized by delayed bone age and maturation with metaphyseal dysplasia resulting in short stature,Â pectus carinatum, and generalized osteopenia. Other features include cutaneous (e.g. eczema or ichthyosis) and dental anomalies, and psychomotor retardation. Mild or severe intellectual disability (50% of patients) causes learning difficulties. Hematologic manifestations may be complicated by bone marrow aplasia, acute myeloid leukemia or a myelodysplastic syndrome (see these terms). In the neonatal period there are generally no symptoms observed but some cases were reported with pancytopenia, respiratory distress, and severe spondylometaphyseal dysplasia (see this term).	NM_001127701.1(SERPINA1):c.415G>A ; NM_001127701.1(SERPINA1):c.839A>T ; NM_001127701.1(SERPINA1):c.272G>A ; NM_001127701.1(SERPINA1):c.194T>C ; NM_001127701.1(SERPINA1):c.187C>T ; NM_001127701.1(SERPINA1):c.230C>T ; NM_001127701.1(SERPINA1):c.347T>A ; NM_001127701.1(SERPINA1):c.415G>A ; NM_001127701.1(SERPINA1):c.839A>T ; NM_001127701.1(SERPINA1):c.272G>A ; NM_001127701.1(SERPINA1):c.194T>C ; NM_001127701.1(SERPINA1):c.187C>T ; NM_001127701.1(SERPINA1):c.230C>T ; NM_001127701.1(SERPINA1):c.347T>A

SERPINA1	Hemorrhagic disease due to alpha-1-antitrypsin Pittsburgh mutation	A rare hereditary, metabolic disease characterized by serum levels of alpha-1-antitrypsin (AAT) that are well below the normal range. In the most severe form, the disease can clinically manifest with chronic liver disorders (cirrhosis, fibrosis), respiratory disorders (emphysema, bronchiectasis), and rarely panniculitis or vasculitis.	The severe form, caused by homozygous Z variant in the geneÂ SERPINA1, is the most clinically relevant and referred to here as Z-AATD. Z-AATD has an extraordinary heterogeneous disease course. Some individuals remain healthy, while others develop a severe lung or liver disease, rarely both. The age of onset is variable in Z-AATD, liver disease presents typically in newborn/early childhood age or later on in adult life (typically at â‰¥ 40 years of age). Z-AATD can lead to neonatal cholestasis in about 10 % of the affected infants and about 30-50% of these will develop chronic progressive liver disease. About 10% of adults develop liver cirrhosis. Onset of lung disease is generally between 20 and 50 years of age. The main pulmonary manifestations include early onset panacinar emphysema, bronchiectasis, bronchial asthma or vasculitis presenting with persistent, dyspnea, cough, wheezing, and production of sputum. Smoking is a major factor affecting the course of the pulmonary manifestations, and is associated with earlier onset. Other features include weight loss, recurrent respiratory infections, and fatigue. Panniculitis of variable severity and developing at any age is a rare disease manifestation. A strongly increased risk of developing liver cirrhosis and hepatocellular carcinoma has been reported. The course may be severe in the absence of appropriate treatment and continued tobacco smoking.	NM_001127701.1(SERPINA1):c.415G>A ; NM_001127701.1(SERPINA1):c.839A>T ; NM_001127701.1(SERPINA1):c.272G>A ; NM_001127701.1(SERPINA1):c.194T>C ; NM_001127701.1(SERPINA1):c.187C>T ; NM_001127701.1(SERPINA1):c.230C>T ; NM_001127701.1(SERPINA1):c.347T>A ; NM_001127701.1(SERPINA1):c.415G>A ; NM_001127701.1(SERPINA1):c.839A>T ; NM_001127701.1(SERPINA1):c.272G>A ; NM_001127701.1(SERPINA1):c.194T>C ; NM_001127701.1(SERPINA1):c.187C>T ; NM_001127701.1(SERPINA1):c.230C>T ; NM_001127701.1(SERPINA1):c.347T>A

SGCA	Alpha-sarcoglycan-related limb-girdle muscular dystrophy R3	Alpha-1-antitrypsin deficiency is an autosomal recessive disorder. The most common manifestation is emphysema, which becomes evident by the third to fourth decade. A less common manifestation of the deficiency is liver disease, which occurs in children and adults, and may result in cirrhosis and liver failure. Environmental factors, particularly cigarette smoking, greatly increase the risk of emphysema at an earlier age.	Hemorrhagic disease due to alpha-1-antitrypsin Pittsburg mutation is a rare, genetic, constitutional coagulation factor defect disorder characterized by a bleeding tendancy of variable severity due to methionine 358 to arginine replacement (Pittsburgh mutation) in the alpha-1-antitrypsin protein. Patients present with spontaneous hematomas, hematomas following minor trauma or surgery and, in female patients, ovarian hematomas after ovulation.	NM_000023.2(SGCA):c.850C>T ; c.903_904dup ; NM_000023.3(SGCA):c.518T>C ; NM_000023.3(SGCA):c.574C>T ; NM_000023.3(SGCA):c.229C>T ; NM_000023.3(SGCA):c.371T>C ; NM_000023.3(SGCA):c.739G>A ; NM_000023.3(SGCA):c.101G>A ; NM_000023.2(SGCA):c.850C>T ; c.903_904dup ; NM_000023.3(SGCA):c.518T>C ; NM_000023.3(SGCA):c.574C>T ; NM_000023.3(SGCA):c.229C>T ; NM_000023.3(SGCA):c.371T>C ; NM_000023.3(SGCA):c.739G>A ; NM_000023.3(SGCA):c.101G>A
SGCB	Beta-sarcoglycan-related limb-girdle muscular dystrophy R4	A subtype of autosomal recessive limb-girdle muscular dystrophy characterized by childhood onset of progressive proximal weakness of the shoulder and pelvic girdle muscles, resulting in difficulty walking, scapular winging, calf hypertrophy and contractures of the Achilles tendon, which lead to a tiptoe gait pattern. Cardiac and respiratory involvement is rare.	Autosomal recessive limb-girdle muscular dystrophy-3 affects mainly the proximal muscles and results in difficulty walking. Most individuals have onset in childhood; the disorder is progressive. Other features may include scapular winging, calf pseudohypertrophy, and contractures. Cardiomyopathy has rarely been reported.	NM_000232.4(SGCB):c.341C>T ; NM_000232.4(SGCB):c.272G>T ; NM_000232.4(SGCB):c.299T>A ; NM_000232.4(SGCB):c.552T>G ; NM_000232.4(SGCB):c.452C>G ; NM_000232.4(SGCB):c.272G>C ; NM_000232.4(SGCB):c.323T>G ; NM_000232.4(SGCB):c.341C>T ; NM_000232.4(SGCB):c.272G>T ; NM_000232.4(SGCB):c.299T>A ; NM_000232.4(SGCB):c.552T>G ; NM_000232.4(SGCB):c.452C>G ; NM_000232.4(SGCB):c.272G>C ; NM_000232.4(SGCB):c.323T>G

SGCG	Gamma-sarcoglycan-related limb-girdle muscular dystrophy R5	A subtype of autosomal recessive limb girdle muscular dystrophy characterized by a childhood to adolescent onset of progressive pelvic- and shoulder-girdle muscle weakness, particularly affecting the pelvic girdle (adductors and flexors of hip). Usually the knees are the earliest and most affected muscles. In advanced stages, involvement of the shoulder girdle (resulting in scapular winging) and the distal muscle groups are observed. Calf hypertrophy, cardiomyopathy, respiratory impairment, tendon contractures, scoliosis, and exercise-induced myoglobinuria may be observed.	All patients presented with proximal symmetric weakness and atrophy of the limb and trunk muscles. The average age at onset was 7.6 years (range 4 to 12), and loss of walking occurred between 12 and 38 years. Calf hypertrophy was also observed. There was marked intrafamilial variability.	NM_000231.2(SGCG):c.787G>A ; c.505+1G>A ; NM_000152.5:c.525delT ; c.89del ; NM_000231.2(SGCG):c.848G>A ; NM_000231.2(SGCG):c.195+4_195+7delAGTA ; NM_000231.2(SGCG):c.787G>A ; c.505+1G>A ; NM_000152.5:c.525delT ; c.89del ; NM_000231.2(SGCG):c.848G>A ; NM_000231.2(SGCG):c.195+4_195+7delAGTA
SGSH	Sanfilippo syndrome type A	A subtype of autosomal recessive limb-girdle muscular dystrophy characterized by a childhood onset of progressive shoulder and pelvic girdle muscle weakness and atrophy frequently associated with calf hypertrophy, diaphragmatic weakness, and/or variable cardiac abnormalities. Mild to moderate elevated serum creatine kinase levels and positive Gowers sign are reported.	Duchenne muscular dystrophy is caused by mutation in the dystrophin gene on the X chromosome. Dystrophin is associated with a large oligomeric complex of sarcolemmal glycoproteins, the dystrophin-glycoprotein complex, which spans the sarcolemma to provide a link between the subsarcolemmal cytoskeleton and the extracellular matrix component, laminin. In DMD, the absence of dystrophin leads to a large reduction in all of the dystrophin-associated proteins.	c.466A>T ; c.320del ; NM_000199.4(SGSH):c.364G>A ; NM_000199.3(SGSH):c.220C>T ; NM_000199.3:c.337_345delinsGCACAGGTGAG ; NM_000199.3(SGSH):c.892T>C ; NM_000199.3(SGSH):c.617G>C ; NM_000199.3(SGSH):c.130G>A ; NM_000199.3(SGSH):c.877C>T ; NM_000199.3(SGSH):c.197C>G ; NM_000199.3(SGSH):c.449G>A ; NM_000199.3(SGSH):c.1298G>A ; NM_000199.3(SGSH):c.383C>T ; NM_000199.3(SGSH):c.1339G>A ; NM_000199.3(SGSH):c.235A>C ; NM_000199.4(SGSH):c.1167C>A ; c.757del ; NM_000199.4(SGSH):c.1380del ; c.466A>T ; c.320del ; NM_000199.4(SGSH):c.364G>A ; NM_000199.3(SGSH):c.220C>T ; NM_000199.3:c.337_345delinsGCACAGGTGAG ; NM_000199.3(SGSH):c.892T>C ; NM_000199.3(SGSH):c.617G>C ; NM_000199.3(SGSH):c.130G>A ; NM_000199.3(SGSH):c.877C>T ; NM_000199.3(SGSH):c.197C>G ; NM_000199.3(SGSH):c.449G>A ; NM_000199.3(SGSH):c.1298G>A ; NM_000199.3(SGSH):c.383C>T ; NM_000199.3(SGSH):c.1339G>A ; NM_000199.3(SGSH):c.235A>C ; NM_000199.4(SGSH):c.1167C>A ; c.757del ; NM_000199.4(SGSH):c.1380del

SLC12A6	Corpus callosum agenesis-neuronopathy syndrome	0	The Sanfilippo syndrome, or mucopolysaccharidosis III, is an autosomal recessive lysosomal storage disease due to impaired degradation of heparan sulfate. The disorder is characterized by severe central nervous system degeneration, but only mild somatic disease. Onset of clinical features usually occurs between 2 and 6 years; severe neurologic degeneration occurs in most patients between 6 and 10 years of age, and death occurs typically during the second or third decade of life. Type A has been reported to be the most severe, with earlier onset and rapid progression of symptoms and shorter survival.	c.213T>G ; c.163+1G>A ; NM_133647.1(SLC12A6):c.1584_1585delCTinsG ; NM_133647.1(SLC12A6):c.3031C>T ; NM_133647.1(SLC12A6):c.2023C>T ; c.213T>G ; c.163+1G>A ; NM_133647.1(SLC12A6):c.1584_1585delCTinsG ; NM_133647.1(SLC12A6):c.3031C>T ; NM_133647.1(SLC12A6):c.2023C>T
SLC17A5	Free sialic acid storage disease, infantile form	Andermann syndrome is an autosomal recessive motor and sensory neuropathy with agenesis of the corpus callosum associated with developmental and neurodegenerative defects and dysmorphic features.	Corpus callosum agenesis-neuronopathy syndrome is a neurodegenerative disorder characterized by severe progressive sensorimotor neuropathy beginning in infancy with resulting hypotonia, areflexia, amyotrophy and variable degrees of dysgenesis of the corpus callosum. Additional features include mild-to-severe intellectual and developmental delays, and psychiatric manifestations that include paranoid delusions, depression, hallucinations, and 'autistic-like' features. Affected individuals are usually wheelchair restricted in the second decade of life and die in the third decade of life. The disease is inherited as an autosomal recessive trait.	NM_012434.4(SLC17A5):c.406A>G ; NM_012434.4(SLC17A5):c.43G>T ; NM_012434.4(SLC17A5):c.1259+1G>A ; NM_012434.4(SLC17A5):c.918T>G ; NM_012434.4(SLC17A5):c.115C>T ; NM_012434.4(SLC17A5):c.406A>G ; NM_012434.4(SLC17A5):c.43G>T ; NM_012434.4(SLC17A5):c.1259+1G>A ; NM_012434.4(SLC17A5):c.918T>G ; NM_012434.4(SLC17A5):c.115C>T

SLC17A5	Intermediate severe Salla disease	Free sialic acid storage disease (free SASD), is a group of lysosomal storage diseases characterized by a spectrum of clinical manifestations including neurological and developmental disorders with severity ranging from the milder phenotype, Salla disease (SD), to the most severe phenotype, infantile free sialic acid storage disease (ISSD).	Sialic acid storage diseases are autosomal recessive neurodegenerative disorders that may present as a severe infantile form (ISSD) or as a slowly progressive adult form that is prevalent in Finland (Salla disease). The main symptoms are hypotonia, cerebellar ataxia, and mental retardation; visceromegaly and coarse features are also present in the infantile cases. Progressive cerebellar atrophy and dysmyelination have been documented by MRI. Enlarged lysosomes are seen on electron microscopic studies, and patients excrete large amounts of free sialic acid in the urine.	NM_012434.4(SLC17A5):c.406A>G ; NM_012434.4(SLC17A5):c.43G>T ; NM_012434.4(SLC17A5):c.1259+1G>A ; NM_012434.4(SLC17A5):c.918T>G ; NM_012434.4(SLC17A5):c.115C>T ; NM_012434.4(SLC17A5):c.406A>G ; NM_012434.4(SLC17A5):c.43G>T ; NM_012434.4(SLC17A5):c.1259+1G>A ; NM_012434.4(SLC17A5):c.918T>G ; NM_012434.4(SLC17A5):c.115C>T
SLC17A5	Salla disease	Free sialic acid storage disease (free SASD), is a group of lysosomal storage diseases characterized by a spectrum of clinical manifestations including neurological and developmental disorders with severity ranging from the milder phenotype, Salla disease (SD), to the most severe phenotype, infantile free sialic acid storage disease (ISSD).	Sialic acid storage diseases are autosomal recessive neurodegenerative disorders that may present as a severe infantile form (ISSD) or as a slowly progressive adult form that is prevalent in Finland (Salla disease). The main symptoms are hypotonia, cerebellar ataxia, and mental retardation; visceromegaly and coarse features are also present in the infantile cases. Progressive cerebellar atrophy and dysmyelination have been documented by MRI. Enlarged lysosomes are seen on electron microscopic studies, and patients excrete large amounts of free sialic acid in the urine.	NM_012434.4(SLC17A5):c.406A>G ; NM_012434.4(SLC17A5):c.43G>T ; NM_012434.4(SLC17A5):c.1259+1G>A ; NM_012434.4(SLC17A5):c.918T>G ; NM_012434.4(SLC17A5):c.115C>T ; NM_012434.4(SLC17A5):c.406A>G ; NM_012434.4(SLC17A5):c.43G>T ; NM_012434.4(SLC17A5):c.1259+1G>A ; NM_012434.4(SLC17A5):c.918T>G ; NM_012434.4(SLC17A5):c.115C>T

SLC25A13	Citrullinemia type II	Free sialic acid storage disease (free SASD), is a group of lysosomal storage diseases characterized by a spectrum of clinical manifestations including neurological and developmental disorders with severity ranging from the milder phenotype, Salla disease (SD), to the most severe phenotype, infantile free sialic acid storage disease (ISSD).	Sialic acid storage diseases are autosomal recessive neurodegenerative disorders that may present as a severe infantile form (ISSD) or as a slowly progressive adult form that is prevalent in Finland (Salla disease). The main symptoms are hypotonia, cerebellar ataxia, and mental retardation; visceromegaly and coarse features are also present in the infantile cases. Progressive cerebellar atrophy and dysmyelination have been documented by MRI. Enlarged lysosomes are seen on electron microscopic studies, and patients excrete large amounts of free sialic acid in the urine.	NM_014251.2(SLC25A13):c.1799dupA ; NM_014251.2(SLC25A13):c.615+1G>C ; NM_014251.2(SLC25A13):c.615+5G>A ; NM_014251.2(SLC25A13):c.674C>A ; c.1231-1G>A ; NM_014251.2(SLC25A13):c.1311+1G>A ; c.1411_1412del ; NM_014251.2(SLC25A13):c.1078C>T ; NM_014251.2(SLC25A13):c.1592G>A ; NM_014251.2(SLC25A13):c.1801G>T ; NM_014251.2(SLC25A13):c.852_855delTATG ; NM_014251.2(SLC25A13):c.1801G>A ; NM_014251.2(SLC25A13):c.1813C>T ; NM_014251.2(SLC25A13):c.1177+1G>A ; NM_014251.2(SLC25A13):c.1799dupA ; NM_014251.2(SLC25A13):c.615+1G>C ; NM_014251.2(SLC25A13):c.615+5G>A ; NM_014251.2(SLC25A13):c.674C>A ; c.1231-1G>A ; NM_014251.2(SLC25A13):c.1311+1G>A ; c.1411_1412del ; NM_014251.2(SLC25A13):c.1078C>T ; NM_014251.2(SLC25A13):c.1592G>A ; NM_014251.2(SLC25A13):c.1801G>T ; NM_014251.2(SLC25A13):c.852_855delTATG ; NM_014251.2(SLC25A13):c.1801G>A ; NM_014251.2(SLC25A13):c.1813C>T ; NM_014251.2(SLC25A13):c.1177+1G>A
SLC25A13	Neonatal intrahepatic cholestasis due to citrin deficiency	A severe subtype of citrin deficiency characterized clinically by adult onset (20 and 50 years of age), recurrent episodes of hyperammonemia and associated neuropsychiatric symptoms such as nocturnal delirium, confusion, restlessness, disorientation, drowsiness, memory loss, abnormal behavior (aggression, irritability, and hyperactivity), seizures, and coma.	Adult-onset type II citrullinemia is an autosomal recessive metabolic disorder characterized clinically by the sudden onset of various neuropsychologic symptoms such as disorientation, abnormal behavior, convulsions, and coma due to hyperammonemia. In some cases, rapid progression can lead to brain edema and death if liver transplantation is not possible. Some patients may present with nonalcoholic hepatic steatosis or may develop hepatic fibrosis or hepatocellular carcinoma. Patients with this disorder have a natural aversion to carbohydrates and favor protein, which is in contrast to protein aversion usually observed in patients with urea cycle defects.	NM_014251.2(SLC25A13):c.1799dupA ; NM_014251.2(SLC25A13):c.615+1G>C ; NM_014251.2(SLC25A13):c.615+5G>A ; NM_014251.2(SLC25A13):c.674C>A ; c.1231-1G>A ; NM_014251.2(SLC25A13):c.1311+1G>A ; c.1411_1412del ; NM_014251.2(SLC25A13):c.1078C>T ; NM_014251.2(SLC25A13):c.1592G>A ; NM_014251.2(SLC25A13):c.1801G>T ; NM_014251.2(SLC25A13):c.852_855delTATG ; NM_014251.2(SLC25A13):c.1801G>A ; NM_014251.2(SLC25A13):c.1813C>T ; NM_014251.2(SLC25A13):c.1177+1G>A ; NM_014251.2(SLC25A13):c.1799dupA ; NM_014251.2(SLC25A13):c.615+1G>C ; NM_014251.2(SLC25A13):c.615+5G>A ; NM_014251.2(SLC25A13):c.674C>A ; c.1231-1G>A ; NM_014251.2(SLC25A13):c.1311+1G>A ; c.1411_1412del ; NM_014251.2(SLC25A13):c.1078C>T ; NM_014251.2(SLC25A13):c.1592G>A ; NM_014251.2(SLC25A13):c.1801G>T ; NM_014251.2(SLC25A13):c.852_855delTATG ; NM_014251.2(SLC25A13):c.1801G>A ; NM_014251.2(SLC25A13):c.1813C>T ; NM_014251.2(SLC25A13):c.1177+1G>A

SLC25A15	Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome	A mild subtype of citrin deficiency characterized clinically by low birth weight, failure to thrive, transient intrahepatic cholestasis, multiple aminoacidemia, galactosemia, hypoproteinemia, hepatomegaly, decreased coagulation factors, hemolytic anemia, variable but mostly mild liver dysfunction, and hypoglycemia.	Neonatal intrahepatic cholestasis caused by citrin deficiency (NICCD) is an autosomal recessive metabolic disorder characterized by poor growth, intrahepatic cholestasis, and increased serum citrulline. Most patients show spontaneous improvement by 1 year of age. However, some patients may have a progressive course with continued failure to thrive and dyslipidemia caused by citrin deficiency (FTTDCD), and some may develop chronic or fatal liver disease.	NM_014252.3(SLC25A15):c.535C>T ; NM_014252.3(SLC25A15):c.212T>A ; NM_014252.3(SLC25A15):c.538G>A ; NM_014252.3(SLC25A15):c.562_564delTTC ; NM_014252.3(SLC25A15):c.824G>A ; NM_014252.3(SLC25A15):c.569G>A ; NM_014252.3(SLC25A15):c.110T>G ; NM_014252.3(SLC25A15):c.658G>A ; NM_014252.3(SLC25A15):c.815C>T ; NM_014252.3(SLC25A15):c.535C>T ; NM_014252.3(SLC25A15):c.212T>A ; NM_014252.3(SLC25A15):c.538G>A ; NM_014252.3(SLC25A15):c.562_564delTTC ; NM_014252.3(SLC25A15):c.824G>A ; NM_014252.3(SLC25A15):c.569G>A ; NM_014252.3(SLC25A15):c.110T>G ; NM_014252.3(SLC25A15):c.658G>A ; NM_014252.3(SLC25A15):c.815C>T
SLC26A2	Achondrogenesis type 1B	A rare, genetic disorder of urea cycle metabolism characterized by either a neonatal-onset with manifestations of lethargy, poor feeding, vomiting and tachypnea or, more commonly, presentations in infancy, childhood or adulthood with chronic neurocognitive deficits, acute encephalopathy and/or coagulation defects or other chronic liver dysfunction.	Age of onset can range from the neonatal period to adulthood and a wide phenotypic spectrum is noted. The neonatal presentation usually begins a few days after birth with lethargy, somnolence, refusal to feed, vomiting, tachypnea with respiratory alkalosis, and/or seizures. Onset of symptoms (ranging from mild to severe) in the majority of patients occurs in infancy, childhood and adulthood with episodes of confusion, forgetfulness, hyperammonemic coma, intellectual disability, developmental delay, spastic paraplegia, cerebellar ataxia, learning difficulties, unexplained seizures, liver dysfunction (rarely failure) and coagulopathy with factor VII-, IX- and X-deficiencies. An aversion to protein-rich foods before diagnosis is often reported.	NM_000112.3(SLC26A2):c.1535C>A ; NM_000112.3(SLC26A2):c.496G>A ; c.833del ; NM_000112.3(SLC26A2):c.532C>T ; NM_000112.3(SLC26A2):c.2033G>T ; c.1878del ; NM_000112.3(SLC26A2):c.1020_1022delTGT ; NM_000112.3(SLC26A2):c.835C>T ; NM_000112.3(SLC26A2):c.1273A>G ; NM_000112.3(SLC26A2):c.1957T>A ; NM_000112.3(SLC26A2):c.1724delA ; NM_000112.3(SLC26A2):c.1361A>C ; NM_000112.3(SLC26A2):c.1535C>A ; NM_000112.3(SLC26A2):c.496G>A ; c.833del ; NM_000112.3(SLC26A2):c.532C>T ; NM_000112.3(SLC26A2):c.2033G>T ; c.1878del ; NM_000112.3(SLC26A2):c.1020_1022delTGT ; NM_000112.3(SLC26A2):c.835C>T ; NM_000112.3(SLC26A2):c.1273A>G ; NM_000112.3(SLC26A2):c.1957T>A ; NM_000112.3(SLC26A2):c.1724delA ; NM_000112.3(SLC26A2):c.1361A>C

SLC26A2	Atelosteogenesis type II	A rare, lethal type of achondrogenesis characterized by severe micromelia with very short fingers and toes, a flat face, a short neck, thickened soft tissue around the neck, hypoplasia of the thorax, protuberant abdomen, a hydropic fetal appearance and distinctive histological features of the cartilage.	In a patient considered to have achondrogenesis type IB,Â it wasÂ found that cartilage extracts showed a reduced content of proteoglycans and that unlike control cartilage they did not stain with toluidine blue and did not bind to DEAE. Impaired synthesis of sulfated proteoglycans was observed in fibroblast cultures from the patient. Radioactive labeling and immunoprecipitation studies indicated that core protein and side chains of proteoglycans were synthesized normally but were not sulfated. Analysis of sulfate metabolism in cultured fibroblasts in the patient's cells showed normal intracellular levels of free sulfate but markedly reduced levels of the 2 intermediate compounds in the sulfate activation pathway, adenosine-phosphosulfate and phosphoadenosine-phosphosulfate.Â IT wasÂ suggested that the results can be explained by deficient activity of one of the enzymes responsible for the biologic activation of sulfate, possibly similar to that observed in cartilage (but not in skin) of the recessive, nonlethal mouse mutant 'brachymorphic' and leading to defective sulfation of macromolecules	NM_000112.3(SLC26A2):c.1535C>A ; NM_000112.3(SLC26A2):c.496G>A ; c.833del ; NM_000112.3(SLC26A2):c.532C>T ; NM_000112.3(SLC26A2):c.2033G>T ; c.1878del ; NM_000112.3(SLC26A2):c.1020_1022delTGT ; NM_000112.3(SLC26A2):c.835C>T ; NM_000112.3(SLC26A2):c.1273A>G ; NM_000112.3(SLC26A2):c.1957T>A ; NM_000112.3(SLC26A2):c.1724delA ; NM_000112.3(SLC26A2):c.1361A>C ; NM_000112.3(SLC26A2):c.1535C>A ; NM_000112.3(SLC26A2):c.496G>A ; c.833del ; NM_000112.3(SLC26A2):c.532C>T ; NM_000112.3(SLC26A2):c.2033G>T ; c.1878del ; NM_000112.3(SLC26A2):c.1020_1022delTGT ; NM_000112.3(SLC26A2):c.835C>T ; NM_000112.3(SLC26A2):c.1273A>G ; NM_000112.3(SLC26A2):c.1957T>A ; NM_000112.3(SLC26A2):c.1724delA ; NM_000112.3(SLC26A2):c.1361A>C

SLC26A2	Diastrophic dwarfism	A rare, lethal perinatal bone dysplasia characterized by limb shortening, normal sized skull with cleft palate, hitchhiker thumbs, distinctive facial dysmorphism and radiographic skeletal features, caused by mutations in the diastrophic dysplasia sulfate transporter gene.	Atelosteogenesis type II, also called neonatal osseous dysplasia I, is characterized by severely shortened limbs, small chest, scoliosis, clubfoot of the equinovarus type (talipes equinovarus), abducted thumbs and great toes, and cleft palate. Radiographic findings include cervical kyphosis, scoliosis, and lumbar hyperlordosis with horizontal sacrum, flattened vertebrae with coronal clefts, and round-shaped iliac bones with flat acetabulae. The distal humerus is typically bifid, and the distal femur rounded. The second and/or third metacarpals and first and second metatarsals are often larger than the other bones of the hand and foot. Patients die of respiratory insufficiency shortly after birth because of the collapse of the airways and pulmonary hypoplasia due to the small rib cage. On the basis of reports of parental consanguinity and recurrence among offspring of unaffected parents, AO II is presumed to be inherited as an autosomal recessive trait.	NM_000112.3(SLC26A2):c.1535C>A ; NM_000112.3(SLC26A2):c.496G>A ; c.833del ; NM_000112.3(SLC26A2):c.532C>T ; NM_000112.3(SLC26A2):c.2033G>T ; c.1878del ; NM_000112.3(SLC26A2):c.1020_1022delTGT ; NM_000112.3(SLC26A2):c.835C>T ; NM_000112.3(SLC26A2):c.1273A>G ; NM_000112.3(SLC26A2):c.1957T>A ; NM_000112.3(SLC26A2):c.1724delA ; NM_000112.3(SLC26A2):c.1361A>C ; NM_000112.3(SLC26A2):c.1535C>A ; NM_000112.3(SLC26A2):c.496G>A ; c.833del ; NM_000112.3(SLC26A2):c.532C>T ; NM_000112.3(SLC26A2):c.2033G>T ; c.1878del ; NM_000112.3(SLC26A2):c.1020_1022delTGT ; NM_000112.3(SLC26A2):c.835C>T ; NM_000112.3(SLC26A2):c.1273A>G ; NM_000112.3(SLC26A2):c.1957T>A ; NM_000112.3(SLC26A2):c.1724delA ; NM_000112.3(SLC26A2):c.1361A>C
SLC26A2	Multiple epiphyseal dysplasia type 4	A rare disorder marked by short stature with short extremities (final adult height is 120cm +/- 10cm), and joint malformations leading to multiple joint contractures (principally involving the shoulders, elbows, interphalangeal joints and hips).	At birth, infants have bilateral clubfoot, short limb deformation of the wrists and abducted thumbs. Cleft palate and mandible hypoplasia are also common findings. Cysts appear on the external ear within the first months of life. Growth is slow and scoliosis is frequent and develops progressively. Joint deformations are severe and can lead to either limitation of joint movement or hyperlaxity. The severity of the clinical manifestations is variable, ranging from very severe to moderate forms that may be diagnosed very late.	NM_000112.3(SLC26A2):c.1535C>A ; NM_000112.3(SLC26A2):c.496G>A ; c.833del ; NM_000112.3(SLC26A2):c.532C>T ; NM_000112.3(SLC26A2):c.2033G>T ; c.1878del ; NM_000112.3(SLC26A2):c.1020_1022delTGT ; NM_000112.3(SLC26A2):c.835C>T ; NM_000112.3(SLC26A2):c.1273A>G ; NM_000112.3(SLC26A2):c.1957T>A ; NM_000112.3(SLC26A2):c.1724delA ; NM_000112.3(SLC26A2):c.1361A>C ; NM_000112.3(SLC26A2):c.1535C>A ; NM_000112.3(SLC26A2):c.496G>A ; c.833del ; NM_000112.3(SLC26A2):c.532C>T ; NM_000112.3(SLC26A2):c.2033G>T ; c.1878del ; NM_000112.3(SLC26A2):c.1020_1022delTGT ; NM_000112.3(SLC26A2):c.835C>T ; NM_000112.3(SLC26A2):c.1273A>G ; NM_000112.3(SLC26A2):c.1957T>A ; NM_000112.3(SLC26A2):c.1724delA ; NM_000112.3(SLC26A2):c.1361A>C

SLC26A4	Athyreosis	Multiple epiphyseal dysplasia type 4 is a multiple epiphyseal dysplasia with a late-childhood onset, characterized by joint pain involving hips, knees, wrists, and fingers with occasional limitation of joint movements, deformity of hands, feet, and knees (club foot, clinodactyly, brachydactyly), scoliosis and slightly reduced adult height. Radiographs display flat epiphyses with early arthritis of the hip, and double-layered patella. Multiple epiphyseal dysplasia type 4 follows an autosomal recessive mode of transmission. The disease is allelic to diastrophic dwarfism, atelosteogenesis type 2 and achondrogenesis type 1B with whom it forms a clinical continuum.		c.961A>T ; NM_000441.1(SLC26A4):c.412G>T ; NM_000441.1(SLC26A4):c.1151A>G ; NM_000441.1(SLC26A4):c.626G>T ; NM_000441.1(SLC26A4):c.1174A>T ; NM_000441.1(SLC26A4):c.1246A>C ; NM_000441.1(SLC26A4):c.281C>T ; NM_000441.1(SLC26A4):c.918+2T>C ; NM_000441.2:c.1198delT ; NM_000441.1(SLC26A4):c.1229C>T ; NM_000441.1(SLC26A4):c.269C>T ; NM_000441.1(SLC26A4):c.1263+1G>A ; NM_000441.1(SLC26A4):c.1003T>C ; NM_000441.1(SLC26A4):c.1489G>A ; NM_000441.1(SLC26A4):c.2048T>C ; NM_000441.1(SLC26A4):c.2162C>T ; NM_000441.1(SLC26A4):c.919-2A>G ; NM_000441.1(SLC26A4):c.1334T>G ; NM_000441.1(SLC26A4):c.916dupG ; NM_000441.1(SLC26A4):c.707T>C ; NM_000441.1(SLC26A4):c.563T>C ; NM_000441.1(SLC26A4):c.1975G>C ; c.1034T>A ; NM_000441.1(SLC26A4):c.1001+1G>T ; NM_000441.1(SLC26A4):c.1001G>T ; NM_000441.1(SLC26A4):c.1226G>A ; NM_000441.1(SLC26A4):c.1707+5G>A ; NM_000441.1(SLC26A4):c.2168A>G ; c.961A>T ; NM_000441.1(SLC26A4):c.412G>T ; NM_000441.1(SLC26A4):c.1151A>G ; NM_000441.1(SLC26A4):c.626G>T ; NM_000441.1(SLC26A4):c.1174A>T ; NM_000441.1(SLC26A4):c.1246A>C ; NM_000441.1(SLC26A4):c.281C>T ; NM_000441.1(SLC26A4):c.918+2T>C ; NM_000441.2:c.1198delT ; NM_000441.1(SLC26A4):c.1229C>T ; NM_000441.1(SLC26A4):c.269C>T ; NM_000441.1(SLC26A4):c.1263+1G>A ; NM_000441.1(SLC26A4):c.1003T>C ; NM_000441.1(SLC26A4):c.1489G>A ; NM_000441.1(SLC26A4):c.2048T>C ; NM_000441.1(SLC26A4):c.2162C>T ; NM_000441.1(SLC26A4):c.919-2A>G ; NM_000441.1(SLC26A4):c.1334T>G ; NM_000441.1(SLC26A4):c.916dupG ; NM_000441.1(SLC26A4):c.707T>C ; NM_000441.1(SLC26A4):c.563T>C ; NM_000441.1(SLC26A4):c.1975G>C ; c.1034T>A ; NM_000441.1(SLC26A4):c.1001+1G>T ; NM_000441.1(SLC26A4):c.1001G>T ; NM_000441.1(SLC26A4):c.1226G>A ; NM_000441.1(SLC26A4):c.1707+5G>A ; NM_000441.1(SLC26A4):c.2168A>G
SLC26A4	Autosomal recessive non-syndromic sensorineural deafness type DFNB	A rare form of thyroid dysgenesis characterized by complete absence of thyroid tissue that results in primary congenital hypothyroidism, a permanent thyroid deficiency that is present from birth.	Clinical manifestations of athyreosis are often subtle or not present at birth, probably as a result of trans-placental passage of some maternal thyroid hormone. More specific symptoms and signs do not develop until several months of age. Common clinical features and signs include decreased activity and increased sleep, feeding difficulty and constipation, prolonged jaundice, myxedematous facies, large fontanels (especially posterior), macroglossia, a distended abdomen with umbilical hernia, and hypotonia. Goiter is always absent. Slow linear growth and developmental delay are usually apparent by 4-6 months of age.	c.961A>T ; NM_000441.1(SLC26A4):c.412G>T ; NM_000441.1(SLC26A4):c.1151A>G ; NM_000441.1(SLC26A4):c.626G>T ; NM_000441.1(SLC26A4):c.1174A>T ; NM_000441.1(SLC26A4):c.1246A>C ; NM_000441.1(SLC26A4):c.281C>T ; NM_000441.1(SLC26A4):c.918+2T>C ; NM_000441.2:c.1198delT ; NM_000441.1(SLC26A4):c.1229C>T ; NM_000441.1(SLC26A4):c.269C>T ; NM_000441.1(SLC26A4):c.1263+1G>A ; NM_000441.1(SLC26A4):c.1003T>C ; NM_000441.1(SLC26A4):c.1489G>A ; NM_000441.1(SLC26A4):c.2048T>C ; NM_000441.1(SLC26A4):c.2162C>T ; NM_000441.1(SLC26A4):c.919-2A>G ; NM_000441.1(SLC26A4):c.1334T>G ; NM_000441.1(SLC26A4):c.916dupG ; NM_000441.1(SLC26A4):c.707T>C ; NM_000441.1(SLC26A4):c.563T>C ; NM_000441.1(SLC26A4):c.1975G>C ; c.1034T>A ; NM_000441.1(SLC26A4):c.1001+1G>T ; NM_000441.1(SLC26A4):c.1001G>T ; NM_000441.1(SLC26A4):c.1226G>A ; NM_000441.1(SLC26A4):c.1707+5G>A ; NM_000441.1(SLC26A4):c.2168A>G

SLC26A4	Pendred syndrome	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	c.961A>T ; NM_000441.1(SLC26A4):c.412G>T ; NM_000441.1(SLC26A4):c.1151A>G ; NM_000441.1(SLC26A4):c.626G>T ; NM_000441.1(SLC26A4):c.1174A>T ; NM_000441.1(SLC26A4):c.1246A>C ; NM_000441.1(SLC26A4):c.281C>T ; NM_000441.1(SLC26A4):c.918+2T>C ; NM_000441.2:c.1198delT ; NM_000441.1(SLC26A4):c.1229C>T ; NM_000441.1(SLC26A4):c.269C>T ; NM_000441.1(SLC26A4):c.1263+1G>A ; NM_000441.1(SLC26A4):c.1003T>C ; NM_000441.1(SLC26A4):c.1489G>A ; NM_000441.1(SLC26A4):c.2048T>C ; NM_000441.1(SLC26A4):c.2162C>T ; NM_000441.1(SLC26A4):c.919-2A>G ; NM_000441.1(SLC26A4):c.1334T>G ; NM_000441.1(SLC26A4):c.916dupG ; NM_000441.1(SLC26A4):c.707T>C ; NM_000441.1(SLC26A4):c.563T>C ; NM_000441.1(SLC26A4):c.1975G>C ; c.1034T>A ; NM_000441.1(SLC26A4):c.1001+1G>T ; NM_000441.1(SLC26A4):c.1001G>T ; NM_000441.1(SLC26A4):c.1226G>A ; NM_000441.1(SLC26A4):c.1707+5G>A ; NM_000441.1(SLC26A4):c.2168A>G ; c.961A>T ; NM_000441.1(SLC26A4):c.412G>T ; NM_000441.1(SLC26A4):c.1151A>G ; NM_000441.1(SLC26A4):c.626G>T ; NM_000441.1(SLC26A4):c.1174A>T ; NM_000441.1(SLC26A4):c.1246A>C ; NM_000441.1(SLC26A4):c.281C>T ; NM_000441.1(SLC26A4):c.918+2T>C ; NM_000441.2:c.1198delT ; NM_000441.1(SLC26A4):c.1229C>T ; NM_000441.1(SLC26A4):c.269C>T ; NM_000441.1(SLC26A4):c.1263+1G>A ; NM_000441.1(SLC26A4):c.1003T>C ; NM_000441.1(SLC26A4):c.1489G>A ; NM_000441.1(SLC26A4):c.2048T>C ; NM_000441.1(SLC26A4):c.2162C>T ; NM_000441.1(SLC26A4):c.919-2A>G ; NM_000441.1(SLC26A4):c.1334T>G ; NM_000441.1(SLC26A4):c.916dupG ; NM_000441.1(SLC26A4):c.707T>C ; NM_000441.1(SLC26A4):c.563T>C ; NM_000441.1(SLC26A4):c.1975G>C ; c.1034T>A ; NM_000441.1(SLC26A4):c.1001+1G>T ; NM_000441.1(SLC26A4):c.1001G>T ; NM_000441.1(SLC26A4):c.1226G>A ; NM_000441.1(SLC26A4):c.1707+5G>A ; NM_000441.1(SLC26A4):c.2168A>G

SLC26A4	Thyroid hypoplasia	A syndromic genetic deafness clinically variable characterized by bilateral sensorineural hearing loss and euthyroid goiter.	Considerable phenotypic variability is found even within families. The main presenting clinical sign is prelingual sensorineural deafness, although occasionally the hearing loss develops later in childhood. The degree of hearing loss is variable: it can be mild-to-moderate and progressive in some patients, and severe-to-profound in others. Fluctuations in hearing are also common and may be associated with or preceded by vertigo. The onset and presentation of euthyroid goiter (75%) is highly variable within and between families, with thyroid enlargement usually developing in late childhood or early adulthood. The thyromegaly reflects a defect in iodide transport from the thyrocyte to the colloid, although organification itself is not impaired. Hypothyroidism may develop if nutritional iodide intake is low. Genetic deafness at the DFNB4 locus is part of the phenotypic spectrum that includes PDS at one extreme and autosomal recessive non-syndromic sensorineural deafness type DFNB4 at the other. In patients with the latter disease, thyroid function is normal.	c.961A>T ; NM_000441.1(SLC26A4):c.412G>T ; NM_000441.1(SLC26A4):c.1151A>G ; NM_000441.1(SLC26A4):c.626G>T ; NM_000441.1(SLC26A4):c.1174A>T ; NM_000441.1(SLC26A4):c.1246A>C ; NM_000441.1(SLC26A4):c.281C>T ; NM_000441.1(SLC26A4):c.918+2T>C ; NM_000441.2:c.1198delT ; NM_000441.1(SLC26A4):c.1229C>T ; NM_000441.1(SLC26A4):c.269C>T ; NM_000441.1(SLC26A4):c.1263+1G>A ; NM_000441.1(SLC26A4):c.1003T>C ; NM_000441.1(SLC26A4):c.1489G>A ; NM_000441.1(SLC26A4):c.2048T>C ; NM_000441.1(SLC26A4):c.2162C>T ; NM_000441.1(SLC26A4):c.919-2A>G ; NM_000441.1(SLC26A4):c.1334T>G ; NM_000441.1(SLC26A4):c.916dupG ; NM_000441.1(SLC26A4):c.707T>C ; NM_000441.1(SLC26A4):c.563T>C ; NM_000441.1(SLC26A4):c.1975G>C ; c.1034T>A ; NM_000441.1(SLC26A4):c.1001+1G>T ; NM_000441.1(SLC26A4):c.1001G>T ; NM_000441.1(SLC26A4):c.1226G>A ; NM_000441.1(SLC26A4):c.1707+5G>A ; NM_000441.1(SLC26A4):c.2168A>G ; c.961A>T ; NM_000441.1(SLC26A4):c.412G>T ; NM_000441.1(SLC26A4):c.1151A>G ; NM_000441.1(SLC26A4):c.626G>T ; NM_000441.1(SLC26A4):c.1174A>T ; NM_000441.1(SLC26A4):c.1246A>C ; NM_000441.1(SLC26A4):c.281C>T ; NM_000441.1(SLC26A4):c.918+2T>C ; NM_000441.2:c.1198delT ; NM_000441.1(SLC26A4):c.1229C>T ; NM_000441.1(SLC26A4):c.269C>T ; NM_000441.1(SLC26A4):c.1263+1G>A ; NM_000441.1(SLC26A4):c.1003T>C ; NM_000441.1(SLC26A4):c.1489G>A ; NM_000441.1(SLC26A4):c.2048T>C ; NM_000441.1(SLC26A4):c.2162C>T ; NM_000441.1(SLC26A4):c.919-2A>G ; NM_000441.1(SLC26A4):c.1334T>G ; NM_000441.1(SLC26A4):c.916dupG ; NM_000441.1(SLC26A4):c.707T>C ; NM_000441.1(SLC26A4):c.563T>C ; NM_000441.1(SLC26A4):c.1975G>C ; c.1034T>A ; NM_000441.1(SLC26A4):c.1001+1G>T ; NM_000441.1(SLC26A4):c.1001G>T ; NM_000441.1(SLC26A4):c.1226G>A ; NM_000441.1(SLC26A4):c.1707+5G>A ; NM_000441.1(SLC26A4):c.2168A>G
SLC26A4	Glycogen storage disease due to glucose-6-phosphatase deficiency type Ib	Thyroid hypoplasia is a form of thyroid dysgenesis (see this term) characterized by incomplete development of the thyroid gland that results in primary congenital hypothyroidism (see this term), a permanent thyroid deficiency that is present from birth.	Clinical manifestations of thyroid hypoplasia are often subtle or not present at birth, probably as a result of trans-placental passage of some maternal thyroid hormone or due to the fact that many infants have some thyroid production of their own. More specific symptoms and signs do not develop until several months of age. Common clinical features and signs include decreased activity and increased sleep, feeding difficulty and constipation, prolonged jaundice, myxedematous facies, large fontanels (especially posterior), macroglossia, a distended abdomen with umbilical hernia, and hypotonia. Goiter is always absent. Slow linear growth and developmental delay are usually apparent by 4-6 months of age. Without treatment thyroid hypoplasia results in severe intellectual deficit and short stature.	c.961A>T ; NM_000441.1(SLC26A4):c.412G>T ; NM_000441.1(SLC26A4):c.1151A>G ; NM_000441.1(SLC26A4):c.626G>T ; NM_000441.1(SLC26A4):c.1174A>T ; NM_000441.1(SLC26A4):c.1246A>C ; NM_000441.1(SLC26A4):c.281C>T ; NM_000441.1(SLC26A4):c.918+2T>C ; NM_000441.2:c.1198delT ; NM_000441.1(SLC26A4):c.1229C>T ; NM_000441.1(SLC26A4):c.269C>T ; NM_000441.1(SLC26A4):c.1263+1G>A ; NM_000441.1(SLC26A4):c.1003T>C ; NM_000441.1(SLC26A4):c.1489G>A ; NM_000441.1(SLC26A4):c.2048T>C ; NM_000441.1(SLC26A4):c.2162C>T ; NM_000441.1(SLC26A4):c.919-2A>G ; NM_000441.1(SLC26A4):c.1334T>G ; NM_000441.1(SLC26A4):c.916dupG ; NM_000441.1(SLC26A4):c.707T>C ; NM_000441.1(SLC26A4):c.563T>C ; NM_000441.1(SLC26A4):c.1975G>C ; c.1034T>A ; NM_000441.1(SLC26A4):c.1001+1G>T ; NM_000441.1(SLC26A4):c.1001G>T ; NM_000441.1(SLC26A4):c.1226G>A ; NM_000441.1(SLC26A4):c.1707+5G>A ; NM_000441.1(SLC26A4):c.2168A>G ; c.961A>T ; NM_000441.1(SLC26A4):c.412G>T ; NM_000441.1(SLC26A4):c.1151A>G ; NM_000441.1(SLC26A4):c.626G>T ; NM_000441.1(SLC26A4):c.1174A>T ; NM_000441.1(SLC26A4):c.1246A>C ; NM_000441.1(SLC26A4):c.281C>T ; NM_000441.1(SLC26A4):c.918+2T>C ; NM_000441.2:c.1198delT ; NM_000441.1(SLC26A4):c.1229C>T ; NM_000441.1(SLC26A4):c.269C>T ; NM_000441.1(SLC26A4):c.1263+1G>A ; NM_000441.1(SLC26A4):c.1003T>C ; NM_000441.1(SLC26A4):c.1489G>A ; NM_000441.1(SLC26A4):c.2048T>C ; NM_000441.1(SLC26A4):c.2162C>T ; NM_000441.1(SLC26A4):c.919-2A>G ; NM_000441.1(SLC26A4):c.1334T>G ; NM_000441.1(SLC26A4):c.916dupG ; NM_000441.1(SLC26A4):c.707T>C ; NM_000441.1(SLC26A4):c.563T>C ; NM_000441.1(SLC26A4):c.1975G>C ; c.1034T>A ; NM_000441.1(SLC26A4):c.1001+1G>T ; NM_000441.1(SLC26A4):c.1001G>T ; NM_000441.1(SLC26A4):c.1226G>A ; NM_000441.1(SLC26A4):c.1707+5G>A ; NM_000441.1(SLC26A4):c.2168A>G

SLC37A4	Glycogen storage disease due to glucose-6-phosphatase deficiency type Ib	Glycogenosis due to glucose-6-phosphatase deficiency (G6P) type b, or glycogen storage disease (GSD) type 1b, is a type of glycogenosis due to G6P deficiency (see this term).	Clinical presentation is similar to that of glycogenosis due to G6P deficiency type a (see this term). In addition, in type b, neutropenia, and neutrophil dysfunction are responsible for tendency towards infections, relapsing aphthous gingivostomatitis, and inflammatory bowel disease.	NM_001164277.1:c.83G>A ; NM_001467.6:c.1042_1043delCT ; NM_001164277.1(SLC37A4):c.703_705delGTG ; NM_001164277.1(SLC37A4):c.1243C>T ; NM_001164277.1(SLC37A4):c.1063G>T ; NM_001164277.1(SLC37A4):c.352T>C ; NM_001164277.1(SLC37A4):c.1015G>T ; NM_001164277.1(SLC37A4):c.1016G>A ; NM_001164277.1:c.83G>A ; NM_001467.6:c.1042_1043delCT ; NM_001164277.1(SLC37A4):c.703_705delGTG ; NM_001164277.1(SLC37A4):c.1243C>T ; NM_001164277.1(SLC37A4):c.1063G>T ; NM_001164277.1(SLC37A4):c.352T>C ; NM_001164277.1(SLC37A4):c.1015G>T ; NM_001164277.1(SLC37A4):c.1016G>A
SLC45A2	Oculocutaneous albinism type 4	Glycogenosis due to glucose-6-phosphatase deficiency (G6P) type b, or glycogen storage disease (GSD) type 1b, is a type of glycogenosis due to G6P deficiency	Clinical presentation is similar to that of glycogenosis due to G6P deficiency type a (see this term). In addition, in type b, neutropenia, and neutrophil dysfunction are responsible for tendency towards infections, relapsing aphthous gingivostomatitis, and inflammatory bowel disease.	NM_016180.4(SLC45A2):c.986del ; NM_016180.4(SLC45A2):c.469G>A ; NM_016180.4(SLC45A2):c.1121del ; NM_016180.4(SLC45A2):c.986del ; NM_016180.4(SLC45A2):c.469G>A ; NM_016180.4(SLC45A2):c.1121del
SLC4A11	Congenital hereditary endothelial dystrophy type II	A form of oculocutaneous albinism characterized by varying degrees of skin and hair hypopigmentation, numerous ocular changes and misrouting of the optic nerves at the chiasm.	Cutaneous hypopigmentation is often visible at birth and signs of nystagmus and strabismus present in the first year of life. Nystagmus is not always present at birth and can develop at 3 to 4 months of age. It can start off as rapid and slow down in later life and it is usually more noticeable when patients are tired, stressed, anxious or angry. Foveal hypoplasia is associated with a reduction in visual acuity. Alternating strabismus and reduced stereoscopic vision are also noted. Visual changes are not progressive and usually stabilize after childhood. A wide range of clinical phenotypes can be found with OCA4. Iris color can range from blue to brown. Photophobia is common. Hair color in newborns ranges from silvery white to light yellow. It may darken slightly with time (to light brown) but usually remains relatively unchanged. Skin color is usually creamy white. Over time, skin can become coarse, thickened and rough and solar keratoses are common in those who have not limited their exposure to the sun. Patients have an increased risk of developing basal and squamous cell carcinomas but melanomas are rare.	NM_001174089.1(SLC4A11):c.2557C>T ; NM_032034.3:c.1038_1039insA ; NM_032034.3(SLC4A11):c.473_480del ; NM_001174089.1(SLC4A11):c.2558G>A ; NM_001174089.1(SLC4A11):c.2480T>C ; ENST00000380056.7:c.2233_2240dup ; NM_001174089.1(SLC4A11):c.1418C>T ; NM_001174089.1(SLC4A11):c.1343G>A ; NM_001174089.1(SLC4A11):c.2216G>A ; NM_001174089.1(SLC4A11):c.2518A>G ; NM_001174089.1(SLC4A11):c.1415G>A ; NM_001174089.1(SLC4A11):c.589T>C ; NM_001174089.1(SLC4A11):c.1765C>T ; NM_001174089.1(SLC4A11):c.2557C>T ; NM_032034.3:c.1038_1039insA ; NM_032034.3(SLC4A11):c.473_480del ; NM_001174089.1(SLC4A11):c.2558G>A ; NM_001174089.1(SLC4A11):c.2480T>C ; ENST00000380056.7:c.2233_2240dup ; NM_001174089.1(SLC4A11):c.1418C>T ; NM_001174089.1(SLC4A11):c.1343G>A ; NM_001174089.1(SLC4A11):c.2216G>A ; NM_001174089.1(SLC4A11):c.2518A>G ; NM_001174089.1(SLC4A11):c.1415G>A ; NM_001174089.1(SLC4A11):c.589T>C ; NM_001174089.1(SLC4A11):c.1765C>T

SLC4A11	Corneal dystrophy-perceptive deafness syndrome	Congenital hereditary endothelial dystrophy II (CHED II) is a rare subtype of posterior corneal dystrophy (see this term) characterized by a diffuse ground-glass appearance of the corneas and marked corneal thickening from birth with nystagmus, and blurred vision.	Diffuse ground glass lesions are present from birth and are accompanied by nystagmus. Tearing and photophobia are minimal or absent. The course is relatively stable. Patients also occasionally have sensorineural deafness. The cornea is swollen due to extensive stromal edema.	NM_001174089.1(SLC4A11):c.2557C>T ; NM_032034.3:c.1038_1039insA ; NM_032034.3(SLC4A11):c.473_480del ; NM_001174089.1(SLC4A11):c.2558G>A ; NM_001174089.1(SLC4A11):c.2480T>C ; ENST00000380056.7:c.2233_2240dup ; NM_001174089.1(SLC4A11):c.1418C>T ; NM_001174089.1(SLC4A11):c.1343G>A ; NM_001174089.1(SLC4A11):c.2216G>A ; NM_001174089.1(SLC4A11):c.2518A>G ; NM_001174089.1(SLC4A11):c.1415G>A ; NM_001174089.1(SLC4A11):c.589T>C ; NM_001174089.1(SLC4A11):c.1765C>T ; NM_001174089.1(SLC4A11):c.2557C>T ; NM_032034.3:c.1038_1039insA ; NM_032034.3(SLC4A11):c.473_480del ; NM_001174089.1(SLC4A11):c.2558G>A ; NM_001174089.1(SLC4A11):c.2480T>C ; ENST00000380056.7:c.2233_2240dup ; NM_001174089.1(SLC4A11):c.1418C>T ; NM_001174089.1(SLC4A11):c.1343G>A ; NM_001174089.1(SLC4A11):c.2216G>A ; NM_001174089.1(SLC4A11):c.2518A>G ; NM_001174089.1(SLC4A11):c.1415G>A ; NM_001174089.1(SLC4A11):c.589T>C ; NM_001174089.1(SLC4A11):c.1765C>T
SLC4A11	Fuchs endothelial corneal dystrophy	Corneal dystrophy-perceptive deafness (CDPD) or Harboyan syndrome is a degenerative corneal disorder characterized by the association of congenital hereditary endothelial dystrophy (CHED; see this term) with progressive, postlingual sensorineural hearing loss.	The ocular manifestations in CDPD include diffuse bilateral corneal edema occurring with severe corneal clouding, blurred vision, visual loss and nystagmus. They are apparent at birth or within the neonatal period and are indistinguishable from the ocular findings characterizing autosomal recessive CHED (CHED2). Hearing deficit in CDPD is slowly progressive and is typically identified in patients between 10 and 25 years of age. There are no reported cases with prelingual deafness, however, significant hearing loss in children as young as 4 years old has been detected by audiometry, suggesting that hearing may be affected early in the disease course, even at birth.	NM_001174089.1(SLC4A11):c.2557C>T ; NM_032034.3:c.1038_1039insA ; NM_032034.3(SLC4A11):c.473_480del ; NM_001174089.1(SLC4A11):c.2558G>A ; NM_001174089.1(SLC4A11):c.2480T>C ; ENST00000380056.7:c.2233_2240dup ; NM_001174089.1(SLC4A11):c.1418C>T ; NM_001174089.1(SLC4A11):c.1343G>A ; NM_001174089.1(SLC4A11):c.2216G>A ; NM_001174089.1(SLC4A11):c.2518A>G ; NM_001174089.1(SLC4A11):c.1415G>A ; NM_001174089.1(SLC4A11):c.589T>C ; NM_001174089.1(SLC4A11):c.1765C>T ; NM_001174089.1(SLC4A11):c.2557C>T ; NM_032034.3:c.1038_1039insA ; NM_032034.3(SLC4A11):c.473_480del ; NM_001174089.1(SLC4A11):c.2558G>A ; NM_001174089.1(SLC4A11):c.2480T>C ; ENST00000380056.7:c.2233_2240dup ; NM_001174089.1(SLC4A11):c.1418C>T ; NM_001174089.1(SLC4A11):c.1343G>A ; NM_001174089.1(SLC4A11):c.2216G>A ; NM_001174089.1(SLC4A11):c.2518A>G ; NM_001174089.1(SLC4A11):c.1415G>A ; NM_001174089.1(SLC4A11):c.589T>C ; NM_001174089.1(SLC4A11):c.1765C>T

SLC6A8	X-linked creatine transporter deficiency	A disorder that is the most frequent form of posterior corneal dystrophy and is characterized by excrescences on a thickened Descemet membrane (corneal guttae), generalized corneal edema, with gradually decreased visual acuity.	The condition is more common and more severe in women (sex ratio 3-4:1). Patients with FECD are initially asymptomatic. Clinical onset is generally in the 5th or 6th decade of life. Discomfort and painful episodes of recurrent corneal erosions occur, along with gradually developing opacification leading to hazy vision. Over time, discomfort may diminish but severe impairment of visual acuity, and even blindness in elderly patients, may be observed. The clinical course often spans 10 to 20 years. The condition is often associated with cataracts. Microbial keratitis and corneal neovascularization are extremely rare complications. Stromal edema produces a blue-gray haze anterior to Descemet membrane followed by eventual thickening of the entire corneal stroma and development of a ground-glass corneal appearance.	NM_005629.3(SLC6A8):c.1540C>T ; NM_005629.3(SLC6A8):c.1222_1224delTTC ; NM_005629.3(SLC6A8):c.1011C>G ; NM_005629.3(SLC6A8):c.1141G>C ; NM_005629.3(SLC6A8):c.321_323delCTT ; NM_005629.3(SLC6A8):c.395G>T ; NM_005629.3(SLC6A8):c.1540C>T ; NM_005629.3(SLC6A8):c.1222_1224delTTC ; NM_005629.3(SLC6A8):c.1011C>G ; NM_005629.3(SLC6A8):c.1141G>C ; NM_005629.3(SLC6A8):c.321_323delCTT ; NM_005629.3(SLC6A8):c.395G>T
SMN1	Proximal spinal muscular atrophy type 1	X-linked creatine transporter deficiency (CRTR-D) is a creatine deficiency syndrome characterized clinically by global developmental delay/ intellectual disability (DD/ID) with prominent speech/language delay, autistic behavior and seizures.	The onset of symptoms occurs during infancy, usually before the age of 2 years. Males are mainly affected, but females can also have various combinations and severities of disease manifestations. CRTR-D is consistently characterized by mild to severe intellectual deficit, and expressive speech and language delay. Behavioral disorders (mainly autism and hyperactivity) are present in all affected individuals. Affected individuals often experience seizures and may present low weight gain, muscular hypotonia, and poor muscle mass. Subtle dysmorphic features such as midface hypoplasia, long face, and prominent chin have been reported in various affected male patients. Epilepsy and extrapyramidal symptoms may also occur occasionally. In adult patients, cardiac and gastrointestinal disorders have been reported. Carrier females are typically asymptomatic, but learning disabilities have been described in some.	functional copy number loss

SMN1	Proximal spinal muscular atrophy type 2	A rare, genetic proximal spinal muscular atrophy characterized by degeneration of alpha motor neurons in the anterior horns of the spinal cord and lower brain stem manifesting with onset of severe and progressive muscle weakness in the first 6 months of life and presenting with severe, generalized hypotonia and weakness,. Dysphagia and respiratory impairment may also be present at presentation or appear at a later stage. Classically, before the advent of recent therapies, type 1 patients never achieved sitting without support.	Disease onset occurs before 6 months of age. The severe, symmetrical muscle weakness affects predominantly proximal limbs but often also involves the extremities. Cries are weak. Poor sucking ability and reduced swallowing are frequent, leading to feeding difficulties. Deep tendon reflexes are absent. Patients have paradoxical breathing, a bell shaped chest and develop respiratory failure. Mild contractures (of the knees and, more rarely, of the elbows), and scoliosis may be present. Classically, patients were not able to achieve sitting without support but this has changed following the availability of new treatments.	functional copy number loss
SMN1	Proximal spinal muscular atrophy type 3	A rare, genetic proximal spinal muscular atrophy characterized by degeneration of alpha motor neurons in the anterior horns of the spinal cord and lower brain stem manifesting with onset between 6 to 18 months of age with progressive, proximal muscle weakness, mild to moderate hypotonia and finger polymyoclonour tremor, with areflexia. Motor milestones are classically limited to independent sitting or standing.	Disease onset occurs between the ages of 6 and 18 months. Classically, before the advent of the new therapies, affected children achieve sitting independently and may acquire standing but do not acquire independent walking. Progressive proximal muscle weakness is symmetrical and greater in the legs than the arms. Finger trembling is frequent. Scoliosis, joint contractures and ankyloses of the mandible are very common . Progressive respiratory muscle weakness can lead to restrictive lung disease. Cognition is normal.	functional copy number loss

SMN1	Proximal spinal muscular atrophy type 4	A rare, genetic proximal spinal muscular atrophy characterized by degeneration of alpha motor neurons in the anterior horns of the spinal cord and lower brain stem manifesting with onset of progressive proximal muscle weakness (legs greater than arms) between 18 months and adulthood. Motor development is heterogeneous but walking is typically acquired.	The disease manifests between 18 months of age and adulthood, typically presenting with frequent falls, difficulty climbing steps and proximal weakness. Patients are subdivided based on age of onset: early onset is between 18 months and 3 years of age (type 3a) and is associated with a plateau in motor development, reduced or absent reflexes, finger polymyoclonus tremor and, frequently, loss of ambulation before or around puberty. Later onset (type 3b), between 3 and 21 years of age, is associated with comparatively milder decline in gross motor function. The muscle weakness predominantly affects the legs and hip muscles and then progresses to the shoulders and arms. Abnormal gait characteristics are common in order to compensate for weakness. Typically, patients are spared scoliosis and respiratory muscle weakness but these may be a feature after loss of ambulation. Cognition is normal.	functional copy number loss
SMPD1	Niemann-Pick disease type A	A rare, genetic proximal spinal muscular atrophy characterized by degeneration of alpha motor neurons in the anterior horns of the spinal cord and lower brain stem manifesting with adult onset, slowly progressive, mild proximal muscle weakness.	Disease onset is typically in the second or third decade of life. The muscle weakness predominantly affects the legs and hip muscles and then progresses to the shoulders and arms. Waddling gait is common. Finger trembling, fasciculation and calf hypertrophy may occur. The clinical picture is similar to that seen in SMA type 3 but the motor weakness is less severe. Cognition is unaffected.	c.740del ; NM_000543.4(SMPD1):c.739G>A ; NM_000543.4(SMPD1):c.1152G>A ; NM_000543.5:c.1828_1830delCGC ; NM_000543.4(SMPD1):c.688C>T ; NM_000543.4(SMPD1):c.557C>T ; NM_000543.5:c.911T>C ; NM_000543.4(SMPD1):c.475T>C ; c.566_582del ; NM_000543.4(SMPD1):c.1117C>T ; NM_000543.4:c.103_119delCTGGTGCTGGCGCTGGC ; NM_000543.4(SMPD1):c.1267C>T ; NM_000543.4(SMPD1):c.842_849dupTCCCCGCA ; NM_000543.4(SMPD1):c.354delC ; NM_000543.5:c.573delT ; NM_000543.4:c.106delG ; NM_000543.4(SMPD1):c.1420_1421delCT ; NM_000543.5:c.996delC ; NM_000543.4(SMPD1):c.1299T>G ; NM_000543.4(SMPD1):c.757G>C ; NM_000543.4(SMPD1):c.1426C>T ; NM_000543.4(SMPD1):c.1092-1G>C ; NM_000543.4(SMPD1):c.785_807del23 ; c.103_107del ; NM_000543.4(SMPD1):c.96G>A ; NM_000543.4(SMPD1):c.730G>A ; c.104_119del ; NM_000543.4(SMPD1):c.788T>A ; NM_000543.5(SMPD1):c.564dup ; NM_000543.4(SMPD1):c.1327C>T ; NM_000543.4(SMPD1):c.564delC ; NM_000543.5(SMPD1):c.1630del ; NM_000543.4(SMPD1):c.1264-1G>T ; NM_000543.4(SMPD1):c.742G>A ; NM_000543.4(SMPD1):c.1805G>A ; NM_000543.4(SMPD1):c.1624C>T ; c.740del ; NM_000543.4(SMPD1):c.739G>A ; NM_000543.4(SMPD1):c.1152G>A ; NM_000543.5:c.1828_1830delCGC ; NM_000543.4(SMPD1):c.688C>T ; NM_000543.4(SMPD1):c.557C>T ; NM_000543.5:c.911T>C ; NM_000543.4(SMPD1):c.475T>C ; c.566_582del ; NM_000543.4(SMPD1):c.1117C>T ; NM_000543.4:c.103_119delCTGGTGCTGGCGCTGGC ; NM_000543.4(SMPD1):c.1267C>T ; NM_000543.4(SMPD1):c.842_849dupTCCCCGCA ; NM_000543.4(SMPD1):c.354delC ; NM_000543.5:c.573delT ; NM_000543.4:c.106delG ; NM_000543.4(SMPD1):c.1420_1421delCT ; NM_000543.5:c.996delC ; NM_000543.4(SMPD1):c.1299T>G ; NM_000543.4(SMPD1):c.757G>C ; NM_000543.4(SMPD1):c.1426C>T ; NM_000543.4(SMPD1):c.1092-1G>C ; NM_000543.4(SMPD1):c.785_807del23 ; c.103_107del ; NM_000543.4(SMPD1):c.96G>A ; NM_000543.4(SMPD1):c.730G>A ; c.104_119del ; NM_000543.4(SMPD1):c.788T>A ; NM_000543.5(SMPD1):c.564dup ; NM_000543.4(SMPD1):c.1327C>T ; NM_000543.4(SMPD1):c.564delC ; NM_000543.5(SMPD1):c.1630del ; NM_000543.4(SMPD1):c.1264-1G>T ; NM_000543.4(SMPD1):c.742G>A ; NM_000543.4(SMPD1):c.1805G>A ; NM_000543.4(SMPD1):c.1624C>T

SMPD1	Niemann-Pick disease type B	A rare, autosomal recessive, acid sphingomyelinase deficiency characterized clinically by onset in infancy or early childhood with failure to thrive, hepatosplenomegaly, interstitial lung disease and rapidly progressive neurodegenerative disorders.	The first symptom in NPD-A is hepatosplenomegaly, usually noted in the first few months of life. Other non-neurological findings include feeding problems, failure to thrive, gastrointestinal complaints (e.g., constipation, diarrhea, and vomiting), recurrent respiratory infections, persistently elevated transaminases, and irritability. Early neurological manifestations include muscular hypotonia, weakness and feeding difficulties. Affected infants have decreased linear growth and body weight. By 6 months of age, global development delay becomes evident and regression of developmental milestones is noted. With advancing age, the loss of motor function and the deterioration of intellectual capabilities are progressively debilitating. A classic cherry-red spot of the macula of the retina is eventually present in all affected children after 6 months of age. Interstitial lung disease results in frequent respiratory infections and often respiratory failure. Osteoporosis is common, presumably due to infiltration and poor nutrition.	c.740del ; NM_000543.4(SMPD1):c.739G>A ; NM_000543.4(SMPD1):c.1152G>A ; NM_000543.5:c.1828_1830delCGC ; NM_000543.4(SMPD1):c.688C>T ; NM_000543.4(SMPD1):c.557C>T ; NM_000543.5:c.911T>C ; NM_000543.4(SMPD1):c.475T>C ; c.566_582del ; NM_000543.4(SMPD1):c.1117C>T ; NM_000543.4:c.103_119delCTGGTGCTGGCGCTGGC ; NM_000543.4(SMPD1):c.1267C>T ; NM_000543.4(SMPD1):c.842_849dupTCCCCGCA ; NM_000543.4(SMPD1):c.354delC ; NM_000543.5:c.573delT ; NM_000543.4:c.106delG ; NM_000543.4(SMPD1):c.1420_1421delCT ; NM_000543.5:c.996delC ; NM_000543.4(SMPD1):c.1299T>G ; NM_000543.4(SMPD1):c.757G>C ; NM_000543.4(SMPD1):c.1426C>T ; NM_000543.4(SMPD1):c.1092-1G>C ; NM_000543.4(SMPD1):c.785_807del23 ; c.103_107del ; NM_000543.4(SMPD1):c.96G>A ; NM_000543.4(SMPD1):c.730G>A ; c.104_119del ; NM_000543.4(SMPD1):c.788T>A ; NM_000543.5(SMPD1):c.564dup ; NM_000543.4(SMPD1):c.1327C>T ; NM_000543.4(SMPD1):c.564delC ; NM_000543.5(SMPD1):c.1630del ; NM_000543.4(SMPD1):c.1264-1G>T ; NM_000543.4(SMPD1):c.742G>A ; NM_000543.4(SMPD1):c.1805G>A ; NM_000543.4(SMPD1):c.1624C>T ; c.740del ; NM_000543.4(SMPD1):c.739G>A ; NM_000543.4(SMPD1):c.1152G>A ; NM_000543.5:c.1828_1830delCGC ; NM_000543.4(SMPD1):c.688C>T ; NM_000543.4(SMPD1):c.557C>T ; NM_000543.5:c.911T>C ; NM_000543.4(SMPD1):c.475T>C ; c.566_582del ; NM_000543.4(SMPD1):c.1117C>T ; NM_000543.4:c.103_119delCTGGTGCTGGCGCTGGC ; NM_000543.4(SMPD1):c.1267C>T ; NM_000543.4(SMPD1):c.842_849dupTCCCCGCA ; NM_000543.4(SMPD1):c.354delC ; NM_000543.5:c.573delT ; NM_000543.4:c.106delG ; NM_000543.4(SMPD1):c.1420_1421delCT ; NM_000543.5:c.996delC ; NM_000543.4(SMPD1):c.1299T>G ; NM_000543.4(SMPD1):c.757G>C ; NM_000543.4(SMPD1):c.1426C>T ; NM_000543.4(SMPD1):c.1092-1G>C ; NM_000543.4(SMPD1):c.785_807del23 ; c.103_107del ; NM_000543.4(SMPD1):c.96G>A ; NM_000543.4(SMPD1):c.730G>A ; c.104_119del ; NM_000543.4(SMPD1):c.788T>A ; NM_000543.5(SMPD1):c.564dup ; NM_000543.4(SMPD1):c.1327C>T ; NM_000543.4(SMPD1):c.564delC ; NM_000543.5(SMPD1):c.1630del ; NM_000543.4(SMPD1):c.1264-1G>T ; NM_000543.4(SMPD1):c.742G>A ; NM_000543.4(SMPD1):c.1805G>A ; NM_000543.4(SMPD1):c.1624C>T

STAR	Classic congenital lipoid adrenal hyperplasia due to STAR deficency	A rare autosomal recessive, chronic, acid sphingomyelinase deficiency characterized clinically by onset in childhood with hepatosplenomegaly, growth retardation, interstitial lung disease and absence of neurodegenerative disorders.	NPD-B is characterized by hepatosplenomegaly with progressive hypersplenism and stable liver dysfunction, gradual deterioration in pulmonary function, osteopenia, and atherogenic lipid profile. Most patients are diagnosed in infancy or childhood. The degree of hepatosplenomegaly ranges from mild to massive. Those with significant organomegaly have hypersplenism with secondary thrombocytopenia. Pulmonary involvement is common in affected individuals of all ages. Most affected individuals have evidence of interstitial lung disease. Abnormal linear growth and delayed skeletal maturation are common in children and adolescents, and can result in significant short stature in adulthood. A proatherogenic lipid profile is seen early in the disease course and some patients develop coronary artery disease. Neurologic manifestations occur infrequently and most of patients had minor and non-progressive findings. Up to one third of individuals with NPD-B have a cherry-red macula.	NM_000349.2(STAR):c.577C>T ; NM_000349.2(STAR):c.545G>A ; NM_000349.2(STAR):c.545G>T ; NM_000349.2(STAR):c.559G>A ; NM_000349.2(STAR):c.562C>T ; NM_000349.2(STAR):c.749G>A ; NM_000349.2(STAR):c.772C>T ; NM_000349.2(STAR):c.577C>T ; NM_000349.2(STAR):c.545G>A ; NM_000349.2(STAR):c.545G>T ; NM_000349.2(STAR):c.559G>A ; NM_000349.2(STAR):c.562C>T ; NM_000349.2(STAR):c.749G>A ; NM_000349.2(STAR):c.772C>T
STAR	Familial glucocorticoid deficiency	A disorder that is one of the most severe forms of congenital adrenal hyperplasia (CAH) characterized by severe adrenal insufficiency and sex reversal in males.	Age of onset typically occurs in the antenatal period but congenital anomalies are typically seen in the perinatal period. Boys are not virilized and demonstrate a complete girl phenotype. The external genitalia of girls are normal. Hypoglycemic seizures, vomiting or symptoms of dehydration are common manifestations in the first few weeks of life and can be life threatening. Acute adrenal insufficiency is an emergency and can occur in some cases.	NM_000349.2(STAR):c.577C>T ; NM_000349.2(STAR):c.545G>A ; NM_000349.2(STAR):c.545G>T ; NM_000349.2(STAR):c.559G>A ; NM_000349.2(STAR):c.562C>T ; NM_000349.2(STAR):c.749G>A ; NM_000349.2(STAR):c.772C>T ; NM_000349.2(STAR):c.577C>T ; NM_000349.2(STAR):c.545G>A ; NM_000349.2(STAR):c.545G>T ; NM_000349.2(STAR):c.559G>A ; NM_000349.2(STAR):c.562C>T ; NM_000349.2(STAR):c.749G>A ; NM_000349.2(STAR):c.772C>T

STAR	Non-classic congenital lipoid adrenal hyperplasia due to STAR deficency	Familial glucocorticoid deficiency (FGD) is a group of primary adrenal insufficiencies characterized clinically by neonatal hyperpigmentation, hypoglycemia, failure to thrive, and recurrent infections, and biochemically by glucocorticoid deficiency without mineralocorticoid deficiency.	FGD usually presents in infancy or early childhood with hyperpigmentation of the skin and gums (present at birth or that develops over time), hypoglycemic seizures and failure to thrive. Recurrent infections are also a common finding (and may be the presenting sign in older children). Weakness, fatigue, weight loss, anorexia, vomiting, flank or abdominal pain, constipation and diarrhea are additional symptoms seen in some patients due to hypocortisolemia. Hypoglycemic crises resulting in convulsions can lead to coma or death if untreated and recurrent hypolglycemia may lead to neurological sequelae (i.e. learning disabilities, intellectual deficit, and sometimes severe, neuronal damage leading to major sensory and motor defects such as quadriplegia). Tall stature has been reported in some patients with FGD, typically those withÂ MC2RÂ gene defects.Â MRAPÂ defects have been associated with a more severe disease and an earlier age of onset while a milder phenotype is seen in those with defects in theÂ MCM4Â gene (Irish Traveler FGD).	NM_000349.2(STAR):c.577C>T ; NM_000349.2(STAR):c.545G>A ; NM_000349.2(STAR):c.545G>T ; NM_000349.2(STAR):c.559G>A ; NM_000349.2(STAR):c.562C>T ; NM_000349.2(STAR):c.749G>A ; NM_000349.2(STAR):c.772C>T ; NM_000349.2(STAR):c.577C>T ; NM_000349.2(STAR):c.545G>A ; NM_000349.2(STAR):c.545G>T ; NM_000349.2(STAR):c.559G>A ; NM_000349.2(STAR):c.562C>T ; NM_000349.2(STAR):c.749G>A ; NM_000349.2(STAR):c.772C>T
STRC	Autosomal recessive non-syndromic sensorineural deafness type DFNB	A disorder that is one of the most severe forms of congenital adrenal hyperplasia (CAH) characterized by severe adrenal insufficiency and sex reversal in males.	Age of onset typically occurs in the antenatal period but congenital anomalies are typically seen in the perinatal period. Boys are not virilized and demonstrate a complete girl phenotype. The external genitalia of girls are normal. Hypoglycemic seizures, vomiting or symptoms of dehydration are common manifestations in the first few weeks of life and can be life threatening. Acute adrenal insufficiency is an emergency and can occur in some cases.	c.4545+1G>C ; c.5168_5171del ; c.3556C>T ; c.5185C>T ; NM_153700.2(STRC):c.5188C>T ; c.4545+1G>C ; c.5168_5171del ; c.3556C>T ; c.5185C>T ; NM_153700.2(STRC):c.5188C>T

STRC	Deafness-infertility syndrome	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	c.4545+1G>C ; c.5168_5171del ; c.3556C>T ; c.5185C>T ; NM_153700.2(STRC):c.5188C>T ; c.4545+1G>C ; c.5168_5171del ; c.3556C>T ; c.5185C>T ; NM_153700.2(STRC):c.5188C>T
TAT	Tyrosinemia type 2	Deafness-infertility syndrome (DIS) is a very rare syndrome associating sensorineural deafness and male infertility.	Onset of hearing loss occurred in early childhood and was nonprogressive (ages of deaf individuals ranged from 35-60 years, and there were records of audiometric tests performed during childhood). The hearing impairment, which involved all frequencies, was moderate in the range of 125-1,000 Hz but severe in higher frequencies. Vestibular function was normal, and there were no symptoms of tinnitus.	NM_000353.2(TAT):c.1297C>T ; NM_000353.2(TAT):c.169C>T ; NM_000353.2(TAT):c.236-5A>G ; NM_000353.2(TAT):c.668C>G ; NM_000353.2(TAT):c.1249C>T ; NM_000353.2(TAT):c.1297C>T ; NM_000353.2(TAT):c.169C>T ; NM_000353.2(TAT):c.236-5A>G ; NM_000353.2(TAT):c.668C>G ; NM_000353.2(TAT):c.1249C>T

TCIRG1	Autosomal dominant severe congenital neutropenia	Tyrosinemia type 2 is an inborn error of tyrosine metabolism characterized by hypertyrosinemia with oculocutaneous manifestations and, in some cases, intellectual deficit.	Skin lesions occur in 80% of cases, ocular involvement in 75% of cases and neurologic findings and some degree of intellectual deficit in up to 60% of cases. Onset is variable but the ocular symptoms (redness, photophobia, excessive tearing and pain) usually develop in the first year of life. Ocular signs include corneal clouding with bilateral dendritiform corneal lesions (pseudodendritic keratitis), neovascularization, corneal ulceration and scarring, which may lead to decreased visual acuity. Cutaneous manifestations usually begin after the first year of life but may develop at the same time as the ocular symptoms. The skin lesions consist of nonpruritic, hyperkeratotic papules and plaques principally located on the palms and soles (palmoplantar hyperkeratosis). These lesions are painful and progressive and are often associated with hyperhidrosis. Central nervous system (CNS) involvement is highly variable with intellectual deficit (ranging from mild to severe) being the most common manifestation. Other signs of CNS involvement include behavioral problems, nystagmus, tremor, ataxia, and convulsions.	NM_006019.3(TCIRG1):c.1213G>A ; c.115_116del ; NM_006019.4:c.1331G>T ; NM_006019.3(TCIRG1):c.1674-1G>A ; NM_006019.3(TCIRG1):c.2236+1G>A ; NM_006019.3(TCIRG1):c.1213G>A ; c.115_116del ; NM_006019.4:c.1331G>T ; NM_006019.3(TCIRG1):c.1674-1G>A ; NM_006019.3(TCIRG1):c.2236+1G>A
TCIRG1	Autosomal recessive malignant osteopetrosis	A rare primary immunodeficiency disorder characterized by autosomal dominant inheritance, absolute neutrophil counts below 0.5x10E9/L in the peripheral blood (on three separate occasions over a six month period), granulopoiesis maturation arrest at the promyelocyte/myelocyte stage and early-onset, severe, recurrent bacterial infections.		NM_006019.3(TCIRG1):c.1213G>A ; c.115_116del ; NM_006019.4:c.1331G>T ; NM_006019.3(TCIRG1):c.1674-1G>A ; NM_006019.3(TCIRG1):c.2236+1G>A ; NM_006019.3(TCIRG1):c.1213G>A ; c.115_116del ; NM_006019.4:c.1331G>T ; NM_006019.3(TCIRG1):c.1674-1G>A ; NM_006019.3(TCIRG1):c.2236+1G>A

TCIRG1	Dysosteosclerosis	Infantile malignant osteopetrosis is a rare congenital disorder of bone resorption characterised by generalised skeletal densification.	Bone marrow failure, fractures and visual impairment are the classical features of the disease, which begins in early infancy or in foetal life. It results from the failure of osteoclasts to resorb immature bone. This leads to abnormal bone marrow cavity formation and to the clinical signs and symptoms of bone marrow failure. It is accompanied by hepatosplenomegaly due to compensatory extramedullary hematopoiesis. Impaired bone remodelling causes bony narrowing of the cranial nerve foramina, which results in cranial nerve (especially optic nerve) compression. Pathologically, there is a persistence of the primary spongiosa characterised by cores of calcified cartilage within bone. Abnormal remodelling of primary, woven bone to lamellar bone results in 'brittle' bone that is prone to fracture. A rare form of the disease is associated with severe central nervous system dysfunction.	NM_006019.3(TCIRG1):c.1213G>A ; c.115_116del ; NM_006019.4:c.1331G>T ; NM_006019.3(TCIRG1):c.1674-1G>A ; NM_006019.3(TCIRG1):c.2236+1G>A ; NM_006019.3(TCIRG1):c.1213G>A ; c.115_116del ; NM_006019.4:c.1331G>T ; NM_006019.3(TCIRG1):c.1674-1G>A ; NM_006019.3(TCIRG1):c.2236+1G>A
TCIRG1	Intermediate osteopetrosis	A rare genetic primary bone dysplasia disease characterized by progressive osteosclerosis and platyspondyly.	The disease is characterized by sclerosis of the skull base, ribs, clavicles, scapulae, mid-diaphyses and increased bone fragility. Patients have a prominent forehead, narrow midface, flattening of the vertebral bodies and dental anomalies. Short stature, optic atrophy, hearing impairment, epilepsy, skin changes, and progressive psychomotor deficit are frequent.	NM_006019.3(TCIRG1):c.1213G>A ; c.115_116del ; NM_006019.4:c.1331G>T ; NM_006019.3(TCIRG1):c.1674-1G>A ; NM_006019.3(TCIRG1):c.2236+1G>A ; NM_006019.3(TCIRG1):c.1213G>A ; c.115_116del ; NM_006019.4:c.1331G>T ; NM_006019.3(TCIRG1):c.1674-1G>A ; NM_006019.3(TCIRG1):c.2236+1G>A

TFR2	Hemochromatosis type 3	Intermediate osteopetrosis is a rare, genetic primary bone dysplasia with increased bone density characterized by susceptibility to fractures after minor trauma, anemia, and characteristic skeletal radiographic changes, such as sandwich vertebra, bone-within-bone appearance, Erlenmeyer-shaped femoral metaphysis, and mild osteosclerosis of the skull base. Dental anomalies and visual impairment secondary to optic nerve compression have been rarely described.	Osteopetrosis (OPT) is a life-threatening disease caused by subnormal osteoclast function, with an incidence of 1 in 250,000 births. The disease usually manifests in the first few months of life with macrocephaly and frontal bossing, resulting in a characteristic facial appearance. Defective bone remodeling of the skull results in choanal stenosis with concomitant respiratory problems and feeding difficulties, which are the first clinical manifestation of disease. The expanding bone encroaches on neural foramina, leading to blindness, deafness, and facial palsy. Complete visual loss invariably occurs in all untreated patients, and hearing loss is estimated to affect 78% of patients with OPT. Tooth eruption defects and severe dental caries are common. Calcium feedback hemostasis is impaired, and children with OPT are at risk of developing hypocalcemia with attendant tetanic seizures and secondary hyperparathyroidism. The most severe complication of OPT, limiting survival, is bone marrow insufficiency. The abnormal .expansion of cortical and trabecular bone physically limits the availability of medullary space for hematopoietic activity, leading to life-threatening cytopenia and secondary expansion of extramedullary hematopoiesis at sites such as the liver and spleen	NM_003227.3(TFR2):c.750C>G ; NM_003227.3(TFR2):c.1231_1233delAAC ; NM_003227.3(TFR2):c.1469T>G ; c.1632_1633del ; c.1473+1G>A ; NM_003227.3(TFR2):c.2374G>A ; c.2343G>A ; NM_003227.3(TFR2):c.1330G>A ; NM_003227.3(TFR2):c.1665delC ; NM_003227.3(TFR2):c.313C>T ; NM_003227.3(TFR2):c.515T>A ; NM_003227.3(TFR2):c.1861_1872delGCCGTGGCCCAG ; NM_003227.3(TFR2):c.1186C>T ; NM_003227.3(TFR2):c.949C>T ; NM_003227.3(TFR2):c.750C>G ; NM_003227.3(TFR2):c.1231_1233delAAC ; NM_003227.3(TFR2):c.1469T>G ; c.1632_1633del ; c.1473+1G>A ; NM_003227.3(TFR2):c.2374G>A ; c.2343G>A ; NM_003227.3(TFR2):c.1330G>A ; NM_003227.3(TFR2):c.1665delC ; NM_003227.3(TFR2):c.313C>T ; NM_003227.3(TFR2):c.515T>A ; NM_003227.3(TFR2):c.1861_1872delGCCGTGGCCCAG ; NM_003227.3(TFR2):c.1186C>T ; NM_003227.3(TFR2):c.949C>T
TH	Autosomal recessive dopa-responsive dystonia	Type 3 hemochromatosis is a form of rare hereditary hemochromatosis (HH) (see this term), a group of diseases characterized by excessive tissue iron deposition of genetic origin.	Type 3 hemochromatosis concerns middle aged-adults but also adolescents and young adults (<30 years old). It resembles type 1 (HFE-related) hemochromatosis (see this term) and presents with liver disease, hypogonadism, arthritis, diabetes and skin pigmentation.	NM_199292.2(TH):c.1234C>A ; NM_199292.2(TH):c.826A>C ; NM_199292.2(TH):c.698G>A ; NM_199292.2(TH):c.707T>C ; NM_199292.2(TH):c.1234C>A ; NM_199292.2(TH):c.826A>C ; NM_199292.2(TH):c.698G>A ; NM_199292.2(TH):c.707T>C

TMC1	Autosomal dominant non-syndromic sensorineural deafness type DFNA	A very rare neurometabolic disorder characterized by a spectrum of symptoms ranging from those seen in dopa-responsive dystonia (DRD) to progressive infantile encephalopathy.	Disease presents in infancy (most frequently in the first year of life) with a progressive hypokinetic-rigid syndrome with generalized dystonia, involuntary jerky movements, postural tremor, or gait disturbances that may fluctuate during the day and show good or excellent responsiveness to levodopa (L-dopa) in most cases (>80%). Eye-rolling movements and/or mild, non-progressive intellectual deficit may be present in some cases. Less frequently, a more severe phenotype of complex encephalopathy can present before the age of 6 months, with marked hypokinesia and progressive truncal hypotonia, combined with focal or generalized dystonia, sometimes with dystonic crises over several days and (often excessive) jerky movements like myoclonus and tremor without diurnal fluctuations. Autonomic disturbances are frequent, such as excessive salivation and sweating, lethargy, constipation, poor feeding and "pyrexia of unknown origin". Intellectual deficit, developmental motor delay, bilateral ptosis and oculogyric crises are also frequent.	NM_138691.2(TMC1):c.1165C>T ; NM_138691.2:c.100C>T ; c.425G>A ; c.1842G>A ; NM_138691.2(TMC1):c.1960A>G ; c.454-1G>C ; NM_138691.2(TMC1):c.1165C>T ; NM_138691.2:c.100C>T ; c.425G>A ; c.1842G>A ; NM_138691.2(TMC1):c.1960A>G ; c.454-1G>C

TMC1	Autosomal recessive non-syndromic sensorineural deafness type DFNB	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	NM_138691.2(TMC1):c.1165C>T ; NM_138691.2:c.100C>T ; c.425G>A ; c.1842G>A ; NM_138691.2(TMC1):c.1960A>G ; c.454-1G>C ; NM_138691.2(TMC1):c.1165C>T ; NM_138691.2:c.100C>T ; c.425G>A ; c.1842G>A ; NM_138691.2(TMC1):c.1960A>G ; c.454-1G>C

TMEM216	Joubert syndrome with oculorenal defect	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	NM_001173990.2(TMEM216):c.218G>A ; c.79_82del ; NM_001173991.2:c.230G>C ; NM_001173990.2(TMEM216):c.253C>T ; NM_001173991.2(TMEM216):c.341T>G ; NM_001173990.3:c.218G>T ; NM_001173990.2(TMEM216):c.218G>A ; c.79_82del ; NM_001173991.2:c.230G>C ; NM_001173990.2(TMEM216):c.253C>T ; NM_001173991.2(TMEM216):c.341T>G ; NM_001173990.3:c.218G>T
TMEM216	Meckel syndrome	A rare subtype of Joubert syndrome (JS) and related disorders (JSRD) characterized by the neurological features of JS associated with both renal and ocular disease.	Patients present retinal involvement (manifesting with either Leber congenital amaurosis (LCA, see this term), or progressive retinal dystrophy) and nephronophthisis (NPH, usually juvenile). Retinal involvement is present at birth (LCA) or may manifest later in life. Juvenile NPH usually becomes clinically symptomatic towards the late first decade or the early second decade of life.	NM_001173990.2(TMEM216):c.218G>A ; c.79_82del ; NM_001173991.2:c.230G>C ; NM_001173990.2(TMEM216):c.253C>T ; NM_001173991.2(TMEM216):c.341T>G ; NM_001173990.3:c.218G>T ; NM_001173990.2(TMEM216):c.218G>A ; c.79_82del ; NM_001173991.2:c.230G>C ; NM_001173990.2(TMEM216):c.253C>T ; NM_001173991.2(TMEM216):c.341T>G ; NM_001173990.3:c.218G>T

TMEM216	Orofaciodigital syndrome type 6	A rare, lethal, genetic, multiple congenital anomaly disorder characterized by the triad of brain malformation (mainly occipital encephalocele), large polycystic kidneys, and polydactyly, as well as associated abnormalities that may include cleft lip/palate, cardiac and genital anomalies, central nervous system (CNS) malformations, liver fibrosis, and bone dysplasia.	Fetuses affected by Meckel syndrome (MKS) survive only a few days to a few weeks at the most, or dieÃ in utero. The main CNS features include occipital encephalocele, hydrocephalus, anencephaly, holoprosencephaly, as well as Dandy-Walker. Large polycystic kidneys with cystic dysplasia are a constant feature of Meckel syndrome. Hepatic dysgenesis and liver fibrosis are frequent. Polydactyly may affect all four extremities and is typically postaxial (80%) or very rarely preaxial. Affected individuals have pulmonary hypoplasia secondary to oligohydramnios. Cleft lip and palate, microphthalmia and micrognathia may be observed. Cardiac malformations may include atrial septal defect, aorta coarctation, patent arterial duct, and valvular pulmonary stenosis. Incomplete development of internal and external genitalia, and cryptorchidism in males are common.	NM_001173990.2(TMEM216):c.218G>A ; c.79_82del ; NM_001173991.2:c.230G>C ; NM_001173990.2(TMEM216):c.253C>T ; NM_001173991.2(TMEM216):c.341T>G ; NM_001173990.3:c.218G>T ; NM_001173990.2(TMEM216):c.218G>A ; c.79_82del ; NM_001173991.2:c.230G>C ; NM_001173990.2(TMEM216):c.253C>T ; NM_001173991.2(TMEM216):c.341T>G ; NM_001173990.3:c.218G>T
TPP1	Childhood-onset autosomal recessive slowly progressive spinocerebellar ataxia	Joubert syndrome with orofaciodigital defect (or oral-facial-digital syndrome type 6, OFD6) is a very rare subtype of Joubert syndrome and related disorders (JSRD, see this term) characterized by the neurological features of JS associated with orofacial anomalies and often polydactyly.	Typical oral findings include bifid or lobulated tongue, lingual hamartomas and multiple oral frenulae, but cleft lip and/or palate can also be present. Polydactyly is typically mesaxial with Y-shaped metacarpals, but can also be preaxial or postaxial. A subset of patients present with hypothalamic hamartoma that has never been reported in other JSRD subgroups.	NM_000391.3(TPP1):c.1340G>A ; NM_000391.3(TPP1):c.851G>T ; NM_000391.3(TPP1):c.622C>T ; NM_000391.3(TPP1):c.827A>T ; NM_000391.3(TPP1):c.509-1G>C ; NM_000391.3(TPP1):c.1093T>C ; c.141_144del ; NM_000391.3(TPP1):c.616C>T ; NM_000391.3(TPP1):c.1340G>A ; NM_000391.3(TPP1):c.851G>T ; NM_000391.3(TPP1):c.622C>T ; NM_000391.3(TPP1):c.827A>T ; NM_000391.3(TPP1):c.509-1G>C ; NM_000391.3(TPP1):c.1093T>C ; c.141_144del ; NM_000391.3(TPP1):c.616C>T

TPP1	CLN2 disease	Autosomal recessive spinocerebellar ataxia is a neurologic disorder characterized by onset of progressive gait difficulties, eye movement abnormalities, and dysarthria in the first or second decade of life.	A rare, genetic, autosomal recessive cerebellar ataxia disease characterized by slowly progressive spinocerebellar ataxia developing during childhood, manifesting with gait and limb ataxia, postural tremor, dysarthria, sensory alterations (e.g. decreased vibration sense), eye movement anomalies (i.e. nystagmus, saccadic pursuit, oculomotor apraxia), upper and lower limb fasciculations, and hyperreflexia with Babinski signs. Brain imaging reveals cerebellar, pontine, vermian and medullar atrophy.	NM_000391.3(TPP1):c.1340G>A ; NM_000391.3(TPP1):c.851G>T ; NM_000391.3(TPP1):c.622C>T ; NM_000391.3(TPP1):c.827A>T ; NM_000391.3(TPP1):c.509-1G>C ; NM_000391.3(TPP1):c.1093T>C ; c.141_144del ; NM_000391.3(TPP1):c.616C>T ; NM_000391.3(TPP1):c.1340G>A ; NM_000391.3(TPP1):c.851G>T ; NM_000391.3(TPP1):c.622C>T ; NM_000391.3(TPP1):c.827A>T ; NM_000391.3(TPP1):c.509-1G>C ; NM_000391.3(TPP1):c.1093T>C ; c.141_144del ; NM_000391.3(TPP1):c.616C>T
TREX1	Aicardi-GoutiÃ¨res syndrome	Neuronal ceroid lipofuscinoses (NCLs) are a group of inherited progressive degenerative brain diseases characterized clinically by a decline of mental and other capacities, epilepsy, and vision loss through retinal degeneration, and histopathologically by intracellular accumulation of an autofluorescent material, ceroid lipofuscin, in the neuronal cells in the brain and in the retina.	The clinical presentation varies widely between forms but the clinical hallmark is a combination of dementia, visual loss, and epilepsy. Manifestations may begin between the neonatal period and young adult age depending on the form, leading to the original classification of NCLs by age at onset into congenital, infantile, late infantile, juvenile and adult NCL subgroups (see these terms). A Northern epilepsy variant (progressive epilepsy-intellectual deficit, Finnish type; see this term), in which the visual problems may be absent or be mild and go unrecognized, has also been described.	NM_033629.2(TREX1):c.490C>T ; NM_033629.2(TREX1):c.490C>T

TREX1	Familial Chilblain lupus	An inherited, subacute encephalopathy characterised by the association of basal ganglia calcification, leukodystrophy and cerebrospinal fluid (CSF) lymphocytosis.	The majority of affected infants are born at full term with normal growth parameters. Onset occurs within the first few days or month of life with severe, subacute encephalopathy (feeding problems, irritability and psychomotor regression or delay) associated with epilepsy (53% of cases), chilblain skin lesions on the extremities (43% of cases) and episodes of aseptic febrile illness (40% of cases). Symptoms progress over several months (with the development of microcephaly and pyramidal signs) before the disease course stabilises. However, less severe forms have been described with onset after 1 year of age and preservation of language skills and cognitive function, and normal head circumference. The phenotype shows inter- and intrafamilial variation.	NM_033629.2(TREX1):c.490C>T ; NM_033629.2(TREX1):c.490C>T

TREX1	Retinal vasculopathy with cerebral leukoencephalopathy and systemic manifestations	A rare monogenic form of cutaneous lupus erythematosus characterized by infantile or childhood onset of cold-induced erythematous papules or plaques predominantly on the fingers, toes, nose, cheeks, and ears. Recurrent ulceration of the lesions may lead to necrotic tissue destruction and mutilation. Patients may experience ischemia of the affected acral regions. Histological findings include cutaneous perivascular inflammatory infiltrates with deposits of immunoglobulins or complement.	Affected individuals presented with painful bluish-red papular or nodular lesions of the skin in acral locations (including the dorsal aspects of fingers and toes, heels, nose, cheeks, ears, and, in some cases, knees) precipitated by cold and wet exposure at temperatures less than 10 degrees centigrade. Sometimes a plaque-like appearance was noted, and ulceration was commonly seen. Although deep ulceration led to necrotic destruction of the distal interphalangeal joint of the left fifth finger in the index patient at age 15 years, the lesions usually healed without scars, occasionally leaving atrophic skin and pigmentary changes. The onset of the skin lesions was in early childhood, and, in most patients, the lesions tended to improve during summer. Mucous membranes and nails were not affected, although subungual lesions were sometimes seen. There was no associated Raynaud phenomenon or photosensitivity. There was no evidence of associated disease of any internal organ (including the CNS), immune deficiency, or malignancy. Arthralgias affected mainly large joints, such as knees and shoulders. There was no increased susceptibility to infection. Histologic findings included a deep inflammatory infiltrate with perivascular distribution and granular deposits of immunoglobulins and complement along the basement membrane. Some affected individuals showed antinuclear antibodies or immune complex formation, whereas cryoglobulins or cold agglutinins were absent. The family study suggested a highly penetrant trait with autosomal dominant inheritance. Chilblain lupus occurs predominantly in adult women and has only rarely been described in children.	NM_033629.2(TREX1):c.490C>T ; NM_033629.2(TREX1):c.490C>T

TREX1	Systemic lupus erythematosus	Retinal vasculopathy and cerebral leukodystrophy (RVCL) is an inherited group of small vessel diseases comprised of cerebroretinal vasculopathy (CRV), hereditary vascular retinopathy (HRV) and hereditary endotheliopathy with retinopathy, nephropathy and stroke (HERNS); all exhibiting progressive visual impairment as well as variable cerebral dysfunction.	Retinal vasculopathy with cerebral leukoencephalopathy and systemic manifestations (RVCLS) is an adult-onset autosomal dominant disorder involving the microvessels of the brain and resulting in central nervous system degeneration with progressive loss of vision, stroke, motor impairment, and cognitive decline. Death occurs in most patients 5. to 10 years after onset. A subset of affected individuals have systemic vascular involvement evidenced by Raynaud phenomenon, micronodular cirrhosis, and glomerular dysfunction	NM_033629.2(TREX1):c.490C>T ; NM_033629.2(TREX1):c.490C>T
TRIM32	Bardet-Biedl syndrome	Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by production of autoantibodies against nuclear, cytoplasmic, and cell surface molecules that transcend organ-specific boundaries. Tissue deposition of antibodies or immune complexes induces inflammation and subsequent injury of multiple organs and finally results in clinical manifestations of SLE, including glomerulonephritis, dermatitis, thrombosis, vasculitis, seizures, and arthritis.		NC_000009.12:g.116699302del ; NM_001099679.1(TRIM32):c.1459G>A ; NC_000009.12:g.116699302del ; NM_001099679.1(TRIM32):c.1459G>A

TRIM32	TRIM32-related limb-girdle muscular dystrophy R8	Bardet-Biedl syndrome (BBS) is a ciliopathy with multisystem involvement.	This disorder is characterized by a combination of clinical signs: obesity, pigmentary retinopathy, post-axial polydactyly, polycystic kidneys, hypogenitalism, and learning disabilities, many of which appear several years after disease onset. Clinical expression is variable but most patients manifest the majority of clinical signs during the disease course. Pigmentary retinopathy is the only constant clinical sign after childhood. BBS may also be associated with several other manifestations including diabetes, hypertension, congenital cardiopathy and Hirschsprung disease (see this term).	NC_000009.12:g.116699302del ; NM_001099679.1(TRIM32):c.1459G>A ; NC_000009.12:g.116699302del ; NM_001099679.1(TRIM32):c.1459G>A
TRIM37	Mulibrey nanism	A mild subtype of autosomal recessive limb girdle muscular dystrophy characterized by slowly progressive proximal muscle weakness and wasting of the pelvic and shoulder girdles with onset that usually occurs during the second or third decade of life. Clinical presentation is variable and can include calf psuedohypertrophy, joint contractures, scapular winging, muscle cramping and/or facial and respiratory muscle involvement.		c.1668-1G>C ; NM_015294.4(TRIM37):c.965G>T ; NM_015294.4(TRIM37):c.227T>C ; NM_015294.4(TRIM37):c.2056C>T ; NM_015294.4(TRIM37):c.1346dupA ; c.1478_1479del ; NM_015294.4(TRIM37):c.2212delG ; NM_015294.4(TRIM37):c.1411C>T ; c.496_500del ; NM_015294.4(TRIM37):c.1037_1040dupAGAT ; NM_001005207.3(TRIM37):c.326G>C ; c.1668-1G>C ; NM_015294.4(TRIM37):c.965G>T ; NM_015294.4(TRIM37):c.227T>C ; NM_015294.4(TRIM37):c.2056C>T ; NM_015294.4(TRIM37):c.1346dupA ; c.1478_1479del ; NM_015294.4(TRIM37):c.2212delG ; NM_015294.4(TRIM37):c.1411C>T ; c.496_500del ; NM_015294.4(TRIM37):c.1037_1040dupAGAT ; NM_001005207.3(TRIM37):c.326G>C

TSEN54	Pontocerebellar hypoplasia type 1	A rare developmental defect during embryogenesis characterized by growth delay and multiorgan manifestations.	Mulibrey nanism (MUL) manifests neonatally and during infancy. It is characterized by pre- and postnatal growth restriction, relative macrocephaly, thin extremities and typical craniofacial features (scaphocephaly, facial triangularity, broad forehead and low nasal bridge). Psychomotor development is mainly normal. Feeding difficulties are common in infants. Children are prone to respiratory problems. Characteristic features also include yellowish dots in the retinal mid peripheral region, a high-pitched voice and cutaneous naevi flammei. Radiologic findings include slender long bones with thick cortex, narrow medullary channel and fibrous dysplasia, J-shaped sella turcica and a small thoracic cage. A restrictive, perimyocardial heart disease is the most serious element of the disorder. Hepatomegaly and fatty liver are common. Insulin resistance is an important metabolic finding. More than 90% of the adults show abnormally high fasting insulin levels resulting in type 2 diabetes in half of the patients. Tumors have been detected in several internal organs. The most frequent malignant tumor is Wilms' tumor. Females are at high risk of developing ovarian fibrothecomas. Primary hypogonadism, both male and female, as well as infertility, are central clinical characteristics.	c.887G>A ; NM_207346.2(TSEN54):c.736C>T ; NM_207346.2(TSEN54):c.919G>T ; NM_207346.2(TSEN54):c.670_671delAA ; NM_207346.2(TSEN54):c.1027C>T ; NM_207346.3(TSEN54):c.1039A>T ; c.887G>A ; NM_207346.2(TSEN54):c.736C>T ; NM_207346.2(TSEN54):c.919G>T ; NM_207346.2(TSEN54):c.670_671delAA ; NM_207346.2(TSEN54):c.1027C>T ; NM_207346.3(TSEN54):c.1039A>T
TSEN54	Pontocerebellar hypoplasia type 2	A severe, genetic form of pontocerebellar hypoplasia (PCH) characterized by spinal cord anterior horn cell degeneration in addition to pontocerebellar hypoplasia. Clinically, patients manifest with a severe global development deficit that is evident early on from difficulties in feeding and swallowing	The clinical course is severe. Neonates with PCH1 present with hypotonia, impaired swallowing with subsequent feeding difficulties, and progressive, postnatal microcephaly. A severe psychomotor deficit subsequently becomes apparent. If patients survive past infancy, patients have oculomotor manifestations including strabismus, nystagmus, occulomotor apraxia. The most severe cases of PCH1 manifest prenatally with polyhydramnios and arthrogryposis multiplex congenital.	c.887G>A ; NM_207346.2(TSEN54):c.736C>T ; NM_207346.2(TSEN54):c.919G>T ; NM_207346.2(TSEN54):c.670_671delAA ; NM_207346.2(TSEN54):c.1027C>T ; NM_207346.3(TSEN54):c.1039A>T ; c.887G>A ; NM_207346.2(TSEN54):c.736C>T ; NM_207346.2(TSEN54):c.919G>T ; NM_207346.2(TSEN54):c.670_671delAA ; NM_207346.2(TSEN54):c.1027C>T ; NM_207346.3(TSEN54):c.1039A>T

TSEN54	Pontocerebellar hypoplasia type 4	A rare, genetic form of pontocerebellar hypoplasia characterized by pontocerebellar hypoplasia and progressive neocortical atrophy that manifests clinically with uncoordinated sucking and swallowing, and generalized clonus in the neonate. In early childhood, spasticity, chorea/dyskinesia, seizures and progressive microcephaly develop. Voluntary motor development is lacking.	After an uneventful pregnancy and birth without dysmorphic features, affected neonates present usually, but not always, with dysphagia due to bucco-pharyngeal incoordination, respiratory and feeding difficulties and generalized clonus. Extrapyramidal dyskinesia with mixed spasticity such as chorea, athetosis and dystonia develop later. From infancy onward, affected children develop progressive microcephaly, central visual impairment, seizures and a severe impairment of cognitive and motor development, marked by an impaired motor development with failing head control, lack of voluntary hand control and the absence of speech and communication. PCH2 is often fatal in early childhood.	c.887G>A ; NM_207346.2(TSEN54):c.736C>T ; NM_207346.2(TSEN54):c.919G>T ; NM_207346.2(TSEN54):c.670_671delAA ; NM_207346.2(TSEN54):c.1027C>T ; NM_207346.3(TSEN54):c.1039A>T ; c.887G>A ; NM_207346.2(TSEN54):c.736C>T ; NM_207346.2(TSEN54):c.919G>T ; NM_207346.2(TSEN54):c.670_671delAA ; NM_207346.2(TSEN54):c.1027C>T ; NM_207346.3(TSEN54):c.1039A>T
TSFM	Fatal mitochondrial disease due to combined oxidative phosphorylation defect type 3	A severe, genetic form of pontocerebellar hypoplasia (PCH) characterized by delayed neocortical maturation with underdeveloped cerebral hemispheres and pontocerebellar hypoplasia and a severely affected vermis. Clinically, the disorder manifests with prenatal onset of polyhydramnios and contractures followed by hypertonia, severe clonus, primary hypoventilation leading to an early postnatal death.	PCH4 is characterized prenatally by polyhydramnios. Neonates present with microcephaly, central apnea requiring respiratory support, dysmorphism (sloping forehead, midface hypoplasia, micrognathia), congenital arthrogryposis (50%), severe clonus, and hypertonia. Weaning from mechanical ventilation is difficult and usually fails. Survival beyond the neonatal period is rare.	c.1_2del ; c.581del ; c.24_25del ; NM_005726.5(TSFM):c.856C>T ; c.1_2del ; c.581del ; c.24_25del ; NM_005726.5(TSFM):c.856C>T

TSHB	Isolated thyroid-stimulating hormone deficiency	Combined oxidative phosphorylation deficiency type 3 is an extremely rare clinically heterogenous disorder described in about 5 patients to date. Clinical signs included hypotonia, lactic acidosis, and hepatic insufficiency, with progressive encephalomyopathy or hypertrophic cardiomyopathy.	The first proband was the child of consanguineous Turkish parents. Muscular hypotonia, sucking weakness, and severe lactic acidosis were the initial clinical signs and symptoms, followed by rhabdomyolysis with elevated creatine kinase values. Generalized convulsions began on the third day of life. Despite intensive treatment, the patient died of progressive encephalomyopathy and respiratory failure at age 7 weeks. The second proband was the offspring of consanguineous Kurdish Jewish parents. The mother reported a paucity of fetal movements throughout pregnancy. At age 36 hours, apathy, irregular breathing, and severe muscular hypotonia were noted. Laboratory investigations revealed severe metabolic acidosis with increased serum lactate level, blood ketone levels, and serum ammonia levels. Echocardiographic examination disclosed severe concentric hypertrophic cardiomyopathy with normal contractility. Death occurred at age 7 weeks.	NM_000549.4(TSHB):c.205C>T ; NM_000549.4(TSHB):c.145G>A ; NM_000549.4(TSHB):c.94G>T ; NM_000549.4(TSHB):c.205C>T ; NM_000549.4(TSHB):c.145G>A ; NM_000549.4(TSHB):c.94G>T
TSHR	Athyreosis	A type of central congenital hypothyroidism, a permanent thyroid deficiency that is present from birth, characterized by low levels of thyroid hormones due to a deficiency in TSH synthesis.	The clinical manifestations are often subtle, probably as a result of trans-placental passage of some maternal thyroid hormone or due to the fact that many infants have some thyroid production of their own. More specific symptoms and signs often do not develop until several months of age. Common clinical features and signs include decreased activity and increased sleep, feeding difficulty and constipation, prolonged jaundice, myxedematous facies, large fontanels (especially posterior), macroglossia, a distended abdomen with umbilical hernia, and hypotonia. Slow linear growth and developmental delay are usually apparent by 4-6 months of age.	NM_000369.2(TSHR):c.326G>A ; NM_000369.2(TSHR):c.1170T>G ; NM_000369.2(TSHR):c.500T>A ; c.1742dup ; NM_000369.2(TSHR):c.122G>C ; NM_000369.2(TSHR):c.484C>G ; NM_000369.2(TSHR):c.326G>A ; NM_000369.2(TSHR):c.1170T>G ; NM_000369.2(TSHR):c.500T>A ; c.1742dup ; NM_000369.2(TSHR):c.122G>C ; NM_000369.2(TSHR):c.484C>G

TSHR	Familial gestational hyperthyroidism	A rare form of thyroid dysgenesis characterized by complete absence of thyroid tissue that results in primary congenital hypothyroidism, a permanent thyroid deficiency that is present from birth.	Clinical manifestations of athyreosis are often subtle or not present at birth, probably as a result of trans-placental passage of some maternal thyroid hormone. More specific symptoms and signs do not develop until several months of age. Common clinical features and signs include decreased activity and increased sleep, feeding difficulty and constipation, prolonged jaundice, myxedematous facies, large fontanels (especially posterior), macroglossia, a distended abdomen with umbilical hernia, and hypotonia. Goiter is always absent. Slow linear growth and developmental delay are usually apparent by 4-6 months of age.	NM_000369.2(TSHR):c.326G>A ; NM_000369.2(TSHR):c.1170T>G ; NM_000369.2(TSHR):c.500T>A ; c.1742dup ; NM_000369.2(TSHR):c.122G>C ; NM_000369.2(TSHR):c.484C>G ; NM_000369.2(TSHR):c.326G>A ; NM_000369.2(TSHR):c.1170T>G ; NM_000369.2(TSHR):c.500T>A ; c.1742dup ; NM_000369.2(TSHR):c.122G>C ; NM_000369.2(TSHR):c.484C>G
TSHR	Familial hyperthyroidism due to mutations in TSH receptor	A rare genetic hyperthyroidism characterized by hyperemesis gravidarum associated with hyperthyroidism due to hypersensitivity of the thyrotropin receptor to chorionic gonadotropin, in the absence of abnormally high serum chorionic gonadotropin levels. Clinical manifestations include severe nausea, vomiting, weight loss, tachycardia, excessive sweating, and hand tremor, but no signs of ophthalmopathy.	Hyperemesis gravidarum is characterized by excessive vomiting in early pregnancy, leading to the loss of 5% or more of body weight. It is usually self-limited and therefore of little clinical consequence. Some women with the disorder have high serum thyroid hormone concentrations, and a few have sufficient clinical manifestations of hyperthyroidism to warrant short-term treatment with antithyroid drugs. Many, but not all, women with hyperemesis gravidarum and hyperthyroidism have high serum chorionic gonadotropin concentrations.	NM_000369.2(TSHR):c.326G>A ; NM_000369.2(TSHR):c.1170T>G ; NM_000369.2(TSHR):c.500T>A ; c.1742dup ; NM_000369.2(TSHR):c.122G>C ; NM_000369.2(TSHR):c.484C>G ; NM_000369.2(TSHR):c.326G>A ; NM_000369.2(TSHR):c.1170T>G ; NM_000369.2(TSHR):c.500T>A ; c.1742dup ; NM_000369.2(TSHR):c.122G>C ; NM_000369.2(TSHR):c.484C>G
TSHR	Hypothyroidism due to TSH receptor mutations	A rare hyperthyroidism characterized by mild to severe hyperthyroidism, presence of goiter, absence of features of autoimmunity, frequent relapses while on treatment and a positive family history.	Resistance to thyroid-stimulating hormone, a hallmark of congenital nongoitrous hypothyroidism, causes increased levels of plasma TSH and low levels of thyroid hormone. Only a subset of patients develop frank hypothyroidism; the remainder are euthyroid and asymptomatic (so-called compensated hypothyroidism) and are usually detected by neonatal screening programs.Â	NM_000369.2(TSHR):c.326G>A ; NM_000369.2(TSHR):c.1170T>G ; NM_000369.2(TSHR):c.500T>A ; c.1742dup ; NM_000369.2(TSHR):c.122G>C ; NM_000369.2(TSHR):c.484C>G ; NM_000369.2(TSHR):c.326G>A ; NM_000369.2(TSHR):c.1170T>G ; NM_000369.2(TSHR):c.500T>A ; c.1742dup ; NM_000369.2(TSHR):c.122G>C ; NM_000369.2(TSHR):c.484C>G

TSHR	Thyroid hypoplasia	A type of primary congenital hypothyroidism, a permanent thyroid hormone deficiency that is present from birth due to thyroid resistance to TSH.	Clinical manifestations are those of other forms of congenital hypothyroidism (CH; see this term). Goiter is always absent.	NM_000369.2(TSHR):c.326G>A ; NM_000369.2(TSHR):c.1170T>G ; NM_000369.2(TSHR):c.500T>A ; c.1742dup ; NM_000369.2(TSHR):c.122G>C ; NM_000369.2(TSHR):c.484C>G ; NM_000369.2(TSHR):c.326G>A ; NM_000369.2(TSHR):c.1170T>G ; NM_000369.2(TSHR):c.500T>A ; c.1742dup ; NM_000369.2(TSHR):c.122G>C ; NM_000369.2(TSHR):c.484C>G
TTN	Autosomal recessive centronuclear myopathy	Thyroid hypoplasia is a form of thyroid dysgenesis (see this term) characterized by incomplete development of the thyroid gland that results in primary congenital hypothyroidism (see this term), a permanent thyroid deficiency that is present from birth.	Clinical manifestations of thyroid hypoplasia are often subtle or not present at birth, probably as a result of trans-placental passage of some maternal thyroid hormone or due to the fact that many infants have some thyroid production of their own. More specific symptoms and signs do not develop until several months of age. Common clinical features and signs include decreased activity and increased sleep, feeding difficulty and constipation, prolonged jaundice, myxedematous facies, large fontanels (especially posterior), macroglossia, a distended abdomen with umbilical hernia, and hypotonia. Goiter is always absent. Slow linear growth and developmental delay are usually apparent by 4-6 months of age. Without treatment thyroid hypoplasia results in severe intellectual deficit and short stature.	NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del ; NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del
TTN	Childhood-onset progressive contractures-limb-girdle weakness-muscle dystrophy syndrome	A rare autosomal recessive congenital myopathy characterized by numerous centrally placed nuclei on muscle biopsy and clinical features of a congenital myopathy including facial weakness, ocular abnormalities (ptosis and external ophthalmoplegia) and predominant proximal muscle weakness of variable severity with possible distal involvement.	The age of onset varies from birth to childhood. AR-CNM is characterized by facial weakness including severe involvement of the masticatory muscles, and ocular abnormalities such as ptosis and external ophthalmoplegia. Muscle weakness is observed with variable severity. It is usually prominently proximal, but there may be additional distal weakness and wasting in the lower limbs. Foot abnormalities are frequent and other skeletal deformities (including high arched palate and scoliosis) are common. Respiratory involvement may be severe. An associated cardiomyopathy has been documented in a few, genetically unresolved cases. Urinary incontinence may be an associated feature.	NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del ; NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del

TTN	Classic multiminicore myopathy	A progressive muscular dystrophy characterized by co-existence of limb-girdle weakness and diffuse joint contractures without cardiomyopathy. Patients present lower limb weakness progressing to involve also upper limbs and axial muscles and eventually leading to permanent loss of ambulation, widespread joint contractures in the limbs and sometimes the spine, and variable respiratory involvement. Morphological changes in muscle biopsies include rimmed vacuoles, increased internal nuclei, cytoplasmic bodies, and a dystrophic pattern.	Patients presented between 13 and 16 years of age with difficulty running and climbing, frequent falls, and Gowers sign. They developed proximal muscle weakness and atrophy affecting the lower and upper limbs. The disorder was progressive, and they developed elbow and ankle joint contractures; none was able to walk or raise their arms above their shoulders after their thirties. One patient also had lordosis. Skeletal muscle biopsy of 1 patient showed variation in fiber diameter, cell necrosis, fibrosis, and some regenerating fibers. Serum creatine kinase was increased in 2 patients. There was no cardiac involvement.	NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del ; NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del
TTN	Early-onset myopathy with fatal cardiomyopathy	A rare hereditary neuromuscular disorder characterized by multiple cores on muscle biopsy and clinical features of a congenital myopathy.	Marked clinical variability corresponds to genetic heterogeneity: the most instantly recognizable classic phenotype characterized by spinal rigidity, early scoliosis and respiratory impairment is due to recessive mutations in the selenoprotein N (SEPN1) gene, whereas recessive mutations in the skeletal muscle ryanodine receptor (RYR1) gene have been associated with a wider range of clinical features comprising external ophthalmoplegia, distal weakness and wasting or predominant hip girdle involvement resembling central core disease (CCD). In the latter forms, there may also be a histopathologic continuum with CCD caused by dominantÃ RYR1Â mutations, reflecting the common genetic background.	NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del ; NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del

TTN	Familial atrial fibrillation	A rare genetic neuromuscular disease characterized by neonatal or infancy onset of delayed motor development, generalized muscle weakness involving also the facial muscles, pseudohypertrophy of lower limb muscles, and joint contractures, associated with childhood onset of rapidly progressive dilated cardiomyopathy with arrhythmias leading to sudden cardiac death. Muscle biopsy in early childhood shows minicore-like lesions and centralized nuclei, with dystrophic features being more conspicuous in the second decade of life.	All patients showed delayed motor development with symmetric, generalized muscle weakness predominantly of proximal and distal lower limbs. Other features included facial muscle weakness, ptosis, and relative calf hypertrophy. Progressive dilated cardiomyopathy with rhythm disturbances developed between ages 5 and 12 years. Death from cardiomyopathy occurred in all 5 patients; 4 survived into their teenage years. Skeletal muscle biopsies showed minicore-like lesions with mitochondrial depletion and sarcomere disorganization, centralized nuclei, and type 1 fiber predominance. Dystrophic changes were more apparent in the second decade. Cardiac muscle biopsies showed disruption of myocardial architecture, nuclear hypertrophy, and endomysial fibrosis. All parents were clinically unaffected.	NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del ; NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del
TTN	Familial isolated arrhythmogenic ventricular dysplasia, biventricular form	Familial atrial fibrillation is a rare, genetically heterogenous cardiac disease characterized by erratic activation of the atria with an irregular ventricular response, in various members of a single family. It may be asymptomatic or associated with palpitations, dyspnea and light-headedness. Concomitant rhythm disorders and cardiomyopathies are frequently reported.		NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del ; NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del

TTN	Familial isolated arrhythmogenic ventricular dysplasia, left dominant form	Familial isolated arrhythmogenic right ventricular dysplasia (ARVC) is the familial autosomal dominant form of ARVC (see this term), a heart muscle disease characterized by life-threatening ventricular arrhythmias with left bundle branch block configuration that may manifest with palpitations, ventricular tachycardia, syncope and sudden fatal attacks, and that is due to dystrophy and fibro-fatty replacement of the right ventricular myocardium that may lead to right ventricular aneurysms.		NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del ; NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del
TTN	Familial isolated arrhythmogenic ventricular dysplasia, right dominant form	Familial isolated arrhythmogenic right ventricular dysplasia (ARVC) is the familial autosomal dominant form of ARVC (see this term), a heart muscle disease characterized by life-threatening ventricular arrhythmias with left bundle branch block configuration that may manifest with palpitations, ventricular tachycardia, syncope and sudden fatal attacks, and that is due to dystrophy and fibro-fatty replacement of the right ventricular myocardium that may lead to right ventricular aneurysms.		NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del ; NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del

TTN	Familial isolated dilated cardiomyopathy	Familial isolated arrhythmogenic right ventricular dysplasia (ARVC) is the familial autosomal dominant form of ARVC (see this term), a heart muscle disease characterized by life-threatening ventricular arrhythmias with left bundle branch block configuration that may manifest with palpitations, ventricular tachycardia, syncope and sudden fatal attacks, and that is due to dystrophy and fibro-fatty replacement of the right ventricular myocardium that may lead to right ventricular aneurysms.		NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del ; NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del
TTN	Hereditary myopathy with early respiratory failure	A rare familial cardiomyopathy characterized by the dilation of left ventricle and progressively impairing of systolic ventricular function, in the absence of abnormal loading conditions or coronary artery disease sufficient to cause global systolic impairment. The disease may cause heart failure or arrhythmia. The disease is isolated when no additional atypical cardiac or extracardiac manifestations are present.	The disease is defined by the presence of two major clinical criteria: left ventricular (LV) fractional shortening less than 25% and/or LV ejection fraction less than 45% with LV end diastolic diameter greater than 117% of the predicted value (corrected for age and body surface area based on Henry's formula), in the absence of abnormal loading conditions or coronary artery disease sufficient to cause global systolic impairment. The disease can develop at any age, in either sex. LV mass is often greatly increased in this disorder but LV wall thickness is normal. Symptoms of heart failure may be present as well as arrhythmias. Other presentations include the incidental detection of asymptomatic cardiomegaly and symptoms related to coexisting conduction disturbance or thromboembolic complications. Typically, there is a history of DCM in the family.	NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del ; NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del

TTN	Familial isolated hypertrophic cardiomyopathy	A rare genetic neuromuscular disease characterized by adult onset of slowly progressive distal and/or proximal muscle weakness in the upper and lower extremities, and early involvement of respiratory muscles leading to respiratory failure. Additional features are neck flexor weakness, foot extensor weakness, and, in rare cases, mildly impaired cardiac function. Muscle biopsy shows eosinophilic myofibrillar inclusions referred to as cytoplasmic bodies, as well as fiber size variation, increased internal nuclei and connective tissue, fiber splitting, and rimmed vacuoles.	Myofibrillar myopathy-9 with early respiratory failure (MFM9) is an autosomal dominant muscle disorder characterized by adult onset of slowly progressive muscle weakness with diaphragmatic involvement causing respiratory insufficiency. Patients present between 20 and 70 years of age with distal or proximal muscle weakness, mainly affecting the lower limbs with foot drop or difficulty walking. The age at onset is highly variable, even within families. Nearly all patients eventually develop significant proximal and distal weakness, as well as respiratory insufficiency requiring nocturnal ventilation. Additional, more variable features may include axial weakness, neck muscle weakness, and rarely, cardiac involvement. Muscle biopsy shows myopathic or dystrophic changes with fiber splitting, eosinophilic cytoplasmic inclusions consistent with myofibrillar myopathy, rimmed vacuoles, and increased connective or fatty tissue.	NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del ; NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del
TTN	Tibial muscular dystrophy			NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del ; NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del

TTN	Titin-related limb-girdle muscular dystrophy R10	Tibial muscular dystrophy (TMD) is a distal myopathy characterized by weakness of the muscles of the anterior compartment of lower limbs, appearing in the fourth to seventh decade of life.	TMD manifests after the age of 35 to 40 (rarely after the age of 60) as slowly progressive weakness and atrophy of the anterior tibial muscles with decreased dorsiflexion. Muscle involvement may remain asymmetrical for many years. After about 10 to 20 years, long toe extensors become involved causing foot drop, tripping and clumsiness while walking. Proximal limb muscles, mainly hamstring muscles, may be involved after the age of 60 to 70 and may necessitate the use of a cane and reduced walking distances. Extensor digitorum brevis muscles are spared and involvement of upper limbs is very rare. Neither cardiomyopathy nor respiratory failure has been encountered. TMD may present in a mild form (may remain unnoticed even in elderly individuals) or as aberrant phenotypic forms in about 9% of cases (proximal leg or posterior lower leg muscle involvement even at onset).	NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del ; NM_001267550.2(TTN):c.60681dupT ; c.21296dup ; c.24568_24571del ; c.25753del ; c.77473del ; c.42725C>G ; c.79451_79452del ; c.3027-1G>T ; c.13149C>A ; c.21634del ; NM_001256850.1(TTN):c.102966delA ; c.65754_65760del ; NC_000002.12:g.178599063C>T ; c.72199_72202del
TTPA	Ataxia with vitamin E deficiency	A form of limb-girdle muscular dystrophy that usually has a childhood onset (but can range from the first to third decade of life) of severe progressive proximal weakness, eventually involving the distal muscles. Some patients may remain ambulatory but most are wheelchair dependant 20 years after onset.	Patients had nonspecific myopathic changes on muscle biopsy and progressive fatty infiltration of involved muscles. Onset of the severe LGMD phenotype was in the first to third decades and involved weakness of all proximal muscles. Severe disability with loss of ambulation occurred within 20 years (third to sixth decades). There was no facial muscle involvement or cardiomyopathy. Some patients later developed distal muscle involvement. Segregation analysis showed that the corrected proportion of affected persons with the severe proximal type was 0.246 and the proportion of affected persons with the distal myopathy was 0.58. The findings were compatible with the hypothesis that the severe LGMD phenotype was the homozygous manifestation of a dominant gene that in the heterozygous state caused the milder distal myopathy.	NM_000370.3(TTPA):c.575G>A ; NM_000370.3(TTPA):c.744delA ; NM_000370.3(TTPA):c.575G>A ; NM_000370.3(TTPA):c.744delA

TYR	Minimal pigment oculocutaneous albinism type 1	A neurodegenerative disease belonging to the inherited cerebellar ataxias mainly characterized by progressive spino-cerebellar ataxia, loss of proprioception, areflexia, and is associated with a marked deficiency in vitamin E.	AVED presents generally between ages 5 and 20 years with variable phenotype and severity. Progressive spino-cerebellar ataxia, areflexia and loss of proprioception, mainly in distal joint position and of vibration sense, induce a noticeable clumsiness and imbalance. Patients may have a characteristic head titubation. Tendon reflexes are dramatically reduced and extensor plantar reflexes are frequent. Cerebellar impairment frequently manifests as dysmetria, dysdiadochokinesia and dysarthria. Decreased visual acuity with retinitis pigmentosa may be seen. In some cases, disease onset is late (> 30 years) and the course is milder. On the contrary, in early-onset cases, the course is more severe, with an increased risk of cardiomyopathy. Overall, the clinical picture of AVED is close to that of Friedreich's ataxia (see this term).	NM_000372.4(TYR):c.1255G>A ; c.1177del ; NM_000372.4(TYR):c.325G>A ; NM_000372.4(TYR):c.1147G>A ; NM_000372.5(TYR):c.1501dup ; NM_000372.4(TYR):c.230G>A ; NM_000372.4(TYR):c.572delG ; NM_000372.4(TYR):c.1336G>A ; NM_000372.5:c.1118C>A ; NM_000372.4(TYR):c.646T>A ; NM_000372.4(TYR):c.1265G>A ; NM_000372.4(TYR):c.616G>A ; NM_000372.4:c.1012_1013insC ; NM_000372.4(TYR):c.1217C>T ; NM_000372.4(TYR):c.823G>T ; NM_000372.4(TYR):c.242C>T ; NM_000372.4(TYR):c.1209G>T ; NM_000372.4(TYR):c.164G>A ; NM_000372.4(TYR):c.1342G>A ; NM_000372.5:c.896G>A ; NM_000372.5:c.140G>A ; NM_000372.4(TYR):c.1467dupT ; NM_000372.4(TYR):c.1A>G ; NM_000372.4(TYR):c.533G>A ; NM_000372.4(TYR):c.1164delT ; NM_000372.4(TYR):c.650G>A ; NM_000372.4(TYR):c.265T>C ; NM_000372.4(TYR):c.272G>A ; NM_000372.4(TYR):c.286dupA ; NM_000372.4(TYR):c.1146C>A ; NM_000372.4(TYR):c.1255G>A ; c.1177del ; NM_000372.4(TYR):c.325G>A ; NM_000372.4(TYR):c.1147G>A ; NM_000372.5(TYR):c.1501dup ; NM_000372.4(TYR):c.230G>A ; NM_000372.4(TYR):c.572delG ; NM_000372.4(TYR):c.1336G>A ; NM_000372.5:c.1118C>A ; NM_000372.4(TYR):c.646T>A ; NM_000372.4(TYR):c.1265G>A ; NM_000372.4(TYR):c.616G>A ; NM_000372.4:c.1012_1013insC ; NM_000372.4(TYR):c.1217C>T ; NM_000372.4(TYR):c.823G>T ; NM_000372.4(TYR):c.242C>T ; NM_000372.4(TYR):c.1209G>T ; NM_000372.4(TYR):c.164G>A ; NM_000372.4(TYR):c.1342G>A ; NM_000372.5:c.896G>A ; NM_000372.5:c.140G>A ; NM_000372.4(TYR):c.1467dupT ; NM_000372.4(TYR):c.1A>G ; NM_000372.4(TYR):c.533G>A ; NM_000372.4(TYR):c.1164delT ; NM_000372.4(TYR):c.650G>A ; NM_000372.4(TYR):c.265T>C ; NM_000372.4(TYR):c.272G>A ; NM_000372.4(TYR):c.286dupA ; NM_000372.4(TYR):c.1146C>A
TYR	Ocular albinism with congenital sensorineural deafness	An extremely rare form of Oculocutaneous albinism type 1 with minimal pigment present, characterized by blond hair (white at birth), variable iris transillumination (blue irides at birth followed by minimal development of pigment during the first decade of life), visual acuity ranging from 20/80-20/200 and white skin, with or without skin nevi.	Oculocutaneous albinism is a genetically heterogeneous congenital disorder characterized by decreased or absent pigmentation in the hair, skin, and eyes. The term 'albinism' includes specific ocular changes that are the results of reduced amounts of melanin in the developing eye; these abnormalities in the eye and optic system are specific and necessary for the diagnosis. Aside from decreased pigment in the iris and retina, optic changes include decreased visual acuity, misrouting of the optic nerves at the chiasm, and nystagmus.	NM_000372.4(TYR):c.1255G>A ; c.1177del ; NM_000372.4(TYR):c.325G>A ; NM_000372.4(TYR):c.1147G>A ; NM_000372.5(TYR):c.1501dup ; NM_000372.4(TYR):c.230G>A ; NM_000372.4(TYR):c.572delG ; NM_000372.4(TYR):c.1336G>A ; NM_000372.5:c.1118C>A ; NM_000372.4(TYR):c.646T>A ; NM_000372.4(TYR):c.1265G>A ; NM_000372.4(TYR):c.616G>A ; NM_000372.4:c.1012_1013insC ; NM_000372.4(TYR):c.1217C>T ; NM_000372.4(TYR):c.823G>T ; NM_000372.4(TYR):c.242C>T ; NM_000372.4(TYR):c.1209G>T ; NM_000372.4(TYR):c.164G>A ; NM_000372.4(TYR):c.1342G>A ; NM_000372.5:c.896G>A ; NM_000372.5:c.140G>A ; NM_000372.4(TYR):c.1467dupT ; NM_000372.4(TYR):c.1A>G ; NM_000372.4(TYR):c.533G>A ; NM_000372.4(TYR):c.1164delT ; NM_000372.4(TYR):c.650G>A ; NM_000372.4(TYR):c.265T>C ; NM_000372.4(TYR):c.272G>A ; NM_000372.4(TYR):c.286dupA ; NM_000372.4(TYR):c.1146C>A ; NM_000372.4(TYR):c.1255G>A ; c.1177del ; NM_000372.4(TYR):c.325G>A ; NM_000372.4(TYR):c.1147G>A ; NM_000372.5(TYR):c.1501dup ; NM_000372.4(TYR):c.230G>A ; NM_000372.4(TYR):c.572delG ; NM_000372.4(TYR):c.1336G>A ; NM_000372.5:c.1118C>A ; NM_000372.4(TYR):c.646T>A ; NM_000372.4(TYR):c.1265G>A ; NM_000372.4(TYR):c.616G>A ; NM_000372.4:c.1012_1013insC ; NM_000372.4(TYR):c.1217C>T ; NM_000372.4(TYR):c.823G>T ; NM_000372.4(TYR):c.242C>T ; NM_000372.4(TYR):c.1209G>T ; NM_000372.4(TYR):c.164G>A ; NM_000372.4(TYR):c.1342G>A ; NM_000372.5:c.896G>A ; NM_000372.5:c.140G>A ; NM_000372.4(TYR):c.1467dupT ; NM_000372.4(TYR):c.1A>G ; NM_000372.4(TYR):c.533G>A ; NM_000372.4(TYR):c.1164delT ; NM_000372.4(TYR):c.650G>A ; NM_000372.4(TYR):c.265T>C ; NM_000372.4(TYR):c.272G>A ; NM_000372.4(TYR):c.286dupA ; NM_000372.4(TYR):c.1146C>A

TYR	Oculocutaneous albinism type 1A	Ocular albinism with congenital sensorineural deafness is a rare, genetic, oculocutaneous disorder characterized by profound, congenital, sensorineural hearing loss in association with moderate to severe hypopigmentation of the ocular fundus, blue irides or partial heterochromia, and patchy or generalized hypopigmentation of the skin. White forelock, premature graying of hair, freckles, lentigines and cafÃ©-au-lait macules are frequently associated. Other highly variable features include reduced visual acuity, strabismus, and an iris transillumination defect.	As in the X-linked Nettleship-Falls form of ocular albinism, patients show reduced visual acuity, photophobia, nystagmus, translucent irides, strabismus, hypermetropic refractive errors, and albinotic fundus with foveal hypoplasia. Skin lesions show macromelanosomes as in X-linked ocular albinism. Deafness, which is accompanied by vestibular hypofunction, lentigines even in unexposed areas, optic nerve dysplasia, and dominant inheritance distinguish this form of ocular albinism.	NM_000372.4(TYR):c.1255G>A ; c.1177del ; NM_000372.4(TYR):c.325G>A ; NM_000372.4(TYR):c.1147G>A ; NM_000372.5(TYR):c.1501dup ; NM_000372.4(TYR):c.230G>A ; NM_000372.4(TYR):c.572delG ; NM_000372.4(TYR):c.1336G>A ; NM_000372.5:c.1118C>A ; NM_000372.4(TYR):c.646T>A ; NM_000372.4(TYR):c.1265G>A ; NM_000372.4(TYR):c.616G>A ; NM_000372.4:c.1012_1013insC ; NM_000372.4(TYR):c.1217C>T ; NM_000372.4(TYR):c.823G>T ; NM_000372.4(TYR):c.242C>T ; NM_000372.4(TYR):c.1209G>T ; NM_000372.4(TYR):c.164G>A ; NM_000372.4(TYR):c.1342G>A ; NM_000372.5:c.896G>A ; NM_000372.5:c.140G>A ; NM_000372.4(TYR):c.1467dupT ; NM_000372.4(TYR):c.1A>G ; NM_000372.4(TYR):c.533G>A ; NM_000372.4(TYR):c.1164delT ; NM_000372.4(TYR):c.650G>A ; NM_000372.4(TYR):c.265T>C ; NM_000372.4(TYR):c.272G>A ; NM_000372.4(TYR):c.286dupA ; NM_000372.4(TYR):c.1146C>A ; NM_000372.4(TYR):c.1255G>A ; c.1177del ; NM_000372.4(TYR):c.325G>A ; NM_000372.4(TYR):c.1147G>A ; NM_000372.5(TYR):c.1501dup ; NM_000372.4(TYR):c.230G>A ; NM_000372.4(TYR):c.572delG ; NM_000372.4(TYR):c.1336G>A ; NM_000372.5:c.1118C>A ; NM_000372.4(TYR):c.646T>A ; NM_000372.4(TYR):c.1265G>A ; NM_000372.4(TYR):c.616G>A ; NM_000372.4:c.1012_1013insC ; NM_000372.4(TYR):c.1217C>T ; NM_000372.4(TYR):c.823G>T ; NM_000372.4(TYR):c.242C>T ; NM_000372.4(TYR):c.1209G>T ; NM_000372.4(TYR):c.164G>A ; NM_000372.4(TYR):c.1342G>A ; NM_000372.5:c.896G>A ; NM_000372.5:c.140G>A ; NM_000372.4(TYR):c.1467dupT ; NM_000372.4(TYR):c.1A>G ; NM_000372.4(TYR):c.533G>A ; NM_000372.4(TYR):c.1164delT ; NM_000372.4(TYR):c.650G>A ; NM_000372.4(TYR):c.265T>C ; NM_000372.4(TYR):c.272G>A ; NM_000372.4(TYR):c.286dupA ; NM_000372.4(TYR):c.1146C>A
TYR	Oculocutaneous albinism type 1B	A severe form of oculocutaneous albinism type 1 (OCA1) characterized by complete absence of melanin and manifesting as white hair and skin, blue, fully translucent irises, nystagmus and misrouting of the optic nerves.	Patients have white skin and hair at birth. Irises are blue to pink and fully translucent. These features do not change throughout a patient's life. Nystagmus may be present at birth or it may develop in the first 3 to 4 months of life. It continues throughout life but usually slows down after childhood and is less noticeable when a person is relaxed and well rested. Visual acuity ranges from 20/100 and 20/400 and an alternating strabismus is often present. The reduction in visual acuity is associated with foveal hypoplasia. Severe photophobia is common. Nevi and ephelides are common but are unpigmented and pink. Patients do not tan, and if proper sun protection methods are not followed, skin becomes rough, coarse, thickened and can have solar keratoses. Patients have an increased risk of developing basal and squamous cell carcinomas but melanomas are rare.	NM_000372.4(TYR):c.1255G>A ; c.1177del ; NM_000372.4(TYR):c.325G>A ; NM_000372.4(TYR):c.1147G>A ; NM_000372.5(TYR):c.1501dup ; NM_000372.4(TYR):c.230G>A ; NM_000372.4(TYR):c.572delG ; NM_000372.4(TYR):c.1336G>A ; NM_000372.5:c.1118C>A ; NM_000372.4(TYR):c.646T>A ; NM_000372.4(TYR):c.1265G>A ; NM_000372.4(TYR):c.616G>A ; NM_000372.4:c.1012_1013insC ; NM_000372.4(TYR):c.1217C>T ; NM_000372.4(TYR):c.823G>T ; NM_000372.4(TYR):c.242C>T ; NM_000372.4(TYR):c.1209G>T ; NM_000372.4(TYR):c.164G>A ; NM_000372.4(TYR):c.1342G>A ; NM_000372.5:c.896G>A ; NM_000372.5:c.140G>A ; NM_000372.4(TYR):c.1467dupT ; NM_000372.4(TYR):c.1A>G ; NM_000372.4(TYR):c.533G>A ; NM_000372.4(TYR):c.1164delT ; NM_000372.4(TYR):c.650G>A ; NM_000372.4(TYR):c.265T>C ; NM_000372.4(TYR):c.272G>A ; NM_000372.4(TYR):c.286dupA ; NM_000372.4(TYR):c.1146C>A

TYR	Temperature-sensitive oculocutaneous albinism type 1	A form of oculocutaneous albinism type 1 (OCA1) characterized by skin and hair hypopigmentation, nystagmus, reduced iris and retinal pigment and misrouting of the optic nerves.	Newborns have white or very light yellow hair but with age the hair can darken to blond or light brown. Eyelash hair can be darker than scalp and eyebrow hair. Skin remains creamy white but a minimal amount of tanning is possible along with freckles and pigmented nevi. Nystagmus is sometimes visible at birth but in others not until 3 to 4 months of age. It continues throughout life but becomes less rapid with age and is usually more noticeable in times of stress, anger or tiredness. Iris color is blue at birth and can change to brownish tan or greenish hazel or remain unchanged. Visual acuity ranges from 20/100 to 20/200. With time, skin can become rough, coarse and thickened if sun protection procedures are not followed. Patients have an increased risk of developing basal and squamous cell carcinomas but melanomas are rare.	NM_000372.4(TYR):c.1255G>A ; c.1177del ; NM_000372.4(TYR):c.325G>A ; NM_000372.4(TYR):c.1147G>A ; NM_000372.5(TYR):c.1501dup ; NM_000372.4(TYR):c.230G>A ; NM_000372.4(TYR):c.572delG ; NM_000372.4(TYR):c.1336G>A ; NM_000372.5:c.1118C>A ; NM_000372.4(TYR):c.646T>A ; NM_000372.4(TYR):c.1265G>A ; NM_000372.4(TYR):c.616G>A ; NM_000372.4:c.1012_1013insC ; NM_000372.4(TYR):c.1217C>T ; NM_000372.4(TYR):c.823G>T ; NM_000372.4(TYR):c.242C>T ; NM_000372.4(TYR):c.1209G>T ; NM_000372.4(TYR):c.164G>A ; NM_000372.4(TYR):c.1342G>A ; NM_000372.5:c.896G>A ; NM_000372.5:c.140G>A ; NM_000372.4(TYR):c.1467dupT ; NM_000372.4(TYR):c.1A>G ; NM_000372.4(TYR):c.533G>A ; NM_000372.4(TYR):c.1164delT ; NM_000372.4(TYR):c.650G>A ; NM_000372.4(TYR):c.265T>C ; NM_000372.4(TYR):c.272G>A ; NM_000372.4(TYR):c.286dupA ; NM_000372.4(TYR):c.1146C>A ; NM_000372.4(TYR):c.1255G>A ; c.1177del ; NM_000372.4(TYR):c.325G>A ; NM_000372.4(TYR):c.1147G>A ; NM_000372.5(TYR):c.1501dup ; NM_000372.4(TYR):c.230G>A ; NM_000372.4(TYR):c.572delG ; NM_000372.4(TYR):c.1336G>A ; NM_000372.5:c.1118C>A ; NM_000372.4(TYR):c.646T>A ; NM_000372.4(TYR):c.1265G>A ; NM_000372.4(TYR):c.616G>A ; NM_000372.4:c.1012_1013insC ; NM_000372.4(TYR):c.1217C>T ; NM_000372.4(TYR):c.823G>T ; NM_000372.4(TYR):c.242C>T ; NM_000372.4(TYR):c.1209G>T ; NM_000372.4(TYR):c.164G>A ; NM_000372.4(TYR):c.1342G>A ; NM_000372.5:c.896G>A ; NM_000372.5:c.140G>A ; NM_000372.4(TYR):c.1467dupT ; NM_000372.4(TYR):c.1A>G ; NM_000372.4(TYR):c.533G>A ; NM_000372.4(TYR):c.1164delT ; NM_000372.4(TYR):c.650G>A ; NM_000372.4(TYR):c.265T>C ; NM_000372.4(TYR):c.272G>A ; NM_000372.4(TYR):c.286dupA ; NM_000372.4(TYR):c.1146C>A
TYRP1	Oculocutaneous albinism type 3	An extremely rare form of oculocutaneous albinism type 1 characterized by temperature sensitive hair pigmentation leading to dark hair on the hands, feet, legs, arms and chest (cooler body areas) and white or pale yellow hair on the scalp, axilla and pubic area (warmer body areas). Nystagmus and reduced visual acuity are also noted.	Oculocutaneous albinism type I is an autosomal recessive disorder characterized by absence of pigment in hair, skin, and eyes, and does not vary with race or age. Severe nystagmus, photophobia, and reduced visual acuity are common features. OCA type I is divided into 2 types: type IA, characterized by complete lack of tyrosinase activity due to production of an inactive enzyme, and type IB, characterized by reduced activity of tyrosinase. Patients have white hair in the warmer areas (scalp and axilla) and progressively darker hair in the cooler areas (extremities) of their bodies.	NM_000550.2(TYRP1):c.1067G>A ; NM_000550.2(TYRP1):c.107del ; c.176C>G ; NM_000550.2(TYRP1):c.1120C>T ; NM_000550.2(TYRP1):c.1103delA ; NM_000550.2(TYRP1):c.497C>G ; c.1372_1375dup ; NM_000550.2(TYRP1):c.1057_1060delAACA ; NM_000550.2(TYRP1):c.1067G>A ; NM_000550.2(TYRP1):c.107del ; c.176C>G ; NM_000550.2(TYRP1):c.1120C>T ; NM_000550.2(TYRP1):c.1103delA ; NM_000550.2(TYRP1):c.497C>G ; c.1372_1375dup ; NM_000550.2(TYRP1):c.1057_1060delAACA

UGT1A1	Crigler-Najjar syndrome type 1	A form of oculocutaneous albinism (OCA) characterized by rufous or brown albinism and occurring mainly in the African population.	Visual anomalies, such as nystagmus, are frequently undetectable and patients usually present with one of two phenotypes: rufous OCA (ROCA), characterized by red-bronze skin color, blue or brown irises and ginger-red hair, or brown OCA (BOCA), characterized by light to brown hair and a light to brown or tan skin color. The clinical features of OCA3 have been considered as rather mild, and in the rare cases of non-African patients, reddish hair color has been reported. A Japanese girl was reported with having OCA3 who presented with blond hair and light skin (with a small Mongolian spot), was able to tan and was negative for nystagmus.	NM_000463.2(UGT1A1):c.1021C>T ; NM_000463.2(UGT1A1):c.1456T>G ; NM_000463.2(UGT1A1):c.1070A>G ; NM_000463.2(UGT1A1):c.44T>G ; NM_000463.2(UGT1A1):c.1021C>T ; NM_000463.2(UGT1A1):c.1456T>G ; NM_000463.2(UGT1A1):c.1070A>G ; NM_000463.2(UGT1A1):c.44T>G
UGT1A1	Crigler-Najjar syndrome type 2	A hereditary disorder of hepatic bilirubin conjugation, characterized by severe neonatal unconjugated hyperbilirubinemia due to a complete absence of hepatic bilirubin glucuronosyltransferase (BGT).	Infants present with persistent jaundice at or soon after birth. Bilirubin encephalopathy (kernicterus manifesting as hypotonia, deafness, oculomotor palsy and lethargy) due to hyperbilirubinemia is a permanent risk. Neurologic defects (injury to basal ganglia, cerebellar and likely hippocampal structures) can occur, generally associated with intellectual and motor impairment.	NM_000463.2(UGT1A1):c.1021C>T ; NM_000463.2(UGT1A1):c.1456T>G ; NM_000463.2(UGT1A1):c.1070A>G ; NM_000463.2(UGT1A1):c.44T>G ; NM_000463.2(UGT1A1):c.1021C>T ; NM_000463.2(UGT1A1):c.1456T>G ; NM_000463.2(UGT1A1):c.1070A>G ; NM_000463.2(UGT1A1):c.44T>G
UGT1A1	NON RARE IN EUROPE: Gilbert syndrome	A hereditary disorder of bilirubin metabolism characterized by unconjugated hyperbilirubinemia due to reduced and inducible activity of hepatic bilirubin glucuronosyltransferase (GT). Crigler-Najjar syndrome type 2 (CNS2) is a milder form of Crigler-Najjar syndrome (CNS) than Crigler-Najjar syndrome type 1 (CNS1).	First clinical manifestations usually appear soon after birth. CNS2 patients are less severely jaundiced than CNS1 patients, have pigmented bile that contains bilirubin glucuronides, and generally do not present neurologic or intellectual impairment. Bilirubin encephalopathy may develop in later life when patients experience a superimposed infection or stress.	NM_000463.2(UGT1A1):c.1021C>T ; NM_000463.2(UGT1A1):c.1456T>G ; NM_000463.2(UGT1A1):c.1070A>G ; NM_000463.2(UGT1A1):c.44T>G ; NM_000463.2(UGT1A1):c.1021C>T ; NM_000463.2(UGT1A1):c.1456T>G ; NM_000463.2(UGT1A1):c.1070A>G ; NM_000463.2(UGT1A1):c.44T>G

UGT1A1	Transient familial neonatal hyperbilirubinemia	The characteristics of Gilbert syndrome are normal liver function tests of the usual type, normal liver histology, delayed clearance of bilirubin from the blood, and mild jaundice that tends to fluctuate in severity, particularly after fasting (Nixon and Monahan, 1967). This disorder is difficult to distinguish from prolonged posthepatic hyperbilirubinemia.Â	The hereditary hyperbilirubinemias include those resulting in predominantly unconjugated hyperbilirubinemia: Gilbert or Arias syndrome, Crigler-Najjar syndrome type I, and Crigler-Najjar syndrome type II; and those resulting in predominantly conjugated hyperbilirubinemia: Dubin-Johnson syndrome, Rotor syndrome, and several forms of intrahepatic cholestasis. Detailed studies show that patients with Gilbert syndrome have reduced activity of bilirubin glucuronosyltransferase.	NM_000463.2(UGT1A1):c.1021C>T ; NM_000463.2(UGT1A1):c.1456T>G ; NM_000463.2(UGT1A1):c.1070A>G ; NM_000463.2(UGT1A1):c.44T>G ; NM_000463.2(UGT1A1):c.1021C>T ; NM_000463.2(UGT1A1):c.1456T>G ; NM_000463.2(UGT1A1):c.1070A>G ; NM_000463.2(UGT1A1):c.44T>G
USH1C	Autosomal recessive non-syndromic sensorineural deafness type DFNB	A rare genetic hepatic disease characterized by very high serum bilirubin levels in a newborn, clinically presenting as jaundice during the first few days of life. The condition is usually self-resolving, although in some cases it can lead to kernicterus with corresponding symptoms (including lethargy, high-pitched crying, hypotonia, missing reflexes, vomiting, or seizures, among others), which may result in chronic disability and even death.		NM_005709.4:c.238dupC ; NM_005709.3(USH1C):c.216G>A ; c.2622_2623del ; c.238del ; NM_005709.4:c.238dupC ; NM_005709.3(USH1C):c.216G>A ; c.2622_2623del ; c.238del

USH1C	Usher syndrome type 1	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in theÂ PDSÂ gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in theÂ COCHÂ gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in theÂ WFS1Â gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	NM_005709.4:c.238dupC ; NM_005709.3(USH1C):c.216G>A ; c.2622_2623del ; c.238del ; NM_005709.4:c.238dupC ; NM_005709.3(USH1C):c.216G>A ; c.2622_2623del ; c.238del

USH2A	Retinitis pigmentosa	Usher syndrome type I is an autosomal recessive condition characterized by profound congenital hearing impairment with unintelligible speech, early retinitis pigmentosa (usually evident within the first decade), and constant vestibular dysfunction. Type I is distinguished from type II on the basis of severity of hearing loss and the extent of vestibular involvement. Type I patients are profoundly deaf, whereas type II patients are 'hard of hearing.' Vestibular function is defective in type I patients, whereas type II patients have normal vestibular function. Patients with type III (USH3) have progressive hearing loss.	A rare ciliopathy characterized by profound congenital deafness, retinitis pigmentosa and vestibular dysfunction. Retinitis pigmentosa results in visual loss and generally manifests as night blindness, progressively constricted visual fields, and impaired visual acuity. Vestibular dysfunction a defining feature of this form, manifests as delayed motor development with affected infants taking longer to sit independently and to walk. Later on, vestibular dysfunction results in difficulty with activities requiring balance.	NM_206933.2(USH2A):c.920_923dupGCCA ; NM_206933.2(USH2A):c.11864G>A ; NM_206933.2(USH2A):c.2167+5G>A ; c.15371del ; NM_206933.3(USH2A):c.15089C>A ; NM_206933.2(USH2A):c.10561T>C ; NM_007123.5(USH2A):c.4338_4339delCT ; NM_206933.2(USH2A):c.2299delG ; NM_206933.2(USH2A):c.10073G>A ; NM_206933.2(USH2A):c.6862G>T ; c.5743_5744del ; NM_206933.2(USH2A):c.2898delG ; NM_206933.2(USH2A):c.9799T>C ; NM_206933.2(USH2A):c.10636G>A ; NM_206933.2(USH2A):c.779T>G ; c.3491_3492del ; c.13709del ; NM_206933.2(USH2A):c.12234_12235delGA ; NM_206933.2(USH2A):c.8981G>A ; c.14442C>A ; NM_206933.2(USH2A):c.2276G>T ; c.5573-2A>G ; c.7364G>A ; NM_206933.2(USH2A):c.15520-1G>A ; NM_206933.2(USH2A):c.820C>T ; NM_206933.2(USH2A):c.14803C>T ; NM_206933.2(USH2A):c.920_923dupGCCA ; NM_206933.2(USH2A):c.11864G>A ; NM_206933.2(USH2A):c.2167+5G>A ; c.15371del ; NM_206933.3(USH2A):c.15089C>A ; NM_206933.2(USH2A):c.10561T>C ; NM_007123.5(USH2A):c.4338_4339delCT ; NM_206933.2(USH2A):c.2299delG ; NM_206933.2(USH2A):c.10073G>A ; NM_206933.2(USH2A):c.6862G>T ; c.5743_5744del ; NM_206933.2(USH2A):c.2898delG ; NM_206933.2(USH2A):c.9799T>C ; NM_206933.2(USH2A):c.10636G>A ; NM_206933.2(USH2A):c.779T>G ; c.3491_3492del ; c.13709del ; NM_206933.2(USH2A):c.12234_12235delGA ; NM_206933.2(USH2A):c.8981G>A ; c.14442C>A ; NM_206933.2(USH2A):c.2276G>T ; c.5573-2A>G ; c.7364G>A ; NM_206933.2(USH2A):c.15520-1G>A ; NM_206933.2(USH2A):c.820C>T ; NM_206933.2(USH2A):c.14803C>T

USH2A	Usher syndrome type 2	Retinitis pigmentosa (RP) is an inherited retinal dystrophy leading to progressive loss of the photoreceptors and retinal pigment epithelium and resulting in blindness usually after several decades.	Retinitis pigmentosa is slowly progressive but relentless. There is however broad variability in age of onset, rate of progression and secondary clinical manifestations. Affected individuals generally first develop night blindness (nyctalopia) due to loss of rod function, often in adolescence or earlier. They then develop peripheral visual field impairment, and over time loss of central vision, usually at late stages, often around midlife. Central visual acuity loss may occur at any age as a result of cystoid macular edema or photoreceptor loss. Posterior subcapsular cataracts are common and severity is age dependent. Reduced color vision may also be found. Fundus examination reveals bone spicule pigment deposits, attenuated retinal vessels, retinal atrophy and waxy optic nerve pallor. Severity is partly correlated with the pattern of inheritance with X-linked cases having the most severe course, autosomal recessive and single occurrence cases having intermediate severity, and autosomal dominant the most favorable course.	NM_206933.2(USH2A):c.920_923dupGCCA ; NM_206933.2(USH2A):c.11864G>A ; NM_206933.2(USH2A):c.2167+5G>A ; c.15371del ; NM_206933.3(USH2A):c.15089C>A ; NM_206933.2(USH2A):c.10561T>C ; NM_007123.5(USH2A):c.4338_4339delCT ; NM_206933.2(USH2A):c.2299delG ; NM_206933.2(USH2A):c.10073G>A ; NM_206933.2(USH2A):c.6862G>T ; c.5743_5744del ; NM_206933.2(USH2A):c.2898delG ; NM_206933.2(USH2A):c.9799T>C ; NM_206933.2(USH2A):c.10636G>A ; NM_206933.2(USH2A):c.779T>G ; c.3491_3492del ; c.13709del ; NM_206933.2(USH2A):c.12234_12235delGA ; NM_206933.2(USH2A):c.8981G>A ; c.14442C>A ; NM_206933.2(USH2A):c.2276G>T ; c.5573-2A>G ; c.7364G>A ; NM_206933.2(USH2A):c.15520-1G>A ; NM_206933.2(USH2A):c.820C>T ; NM_206933.2(USH2A):c.14803C>T ; NM_206933.2(USH2A):c.920_923dupGCCA ; NM_206933.2(USH2A):c.11864G>A ; NM_206933.2(USH2A):c.2167+5G>A ; c.15371del ; NM_206933.3(USH2A):c.15089C>A ; NM_206933.2(USH2A):c.10561T>C ; NM_007123.5(USH2A):c.4338_4339delCT ; NM_206933.2(USH2A):c.2299delG ; NM_206933.2(USH2A):c.10073G>A ; NM_206933.2(USH2A):c.6862G>T ; c.5743_5744del ; NM_206933.2(USH2A):c.2898delG ; NM_206933.2(USH2A):c.9799T>C ; NM_206933.2(USH2A):c.10636G>A ; NM_206933.2(USH2A):c.779T>G ; c.3491_3492del ; c.13709del ; NM_206933.2(USH2A):c.12234_12235delGA ; NM_206933.2(USH2A):c.8981G>A ; c.14442C>A ; NM_206933.2(USH2A):c.2276G>T ; c.5573-2A>G ; c.7364G>A ; NM_206933.2(USH2A):c.15520-1G>A ; NM_206933.2(USH2A):c.820C>T ; NM_206933.2(USH2A):c.14803C>T

VPS13A	Choreoacanthocytosis	Usher syndrome type I is an autosomal recessive condition characterized by profound congenital hearing impairment with unintelligible speech, early retinitis pigmentosa (usually evident within the first decade), and constant vestibular dysfunction. Type I is distinguished from type II on the basis of severity of hearing loss and the extent of vestibular involvement. Type I patients are profoundly deaf, whereas type II patients are 'hard of hearing.' Vestibular function is defective in type I patients, whereas type II patients have normal vestibular function. Patients with type III (USH3) have progressive hearing loss.	A rare ciliopathy characterized by congenital moderate-to-severe deafness, retinitis pigmentosa developing in the first or second decade, and normal vestibular function. Congenital bilateral sensorineural hearing loss is mild to moderate in the low frequencies and severe to profound in the higher frequencies. Additional manifestations include night blindness, constricted visual field (tunnel vision), and later on decreased visual acuity sometimes ending with bare light perception.	c.2898T>G ; c.9275+1G>T ; c.9109C>T ; c.3091del ; NM_033305.2(VPS13A):c.622C>T ; c.2898T>G ; c.9275+1G>T ; c.9109C>T ; c.3091del ; NM_033305.2(VPS13A):c.622C>T

WAS	Wiskott-Aldrich syndrome	Chorea-acanthocytosis (ChAc) is a form of neuroacanthocytosis (see this term) and is characterized clinically by a Huntington disease-like phenotype with progressive neurological symptoms including movement disorders, psychiatric manifestations and cognitive disturbances.	Onset is in early adulthood and the initial presentation is often subtle cognitive or psychiatric symptoms. However, patients may have developed related psychiatric disorders several years before neurological manifestations. In at least 1/3 of patients, seizures, typically generalized, are the first manifestation. In some cases, seizures may precede the appearance of movement disorders by as much as a decade. During the course, most patients develop a characteristic phenotype including chorea, a very peculiar "feeding dystonia" with tongue protrusion, orofacial dyskinesias, limb dystonia, involuntary vocalizations, dysarthria and involuntary tongue- and lip-biting. Gait may have a "rubber man" appearance with truncal instability and sudden, violent trunk spasms. Most patients develop generalized chorea and some degree of parkinsonism. Impairment of memory and executive functions is frequent. Psychiatric manifestations are common and may present as schizophrenia-like psychosis or obsessive compulsive disorder (OCD). Myopathy and axonal neuropathy are usually mild. Clinical neuromuscular manifestations include areflexia, sensorimotor neuropathy, and variable weakness and atrophy. ChAc usually progresses slowly over 15-30 years, but sudden death, presumably caused by seizures or autonomic involvement, may occur.	NM_000377.2(WAS):c.814T>C ; NM_000377.2(WAS):c.173C>G ; NM_000377.2(WAS):c.881T>C ; NM_000377.2(WAS):c.1442T>A ; NM_000377.2(WAS):c.134C>T ; NM_000377.2(WAS):c.809T>C ; NM_000377.2(WAS):c.814T>C ; NM_000377.2(WAS):c.173C>G ; NM_000377.2(WAS):c.881T>C ; NM_000377.2(WAS):c.1442T>A ; NM_000377.2(WAS):c.134C>T ; NM_000377.2(WAS):c.809T>C

WAS	X-linked severe congenital neutropenia	A primary immunodeficiency disease characterized by microthrombocytopenia, eczema, infections and an increased risk for autoimmune manifestations and malignancies.	WAS usually manifests in infancy but onset may also occur during the neonatal period. In most cases the first clinical features are hemorrhagic manifestations with petechiae, bruising, purpura, epistaxis, oral bleeding, bloody diarrhea and intracranial bleeding. Acute or chronic eczema is the second characteristic finding of WAS. Due to combined immunodeficiency, most patients also have airway, gut or skin infections caused by regular or opportunistic germs. Autoimmune manifestations are seen in approximately 40% of cases and include autoimmune hemolytic anemia, neutropenia, vasculitis, inflammatory bowel disease, renal disease, and arthritis. WAS patients have a higher risk of developing tumors (mainly B-cell lymphomas) at any age.	NM_000377.2(WAS):c.814T>C ; NM_000377.2(WAS):c.173C>G ; NM_000377.2(WAS):c.881T>C ; NM_000377.2(WAS):c.1442T>A ; NM_000377.2(WAS):c.134C>T ; NM_000377.2(WAS):c.809T>C ; NM_000377.2(WAS):c.814T>C ; NM_000377.2(WAS):c.173C>G ; NM_000377.2(WAS):c.881T>C ; NM_000377.2(WAS):c.1442T>A ; NM_000377.2(WAS):c.134C>T ; NM_000377.2(WAS):c.809T>C
WAS	X-linked thrombocytopenia with normal platelets	X-linked severe congenital neutropenia is an immunodeficiency syndrome characterized by recurrent major bacterial infections, severe congenital neutropenia, and monocytopenia. It has been described in five males spanning three generations of one family. It is transmitted as an X-linked recessive trait and is caused by mutations in the WAS gene, encoding the WASP protein.	X-linked immunodeficiency syndrome characterized by recurrent major bacterial infections, severe congenital neutropenia, and monocytopenia. Although X-linked inheritance and shifts in lymphocyte subsets were not known to be features of severe congenital neutropenia, affected males in this pedigree had increased numbers of activated CD8+ T cells in the peripheral blood resulting in decreased CD4+/CD8+ ratios of 0.5 or less. Immunoglobulin levels and T-lymphocyte activation were normal. Platelets were not decreased, and there was no history of eczema in affected individuals. Bone marrow examination demonstrated a maturation arrest at the promyelocyte/myelocyte stage, without gross abnormalities in megakaryopoiesis or erythropoiesis.	NM_000377.2(WAS):c.814T>C ; NM_000377.2(WAS):c.173C>G ; NM_000377.2(WAS):c.881T>C ; NM_000377.2(WAS):c.1442T>A ; NM_000377.2(WAS):c.134C>T ; NM_000377.2(WAS):c.809T>C ; NM_000377.2(WAS):c.814T>C ; NM_000377.2(WAS):c.173C>G ; NM_000377.2(WAS):c.881T>C ; NM_000377.2(WAS):c.1442T>A ; NM_000377.2(WAS):c.134C>T ; NM_000377.2(WAS):c.809T>C
WNT10A	Odonto-onycho-dermal dysplasia	Hereditary nonsyndromic thrombocytopenia is characterized by decreased numbers of platelets and bleeding tendency	0	WNT10A

WNT10A	Oligodontia	Odontoonychodermal dysplasia (OODD) is an autosomal recessive disorder characterized by dry hair, severe hypodontia, smooth tongue with marked reduction of fungiform and filiform papillae, onychodysplasia, keratoderma and hyperhidrosis of palms and soles, and hyperkeratosis of the skin.	A rare, genetic, ectodermal dysplasia syndrome characterized by dental abnormalities (primarily agenesis of the permanent and deciduous teeth with cone-shaped incisors and canines), onychodysplasia, palmoplantar hyperkeratosis, dry skin and, more variably, hypotrichosis, and sweat gland dysfunction (hyper- or hypohidrosis).	WNT10A
WNT10A	SchÃ¶pf-Schulz-Passarge syndrome	Oligodontia is a rare developmental dental anomaly in humans characterized by the absence of six or more teeth.	Clinical features of oligodontia include six or more missing teeth, lack of development of maxillary and mandibular alveolar bone height and reduced lower facial height. Variation in tooth morphology is also observed along with problems in tooth development, eruption and exfoliation.	WNT10A

XPA	Xeroderma pigmentosum	SchÃ¶pf-Schulz-Passarge syndrome (SSPS) is a rare autosomal recessive ectodermal dysplasia characterized by multiple eyelid apocrine hidrocystomas, palmoplantar keratoderma, hypotrichosis, hypodontia and nail dystrophy.	SSPS refers to a discrete phenotype of ectodermal dysplasia with a relatively benign course and late diagnosis, often established in adulthood. The onset of symptoms occurs in childhood and early adolescence, but they consist of relatively unspecific features, including various degrees of hypodontia, hypotrichosis, palmoplantar keratoderma and nail dystrophy. Telangiectatic rosacea is a further relatively common feature. Multiple eyelid apocrine hidrocystomas commonly appear in (late) adulthood. Palmoplantar keratoderma with histologic features of eccrine syringofibroadenoma is observed in nearly half of cases and occasionally develops a malignant potential. Other adnexal tumors described include basal cell carcinoma, eccrine poroma, benign acanthoma and follicular infundibulum tumor. Some patients have been described to have a bird-like facies. Within theÂ WNT10AÂ mutational spectrum, odonto-onycho-dermal dysplasia and SSPS are regarded as discrete entities, while an increasing number of patients are described with incomplete phenotypes of the odonto-onychial, tricho-odonto and tricho-odonto-onychial types.	c.501del ; NM_000380.3(XPA):c.348T>A ; c.727C>T ; NM_000380.3(XPA):c.619C>T ; c.501del ; NM_000380.3(XPA):c.348T>A ; c.727C>T ; NM_000380.3(XPA):c.619C>T

ZFYVE26	Autosomal recessive spastic paraplegia type 15	Xeroderma pigmentosum (XP) is a rare genodermatosis characterized by extreme sensitivity to ultraviolet (UV)-induced changes in the skin and eyes, and multiple skin cancers. It is subdivided into 8 complementation groups, according to the affected gene: classical XP (XPA to XPG) and XP variant (XPV) (see these terms).	The severity of the clinical manifestations and the age of onset are extremely variable and are in part dependent on exposure to sunlight and the complementation group. Approximately 50% of affected individuals have acute sun sensitivity from the first few months of life, presenting with severe sunburn and/or persistent erythema which takes weeks to resolve. Others do not show any sunburn reaction and gradually develop marked freckling at sun exposed sites. Individuals have dry skin and hypo- or hyperpigmented lesions. There is a greater than 10,000-fold increased risk of non-melanoma skin cancers, and a 2,000 fold increased risk of melanoma under the age of 20 when compared to the general population. Patients with classical XP develop skin cancer generally before the age of 20, while patients with XP variant start to develop skin cancer at about 20-30 years of age. Ocular abnormalities include keratitis resulting in corneal opacification and vascularization. Photophobia is common. Ocular squamous cell carcinoma and melanoma are common. Neurologic abnormalities of varying severity have been reported in about 30% of cases. These include acquired microcephaly, diminished or absent deep tendon stretch reflexes, progressive sensorineural hearing loss, spasticity, ataxia, seizures and progressive cognitive impairment. De Sanctis-Cacchione syndrome is a term that was originally attributed to XP cases with severe neurological abnormalities but it is no longer in general use.	c.501del ; NM_000380.3(XPA):c.348T>A ; c.727C>T ; NM_000380.3(XPA):c.619C>T ; c.501del ; NM_000380.3(XPA):c.348T>A ; c.727C>T ; NM_000380.3(XPA):c.619C>T

FMR1	Fragile X syndrome	A rare genetic disease associated with mild to severe intellectual deficit that may be associated with behavioral disorders and characteristic physical features including a high forehead, prominent and large ears, hyperextensible finger joints, flat feet with pronation and, in adolescent and adult males, macroorchidism.	Fragile X syndrome (FXS) presents with a variable clinical phenotype. In males, the disease presents during childhood with delayed developmental milestones. Intellectual deficit can be of variable severity and may include problems with working and short-term memory, executive function, language, mathematics and visuospatial abilities. Behavioral anomalies can be mild (e.g. anxiety, mood instability) to severe (e.g. aggressive behavior, autism). Autistic-like behavior can include hand flapping, poor eye contact, hand biting, gaze avoidance, social phobia, social and communication deficits and tactile defensiveness. In females, intellectual and behavioral disorders are typically mild and usually consist of shyness, social anxiety, and mild learning problems with a normal IQ, although 25% of girls have an IQ less than 70. Attention deficit hyperactivity disorder (ADHD) is present in over 89% of males and 30% of females and behavioral disinhibition is very common. Recurrent otitis (60%) and seizures (16 to 20%) can also be observed.	Premutation allele (CGG)n
FMR1	Fragile X-associated tremor/ataxia syndrome	Fragile X-associated tremor/ataxia syndrome (FXTAS) is a rare neurodegenerative disorder characterized by adult-onset progressive intention tremor and gait ataxia.	The age of onset of tremor and/or ataxia in males is about 60 years. The clinical presentation is heterogeneous with variable dominant manifestations including: intention tremor, progressive cerebellar gait ataxia, frontal executive dysfunction, cognitive decline, peripheral neuropathy, and dysautonomia. Other signs include mild parkinsonism and psychiatric manifestations (depression, anxiety, agitation) with possible progression to dementia. Carrier females generally have less severe manifestations than males but also have an increased risk of primary ovarian insufficiency, chronic muscle pain, and hypothyroidism.	Premutation allele (CGG)n

FMR1	Symptomatic form of fragile X syndrome in female carrier	A rare genetic disease characterized by a variable clinical phenotype which includes similar features but is typically less severe than in affected males. Patients may present with mild to borderline intellectual disability, anxiety, social phobia, selective mutism, attention deficit hyperactivity disorder, language deficit, neurologic signs and symptoms (such as seizures, hypotonia, and clonus), ophthalmologic anomalies (strabismus, refractive errors), and facial dysmorphism (including long face, prominent forehead, large, prominent ears, and mandibular prognathism).	.	Premutation allele (CGG)n
FMR1	Xq27.3q28 duplication syndrome	Xq27.3q28 duplication syndrome is a recently described syndrome characterized by short stature, hypogonadism, developmental delay and facial dysmorphism.	Facial features include deep-set eyes, bulbous nasal tip and thin lips. Hypogonadism is due to primary gonadal failure. Patients also had some features which are probably caused by testosterone deficiency such as a high-pitched voice, sparse body hair and small hands and feet. Carrier females present with a short stature and early menopause.	Premutation allele (CGG)n

GJB3	Autosomal dominant non-syndromic sensorineural deafness type DFNA	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in the PDS gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in the COCH gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in the WFS1 gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	NM_024009.2(GJB3):c.529T>G; NM_024009.2(GJB3):c.580G>A; NM_024009.2(GJB3):c.94C>T

GJB3	Autosomal dominant non-syndromic sensorineural deafness type DFNB	Deafness is the most frequent form of sensorial deficit. In the vast majority of cases, the deafness is termed nonsyndromic or isolated and the hearing loss is the only clinical anomaly reported. In developed counties, 60-80% of cases of early-onset hearing loss are of genetic origin.	The majority of cases presenting at birth concern perceptive deafness (with a neurosensory origin associated with the inner ear) rather than conductive deafness (anomalies in the amplification of sound waves between the middle ear - tympanum and auditory ossicles - and the outer ear). Autosomal dominant forms are characterised by very early onset and bilateral hearing loss with varying degrees of severity (ranging from mild to profound). No malformations of the inner ear can be detected by CT scan. Mutations in the PDS gene are responsible for 7% of cases of childhood deafness. In these cases, the deafness is marked by early-onset, usually bilateral (but sometimes asymmetric) hearing loss with autosomal recessive transmission. This form of deafness is always associated with malformations of the inner ear that can be detected by CT scan. In rare cases, thyroid gland disease may also be present. For the autosomal dominant forms of deafness, mutations in the COCH gene result in progressive postlingual deafness associated with severe attacks of vertigo and subjective tinnitus. This form of deafness should be distinguished from Meniere's disease (see this term). Autosomal dominant mutations in the WFS1 gene cause either a form of hearing loss affecting mainly low frequency sounds or deafness associated with optic atrophy.	NM_024009.2(GJB3):c.529T>G; NM_024009.2(GJB3):c.580G>A; NM_024009.2(GJB3):c.94C>T

GJB3	Â Erythrokeratodermia variabilis	Erythrokeratoderma variabilis progressiva (EKVP) is a type of erythrokeratoderma characterized by the association of hyperkeratosis and erythema in persistent, although sometimes variable, circumscribed lesions. Progressive symmetric erythrokeratoderma (PSEK) and erythrokeratoderma variabilis (EKV) are probably no longer two distinctive diseases but rather the two clinical manifestations of a same disease, now known as EKVP.	The disease usually starts in the early months of life or later in infancy. Erythema at birth has been described. Patients present with well-demarcated, erythematous patches and hyperkeratotic plaques that are arranged symmetrically. The lesions favor the extensor surface of the upper and lower extremities, buttocks and face. The plaques tend to progress during childhood, with lesions stabilizing thereafter. Considerable clinical overlap exists between PSEK and EKV, the main distinguishing feature being the presence of migratory erythema in patients with EKV. The migratory aspects of the lesions may also change over time, according to lifetime periods. The palms and soles are usually normal but some patients may have palmoplantar keratoderma. Minimal pruritus may be noted. Improvement has rarely been reported.	NM_024009.2(GJB3):c.529T>G; NM_024009.2(GJB3):c.580G>A; NM_024009.2(GJB3):c.94C>T
GJB3	Neuropathy with hearing impairment	This syndrome is characterized by the association of sensorineural hearing impairment and peripheral neuropathy.	The hearing impairment was mild and often asymmetrical. The neuropathy was demyelinating with predominantly sensory involvement but severity was variable ranging from asymptomatic individuals to patients with skin ulcers and osteomyelitis requiring amputation.	NM_024009.2(GJB3):c.529T>G; NM_024009.2(GJB3):c.580G>A; NM_024009.2(GJB3):c.94C>T