PGT A Seq

JUNO GENETICS

PGT A Seq

PGT[A]Seq, increases the chance of a healthy birth per embryo transfer

The most powerful and accurate embryo analysis on the market

Juno uses a unique PGT[A]Seq methodology, which is the only method in the world to have successfully demonstrated clinical validity in a non-selection study.

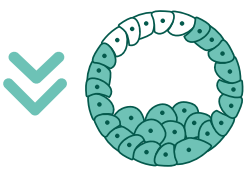
Our PGT[A]Seq strategy employs the latest next-generation sequencing methods, increasing the quality of the data obtained and yielding results of unparalleled accuracy.

PGT[A]Seq has been developed following extensive analytical and clinical validation

PGT[A]Seq

What is PGT[A]Seq?

Aneuploidy screening through Juno Genetics utilizes targeted next-generation sequencing. PGT[A]Seq has been developed following extensive analytical and clinical validation studies and identifies whole chromosome aneuploidy (extra or missing whole chromosomes). PGT[A]Seq is greater than 98% accurate in screening for whole chromosome aneuploidy. PGT[A]Seq also can detect some cases of segmental aneuploidy.

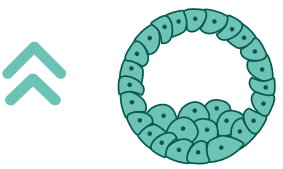


REDUCTION IN MOSAIC EMBRYOS

The enhanced accuracy of PGT[A]Seq prevents viable embryos from being incorrectly classified mosaic.

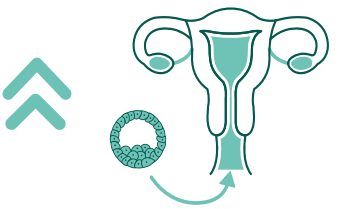
8,00%

ONGOING PREGNANCIES



5,30%

MORE EUPLOID EMBRYOS REPORTED



+ 5,30%

EMBRYOS AVAILABLE TO TRANSFER

PGT A Seq

What is segmental aneuploidy?

Segmental aneuploidy refers to extra or missing genetic material from a part of a chromosome rather than from the whole chromosome.

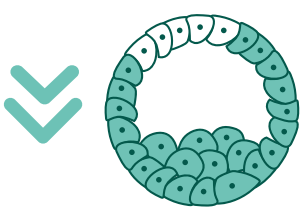
In an internal study where embryos had multiple biopsies performed, the segmental aneuploidy was identified in approximately 50% of rebiopsy samples. Studies have also shown that embryos with segmental aneuploidies can result in a normal pregnancy. However, there have been reports of segmental aneuploidies identified in an embryo biopsy sample that were confirmed to be present in the fetus and resulted in abnormal ultrasound findings.

What is mosaicism?

Mosaicism refers to a potential combination chromosomally normal and chromosomally abnormal cells in a single embryo biopsy sample. Some studies suggest a mosaic result is associated with an increased risk for implantation failure and miscarriage. However, there is no consensus, and these studies are not conclusive. Additionally, embryos with mosaic results have resulted in children who were healthy at birth.

Since the significance of mosaic range results is uncertain, Juno Genetics refers to them as secondary findings of uncertain clinical significance. You and your provider have the option to decide whether you would like Juno Genetics to report results in the mosaic range.

Mosaicisms overestimated by some PGT-A tests



REDUCTION IN MOSAIC EMBRYOS

The enhanced accuracy of PGT[A]Seq prevents viable embryos from being incorrectly classified mosaic.

PGT [A] Seq

Advantages of using Juno PGT[A]Seq

A higher number of euploid embryos reported

Improved clinical outcomes

Predictive value proven in well-designed published studies. The most powerful embryo selection tool currently available

High accuracy, including detection of triploid embryos and detection of DNA contamination

Avoids unsuccessful transfer of non-viable aneuploid embryos

Permits high efficiency single embryo transfer (SET)

Faster time to pregnancy

Provides information on likely potential of stored material and avoids storage of non-viable embryo

Reduced miscarriage rate

Reduced risk of aneuploid syndromes

Avoids incorrect classification of euploid embryos as abnormal or mosaic

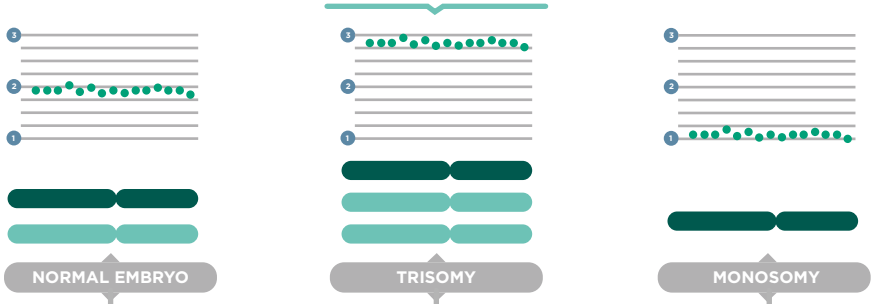
Compared to other methods, Juno PGT[A]Seq is associated with a higher proportion of embryos categorised as euploid

PGT [A] Seq

Increased proportion of embryos classified euploid with respect to some other methods

1 NGS

Juno uses next-generation sequencing to measure the amount of DNA at thousands of sites on each chromosome. This allows the number of copies of the chromosome to be calculated with high accuracy.



2 SNPs

Juno looks at thousands of places where the DNA sequence can differ between individual chromosomes. Each of these sites of variation can be type 'A' or type 'B'. Normal, Trisomy and monosomy each have characteristic patterns of As and Bs

Together, the measurement of the amount of DNA and the analysis of the DNA sequence greatly increases the accuracy of PGT[A]Seq

JUNO'S PGT[A]SEQ METHOD

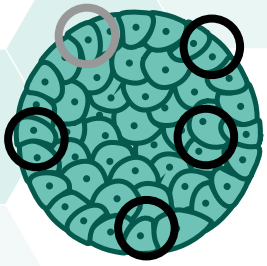
The most accurate available

PGT[A]Seq has been developed following extensive analytical and clinical validation studies and identifies whole chromosome aneuploidy (extra or missing whole chromosomes). PGT[A]Seq is greater than 98% accurate in screening for whole chromosome aneuploidy. PGT[A]Seq also can detect some cases of segmental aneuploidy.

Blastocysts with a routine PGT[A]Seq result

Donated for research

Biopsied an additional 4 times



Original PGT[A]Seq Result

The concordance rates of an initial trophectoderm biopsy with the rest of the embryo using PGT[A]Seq, a targeted next-generation sequencing platform for preimplantation genetic testing-aneuploidy

	EUPLOID	ANEUPLOID
PGT[A]Seq result confirmed in ≥1 other biopsy*	100%	99.6%
PGT[A]Seq result confirmed in all other biopsy*	98.5%	96.7%

Julia Kim, M.D., M.P.H. Xin Tao, Ph.D. Michael Cheng, M.S. Ayesha Steward, M.S. Vanessa Guo, B.A. Yiping Zhan, Ph.D. Richard T. Scott Jr., M.D., H.C.L.D. Chaim Jalas

Published: December 31, 2021
DOI:https://doi.org/10.1016/j.fertnstert.2021.10.011

JUNO'S PGT[A]SEQ METHOD

vs other PGT-A methods

Looking at multiple biopsies from the same embryo using competitors PGT-A methods, have often reported disagreement between different biopsies in 10-20% of embryos*

10-20%

More accurate than other methods

***Preimplantation genetic testing for aneuploidy: A review of published blastocyst reanalysis concordance data**

Diego Marin, Jia Xu, Nathan R Treff
Published: 2021 Apr
https://pubmed.ncbi.nlm.nih.gov/32920823/

JUNO'S PGT[A]SEQ METHOD

How do we know a PGT method is accurate?

Tiegs et al., 2020 using PGT[A]Seq method
(Juno Genetics)

315 TRANSFERRED EMBRYOS WERE FOUND TO BE EUPLOID

	Delivered	Failed	Total
EUPLOID	205	110	315

Predictive Value of 'euploid' delivering = 65.1% P<0.0001

102 TRANSFERRED EMBRYOS WERE FOUND TO BE ANEUPLOID

	Delivered	Failed	Total
ANEUPLOID	0	102	102

Aneuploid diagnosis predicted failure to deliver in 100% of cases P<0.0001

Juno is the only lab with a non-selection study proving that its PGT[A]Seq method doesn't cause viable embryos to be wrongly discarded

In summary:
They biopsied embryos but did not immediately examine the biopsy specimen. Instead, embryos were transferred based upon standard morphological criteria. After the outcome of the cycle was known the embryo biopsy specimens were tested, revealing that some would have been classified as aneuploid using PGT-A.

More than 100 embryos classified 'aneuploid' were transferred - None produced a child.

It shows that embryos classified 'aneuploid' by Juno have little or no chance of producing a baby.

No other PGT-A method has data confirming that embryos classified aneuploid are not viable.

In fact, considering that Juno's aneuploidy rate is lower than other labs, and yet pregnancy rates in PGT-A cycles tend to be superior with Juno, the obvious conclusion is that other labs are over-calling aneuploidy, leading to viable embryos being discarded.

***A multicenter, prospective, blinded, nonselection study evaluating the predictive value of an aneuploid diagnosis using a targeted next-generation sequencing–based preimplantation genetic testing for aneuploidy assay and impact of biopsy**

Ashley W. Tiegs, M.D. Xin Tao, Ph.D. Yiping Zhan, Ph.D. Christine Whitehead, R.N. Julia Kim, M.D. Brent Hanson, M.D. Emily Osman, M.D. Thomas J. Kim, M.D. George Patounakis, M.D., Ph.D. Jacqueline Gutmann, M.D. Arthur Castelbaum, M.D. Emre Seli, M.D. Chaim Jalas Richard T. Scott Jr., M.D.

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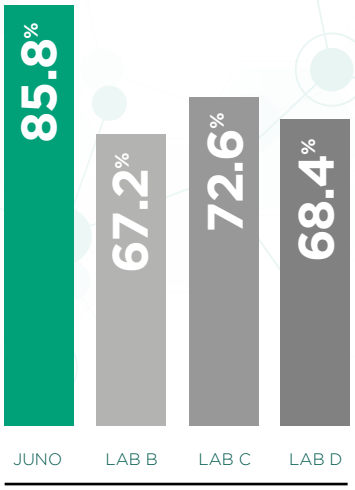
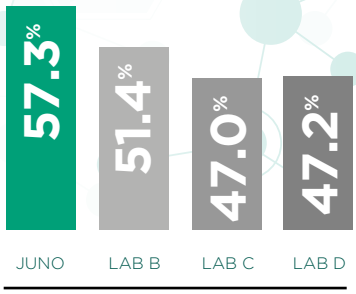
PGT-A SEQ METHOD

JUNO VS OTHER LABS



EMBRYOS CHARACTERISED EUPLOID
P VALUE <0.001 all versus JUNO



LIVE BIRTH RATE/OPR
P VALUE 0.060 other combined versus JUNO

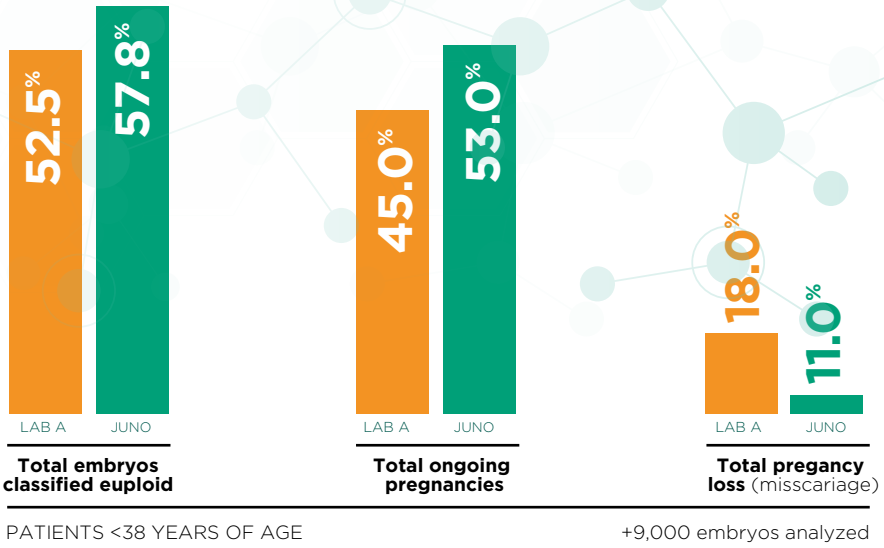
Independent study conducted by Bardos et al (ASRM, 2021), comparing four PGT-A providers (one of which was Juno).

The study, involving oocyte donation cycles, confirms that Juno classifies 10-20% more embryos euploid in young patients.

Birth rates appear higher for Juno cycles (6-10%), although the study was not powered to look at that outcome.

PGT-A SEQ METHOD

Improved clinical outcomes for cycles using preimplantation genetic testing for aneuploidy (PGT-A) may be associated with a change in genetic service provider



BACKGROUND

An increasing number of IVF cycles include PGT-A to assist in the selection of euploid embryos for transfer to the uterus. All modern PGT laboratories utilise next generation sequencing (NGS) to predict the copy number of each chromosome. Given this technical convergence, it has generally been supposed that the choice of PGT-A provider need only depend on factors such as the quality of the user experience, convenience and price. Here we consider whether the choice of PGT-A provider might have more profound affects, potentially impacting clinical results.

METHODS

A large network of IVF clinics switched from PGT-A provider 'A' to provider 'B'. The final 6 months of clinical data using A was compared to 6 months of data after the switch to B. No significant changes in any aspect of patient population, treatment or embryological practice occurred between the two time periods evaluated.

RESULTS

Within the two time periods considered, 9,091 embryos underwent PGT-A using A and 9,550 using B. The average female age was 39.0 and 39.3, respectively. Differences in important clinical outcomes were observed, which were particularly apparent for female patients <38 years of age. For that group, A versus B results were: 52.5% of embryos classified euploid vs. 57.8% ($p<0.0001$); 45% ongoing pregnancy after the first embryo transfer vs. 53% ($p=0.04$); 18% miscarriage rate vs. 11% ($p=0.048$).

CONCLUSIONS

PGT-A and NGS are umbrella terms encompassing different methods with widely varying levels of validation and accuracy. The results of this study suggest that the choice of PGT-A provider has implications for clinical results. One possible interpretation of the data is that higher rates of euploidy and pregnancy with B might be a consequence of embryos being wrongly classified as aneuploid by A, while incorrect labelling of abnormal embryos as euploid could explain the relative increase in miscarriage rates when using that provider.

JUNO PGT[A]SEQ INCREASES THE CHANCE OF A HEALTHY BIRTH PER EMBRYO TRANSFER

The best-in-class accuracy of PGT[A]Seq means an increased number of euploid embryos are correctly reported, leading to more viable embryos being transferred with higher pregnancy rates than is achieved using less accurate PGT-A methods

WHEN IS THE TEST PERFORMED?

Day 1 embryo

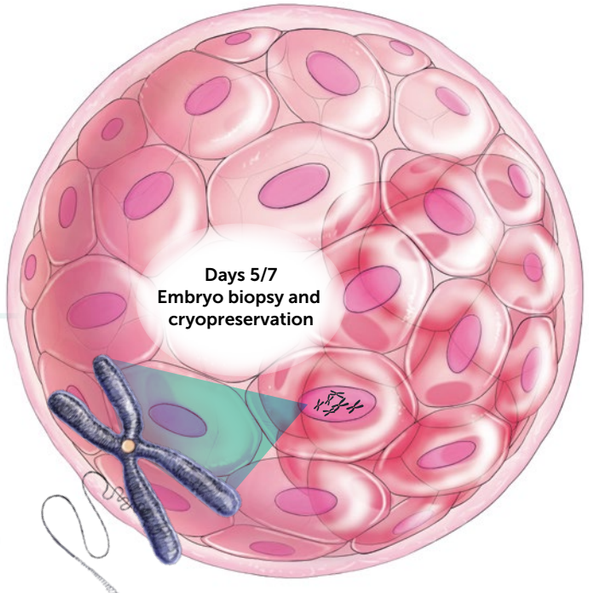
In vitro fertilisation takes place and embryo development begins

Day 2

Day 3

Day 4

On the **fifth day**, a cell sample of the embryo is obtained and analysed



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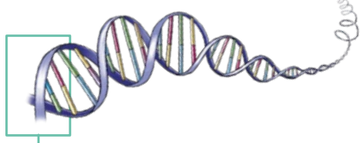
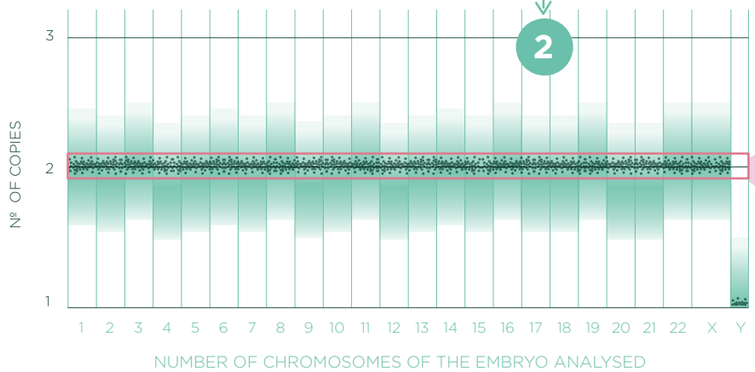


NGS

(The amount of DNA measured in thousands of individual points)

Juno uses next-generation sequencing to measure the amount of DNA at thousands of sites on each chromosome. This allows the number of copies of the chromosome to be calculated with high accuracy

2



NGS + SNPs

Together, the measurement of the amount of DNA and the analysis of the DNA sequence greatly increases the accuracy of PGT[A]Seq

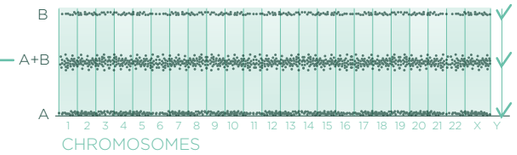
Juno looks at thousands of places where the DNA sequence can differ between individual chromosomes, called single nucleotide polymorphismus or "SNPs"

3

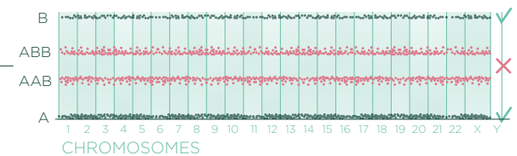
SNPs

(The amount of DNA measured in thousands of individual points)

Each of these sites of variation can be type 'A' or type 'B'. Normal, Trisomy and monosomy each have characteristic patterns of As and Bs

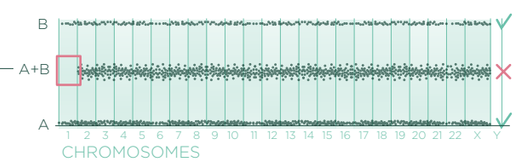


NORMAL
Some sites have only A or B, but others have A and B equally



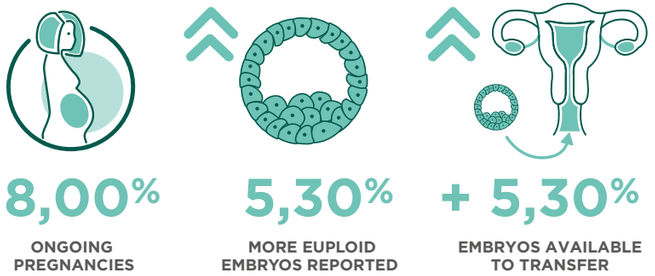
RESULT

TRIPLOID
(extra chromosome)
No sites have A and B equally, but some are AAB or BBA



RESULT

MONOSOMY
(Chromosome loss)
All sites have either A or B, but never both types (no A+B)



8,00%
ONGOING PREGNANCIES

5,30%
MORE EUPLOID EMBRYOS REPORTED

+ 5,30%
EMBRYOS AVAILABLE TO TRANSFER

Day 7

Following PGT[A]Seq, embryos with the correct numbers of chromosomes can be thawed and transfer to the uterus or stored for future use

The study of NGS + SNPs can greatly increase the accuracy of PGT-A

4

ADVANTAGES OF USING JUNO PGT[A]SEQ

A higher number of euploid embryos reported

Improved clinical outcomes

Predictive value proven in well-designed published studies. The most powerful embryo selection too currently availablel

High accuracy, including detection of triploid embryos and detection of DNA contamination

Avoid unsuccessful transfer of non-viable aneuploid embryos

Permits high efficiency single embryo transfer (SET)

Faster time to pregnancy

Provides information on likely potential of stored material and avoids storage of non-viable embryo

Reduced miscarriage rate

Reduced risk of aneuploid syndromes

Avoids incorrect classification of euploid embryos as abnormal or mosaic

Compared to other methods, Juno PGT[A]Seq is associated with a higher proportion of embryos categorised as euploid

Infografía:
Pedro Jiménez

ABOUT JUNO

Juno has developed unique algorithms, techniques and processes, with the aim of increasing the chances for a healthy pregnancy

+30
years of research carried out

+350
scientific publications

3
research centers

UK USA SPAIN ITALY
state-of-the-art laboratories

Juno Genetics is a state-of-the-art laboratory specialising in genetic testing. Our mission is to provide clinically useful information of the highest quality for couples who are planning to start a family, patients undergoing fertility treatments, and for women who are already pregnant.

The innovative tests offered by Juno Genetics are amongst the most technologically advanced and accurate available anywhere in the world.

The cutting-edge tests provided by Juno are the result **of world-class research carried out by an internationally renowned team of scientists.**

JUNO GENETICS

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