

# PGT **A** Seq

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PGT **M** Seq

PGT **SR** Seq

# JUNO

GENETICS



**YOUR PARTNERS  
in GENETIC HEALTH**



# PGT Seq

## EVIDENCE-BASED PGT

**PGT[A]Seq has proven clinical value in expertly-designed, published studies**

### **The most powerful and accurate embryo analysis on the market**

Juno uses a unique combination of custom-developed PGT[A]Seq technologies and is the only PGT-A method in the world to have successfully demonstrated clinical validity in a non-selection study.

Our strategy employs both targeted next-generation sequencing (NGS) and single nucleotide polymorphism (SNP) methods to yield results of unparalleled accuracy and clinical quality.



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

# PGT Seq

## Whole Chromosome Aneuploidy

PGT-A through Juno Genetics utilizes targeted next-generation sequencing and SNP genotyping to achieve very high accuracy for the primary purpose of PGT-A: detecting whole chromosome aneuploidy. These findings are reported on every embryo, and the use of SNPs also enables the detection of all forms of triploidy and haploidy.

## Segmental Aneuploidy

**Segmental aneuploidy refers to extra or missing genetic material (deletion or duplication) from part of a chromosome rather than from the whole chromosome.**

In a Juno Genetics study in which embryos had multiple biopsies performed, segmental aneuploidies that had been detected in clinical PGT-A results were confirmed in approximately 50% of rebiopsy samples (2). Embryos with segmental aneuploidy can result in a normal pregnancy; however, there have also been reports of segmental aneuploidies identified on PGT-A that were confirmed to be present in the fetus and resulted in abnormal ultrasound findings. Because the positive predictive value of segmental aneuploidy is not as high as that for whole chromosome aneuploidy, Juno reports these results separately.



# PGT **A** Seq

## Juno PGT[A]Seq VS other PGT-A

**Our  
PGT[A]Seq  
is unique**

- 1 CUSTOM DEVELOPED IN-HOUSE ASSAY
- 2 TARGETED NGS + SNPS
- 3 HAPLOIDY + TRIPLOIDY DETECTION
- 4 ENABLES DNA FINGERPRINTING
- 5 EXTENSIVELY VALIDATED

### 1 CUSTOM DEVELOPED IN-HOUSE ASSAY

Unlike most laboratories, who use commercially available kits, we have developed a custom in-house assay that overcomes many of the limitations associated with of-the-shelf PGT-A platforms.

### 2 TARGETED NGS + SNPS

Instead of using whole genome amplification - a major contributor to noise and false-positives - we utilize a targeted next-generation sequencing (NGS) technique. Targeted NGS interrogates only areas of the genome that we know are able to provide us with an accurate assessment of whole chromosome aneuploidy, without introducing artifact.

### 3 HAPLOIDY + TRIPLOIDY DETECTION

In addition, we perform a custom single nucleotide polymorphism (SNP) genotyping assay in parallel on every biopsy. This allows for a second, independent confirmation of the number of chromosomes. SNPs also provide the added benefit of detecting all forms of haploidy and triploidy (including XXX triploidy, which is missed by NGS alone) without the need for parental samples\*. Our SNP assay also allows us to detect DNA contamination in the biopsy, and provides confirmation that all embryos within a tested cohort are full genetic siblings, an important QC measure.

### 4 ENABLES DNA FINGERPRINTING

When desired, we are also able to perform parental fingerprinting to confirm gamete sources.

### 5 EXTENSIVELY VALIDATED

PGTSeq has undergone more extensive analytical and clinical validation than any other assay in the industry, proving that embryos diagnosed with whole chromosome aneuploidies by PGTSeq have almost zero reproductive potential and providing critical data for evidence-based counseling on mosaic and segmental aneuploidy, applicable only to our assay (1,2).

\* Assessment of genetic ploidy of triprenuclear embryos identifies few diploid blastocysts. Nicole D. Yoder, MD, Collin Robins, BS, Chaim Jalas, Caroline McCaffrey, PhD, Andria Besser, MS, Jennifer K. Blakemore, MD, Yiping Zhan, PhD, Xin Tao, PhD, James A. Grifo, MD, PhD. Fertility & Sterility Sept 2021 Vol 116(3) Supp, e172-e173.

# PGT [A] Seq

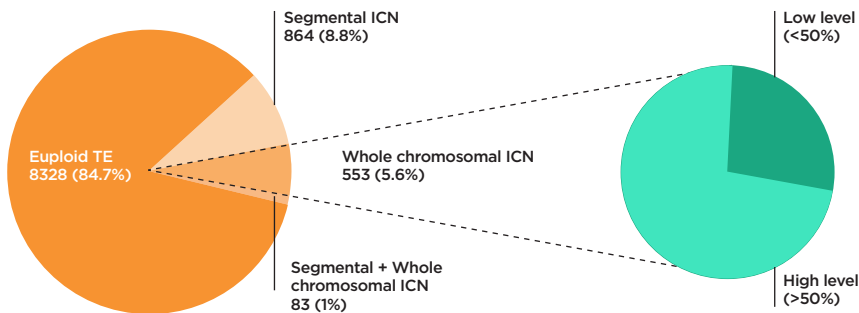
## What is mosaicism?

Mosaicism refers to a potential combination of chromosomally normal and abnormal cells in a single embryo biopsy sample. However, mosaic results on PGT-A are only inferred from “intermediate copy number” results on next-generation sequencing and do not necessarily indicate that the biopsy and/or embryo are truly mosaic.

Juno has investigated the clinical significance of mosaic PGT-A findings in an evidence-based manner, by conducting the largest multisite prospective study on clinical outcomes from nearly 10,000 embryo transfers that were tested on PGT[A]Seq and blinded to the presence or absence of mosaic findings.

Embryos transferred were all negative for whole chromosome aneuploidy: 85% non-mosaic; 5% whole chromosomal mosaicism (WCM); 9% segmental mosaicism (SM); 1% with both WCM and SM. Embryos were chosen for transfer based on morphology only.

### Results: Incidence of intermediate copy number (ICN)

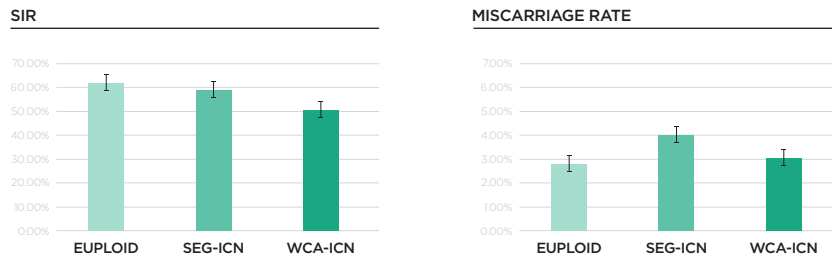


(1) Clinical utility of putative mosaicism detected using concurrent copy number and genotyping PGT method: Outcomes from multisite, prospective, non-selection study including 9828 single embryo transfer cycles. Dhruvi Babariya (1), Pavan Gill, Xin Tao, Yiping Zhan, Matteo Figliuzzi, Marie Werner, Chaim Jalas, Antonio Capalbo. Human Reproduction, 38 (Supp 1), June 2023.

# PGT A Seq

The sustained implantation rates (>8 wks) in non-mosaics, SMs, and WCMs were 62%, 58%, and 50%, respectively

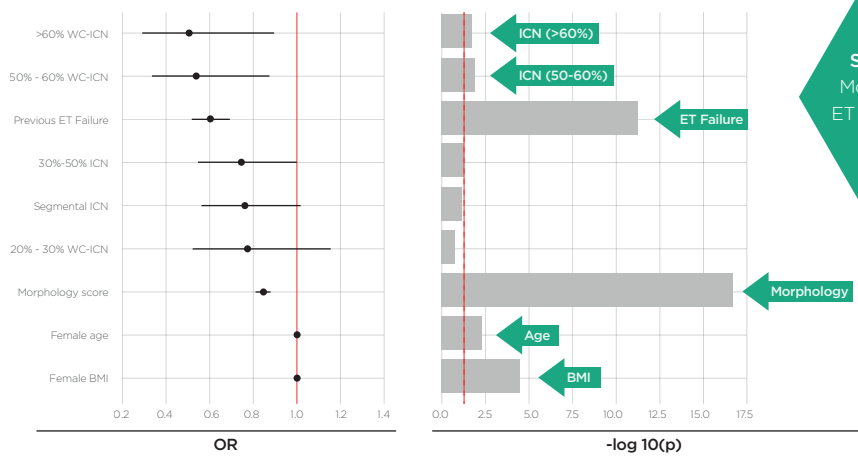
## Sustained implantation rates (SIR) and miscarriage rates



High level WCM embryos (>50%) had a significantly lower sustained implantation rate than non-mosaic embryos but comprise only 1.5% of all embryos. (SIRs of low-level (<50%) WCMs, and all SMs, were not significantly different from the non-mosaic SIR)

Many other clinical & embryology factors were more strongly associated with poorer outcomes than mosaicism.

## Factors associated with SIR



**Sir correlated with:**  
Morphology, Previous ET failures, Female BMI, Female Age, ICN >50%

WC-ICN = Whole chromosomal intermediate-copy-number

Statistical modeling indicated that mosaic reporting does not improve the clinical performance of PGT-A on PGTSeq.

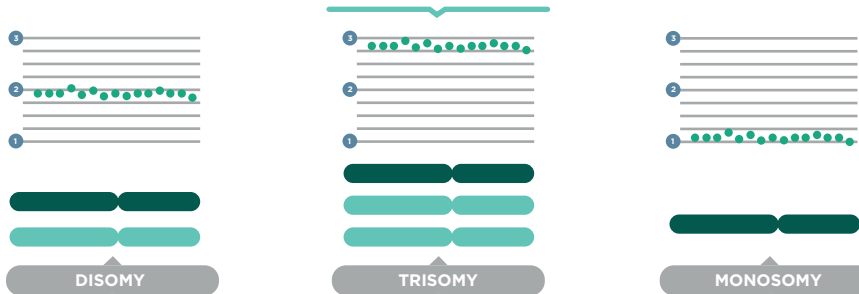
**As a default, mosaic findings are not reported on PGT-A results at Juno and are deemed “negative for whole chromosome aneuploidy”; however, providers may opt in to this information.**

# PGT **A** Seq

Juno uses a combination of custom-developed, targeted next-generation sequencing and SNP genotyping methodologies to make a PGT-A call on every embryo

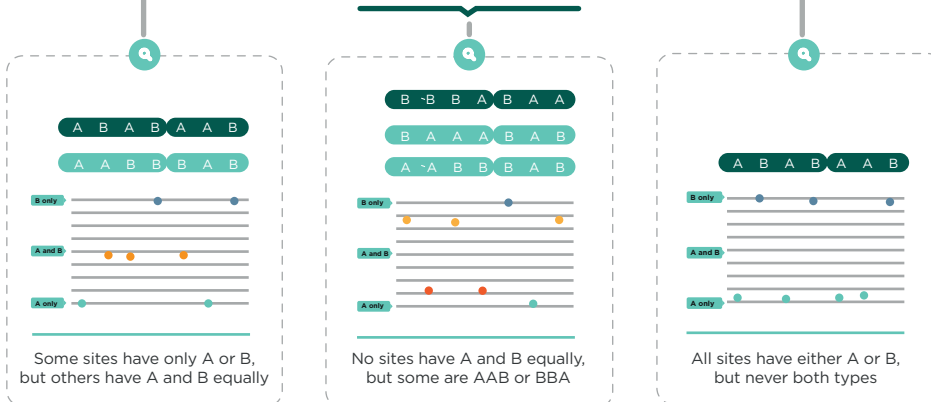
## 1 NGS

Next-generation sequencing measured 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

Thousands of locations where the DNA sequence can differ between individuals are examined. 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



# JUNO'S PGT[A]SEQ METHOD

## How do we know whether a PGT method is accurate?

Analytical and clinical validation studies are necessary to prove the accuracy of each specific PGT-A assay

### 1. Analytical validation

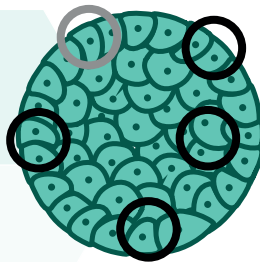
To validate PGT[A]Seq analytically, an extensive rebiopsy study was performed. This methodology evaluated whether the PGT[A]Seq test provides the same clinical result for whole chromosome aneuploidy when multiple different biopsies from the same embryo were tested.

The study concluded that PGT[A]Seq is 97-98% accurate in screening for whole chromosome aneuploidy.

Blastocysts with a routine PGT[A]Seq result

↓  
Donated for research

↓  
Biopsied 4 additional times



### Original PGT[A]Seq Result

	EUPLOID	ANEUPLOID
PGT[A]Seq result confirmed in $\geq 1$ other biopsy	100%	99.6%
PGT[A]Seq result confirmed in all other biopsy	98.5%	96.7%

### (2) 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

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. Fertil Steril. 2022 Feb;117(2):315-323.

# JUNO'S PGT[A]SEQ METHOD

## How do we know whether a PGT method is accurate?

Analytical and clinical validation studies are necessary to prove the accuracy of each specific PGT-A assay

## 2. Clinical validation

To validate PGT[A]Seq clinically, a non-selection study was undertaken in which embryos were biopsied, but embryos were chosen for transfer based on standard morphological criteria only. After the outcome of the transfer was known, PGT[A]Seq was run and the true positive predictive value of the test was revealed.

None of the embryos deemed abnormal by PGT[A]Seq resulted in an ongoing pregnancy, confirming that embryos classified 'aneuploid' by Juno have little or no chance of producing a baby.

Like the rebiopsy study, this study also concluded that PGT[A]Seq is >98% accurate in screening for whole chromosome aneuploidy.

### 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 laboratory with a non-selection study proving that its PGT-A method does not result in the discarding of potentially viable embryos**

### (3) 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. Fertil.

Steril. 2021 Mar;115(3):627-637.

# PGT **A** Seq

## Advantages of using Juno PGT[A]Seq



Proven clinical value in well-designed, published studies



More euploid embryos reported than other assays



Minimizes embryo wastage from over-calling.

High reproducibility in rebiopsy studies.

Detection of DNA contamination and sibling embryo confirmation with SNPs.

Rapid turnaround time and fully transparent data-sharing.

Complete follow-up on discrepant prenatal findings.

Extensive PGT-M expertise and ability to accept complex cases.

The only commercial PGT-A assay that does not rely on whole genome amplification.

Chromosome copy number analysis via NGS and SNPs.

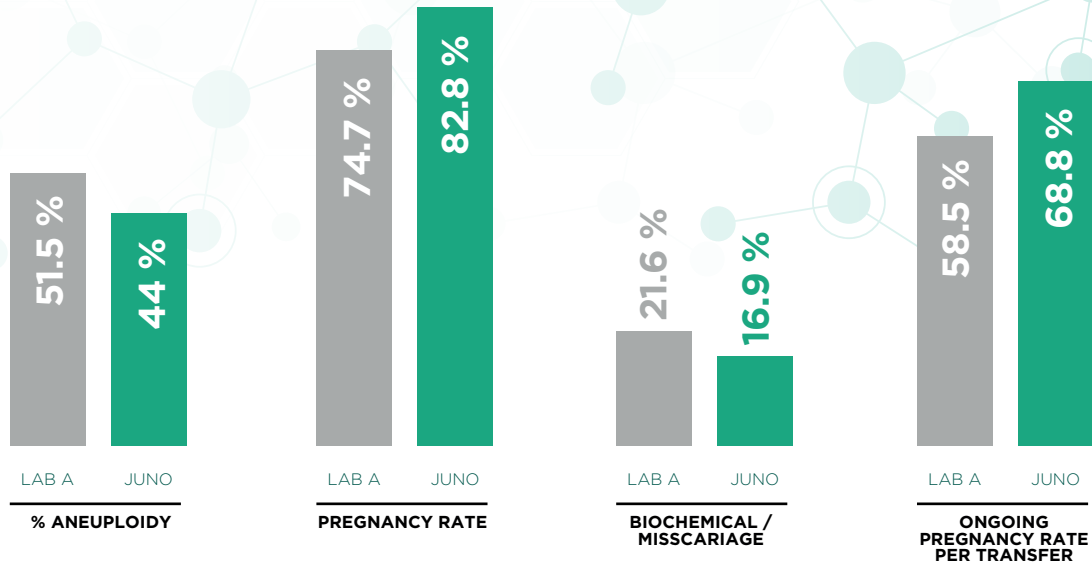
Evidence-based mosaicism and segmental aneuploidy reporting.

Molecular fertilization (pn) check for ploidy status.

# PGT A Seq

## Abstract ESHRE 2023: Genetic laboratories report significantly different aneuploidy rates for identical patient populations, a finding with important implications for clinics using PGT-A

K. Glynn<sup>1</sup>, D. Wells<sup>2</sup>, J. Nicopoulos<sup>3</sup>, S. Batha<sup>1</sup>, <sup>1</sup>Lister Fertility Clinic, Embryology, London, United Kingdom. <sup>2</sup>Juno Genetics, PGT-Laboratory, Oxford, United Kingdom. <sup>3</sup>Lister Fertility Clinic, Consultant, London, United Kingdom.



**EMBRYOS**  
LAB A: 1136  
JUNO: 784

Average maternal age 38 years

### Main results and the role of chance:

The first PGT-A company classified 44.4% of blastocysts euploid, 4.1% low-level mosaic, 51.5% aneuploid. In contrast, the second company reported significantly fewer embryos aneuploid (44.0%;  $P=0.0019$ ). Even if the mosaics reported by the first company are considered for transfer, the second company is still associated with more potentially transferable embryos (relative increase greater than one-sixth). If PGT-A results from the second company are correct, it implies that potentially viable embryos may have been misclassified by the first company, risking their exclusion and loss of the pregnancies they might have produced. Conversely, if the first company is correct, the second company may be

failing to detect some aneuploidies, leading to inadvertent transfer of abnormal embryos, lower pregnancy rates and a higher incidence of miscarriage. 299 transfers following PGT-A using the first company produced 171 pregnancies (74.7%), while 64 single embryo transfers have taken place after PGT-A with the second company, resulting in 53 pregnancies (82.8% per transfer). Losses (biochemical or miscarriage) affected 21.6% and 16.9% of pregnancies after PGT-A conducted by the first and second companies, respectively (ongoing pregnancy rates of 58.5% and 68.8% per transfer, respectively) Thus, there is no evidence that aneuploidies are being missed by the second company.

# PGT A Seq

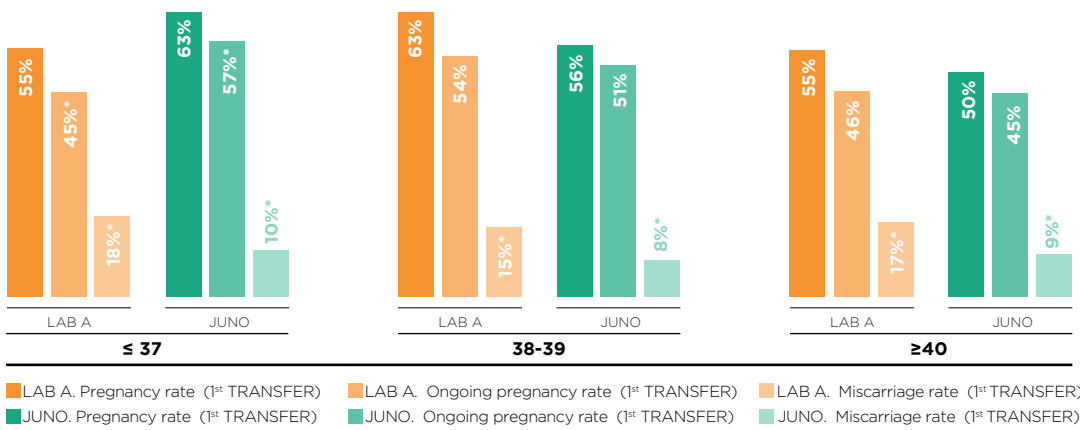
## Abstract ESHRE 2023: The choice of genetic service provider can have significant implications for the outcome of IVF cycles using preimplantation genetic testing for aneuploidy (PGT-A)

Manuel Fernández Sánchez<sup>1</sup>, Esther Santamaría López<sup>1</sup>, Nicolás Prados Dodd<sup>2</sup>, Dagan Wells<sup>3</sup>  
<sup>1</sup>VIRMA Seville <sup>2</sup>VIRMA Headquarters <sup>3</sup>Juno Genetics

	Number of cycles	Number of embryos tested with PGT-A	Euploid result	Mosaic (transferable) result	Mosaic (non transferable) result	Abnormal result	Euploidy rate
LAB A	2734	9091	3586	---	---	5422	39.8%*
JUNO	3036	10281	4991	136	139	4864	49.2%*

Genetic results from both providers for 6 months

\*  $\chi^2$  test: Significant difference between groups (P<0.0001)



Comparison of the clinical results of patients divided by age

\*  $\chi^2$  test: Significant difference between groups (P<0,05)



### RESULTS

A significantly higher proportion of embryos were classified euploid by provider B in comparison to A (Figure 1). Differences in reported aneuploidy were particularly striking for patients 37 years: 67,5% euploid according to B versus 52,5% reported by A (p< 0,0001). For female patients over 38 years of age, the lower aneuploidy frequency reported by B resulted in fewer cycles with all embryos classified 'and more cycles with a transfer: 52,2% of 2115 cycles in this age group had a transfer, compared to 48,6% of 1915 cycles for A (p= 0,02). Having more embryos classified euploid also benefitted younger patients, providing greater opportunity to combine morphological selection with genetic evaluation. Improved selection may explain a higher ongoing pregnancy rate observed for patients 37 years after the first embryo transfer (p=0,026) (Figure 2). Significant differences in miscarriage rates were also observed (patients 37 p= 0,038; patients between 38-39 years, p= 0,018; and patients older than 40 years, p= 0,002) (Figure 2).



### CONCLUSIONS

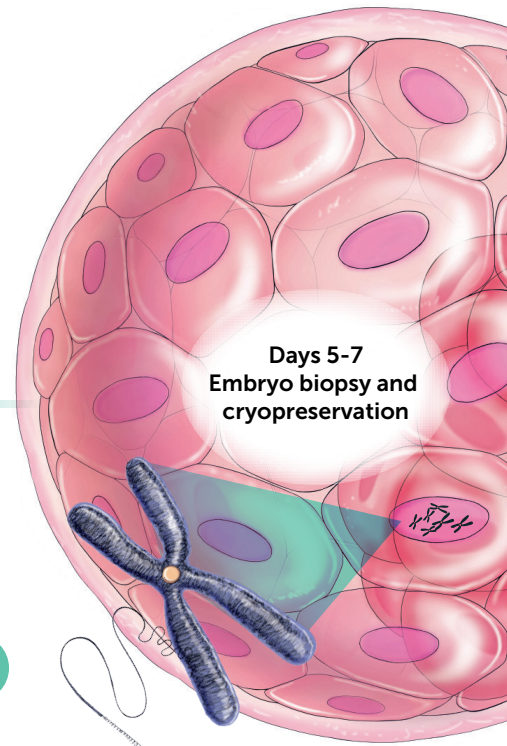
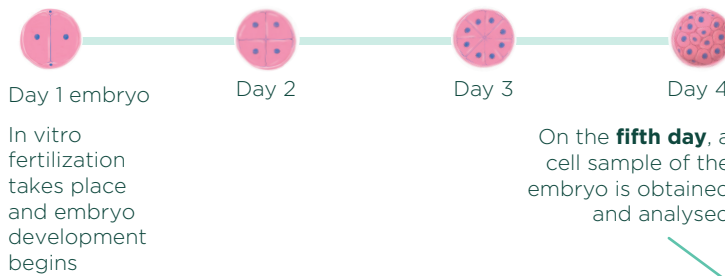
Our results suggest that the choice of PGT A provider has important implications for clinical results, affecting the number of transferable embryos, pregnancy, and miscarriage rates.

- The higher euploidy and pregnancy rates observed when using Provider B could potentially be explained if Provider A misclassified some euploid embryos as 'leading to exclusion of viable embryos. In addition, a failure of Provider A to detect some aneuploidies, resulting in transfer of abnormal embryos, might explain the higher rate of miscarriages seen when using that laboratory. These possibilities cannot be confirmed from our dataset and remain speculative.
- Importantly, it should be understood that PGT A and NGS are umbrella terms encompassing multiple methods with widely varying levels of validation and accuracy. For this reason, PGT A providers are not equivalent and should be chosen with care.

# JUNO PGT[A]SEQ INCREASES THE CHANCE OF A HEALTHY BIRTH PER IVF CYCLE

The best-in-class accuracy of PGT[A]Seq means an increased number of euploid embryos are correctly reported, leading to the availability of more viable embryos for transfer and better outcomes than other PGT-A methods.

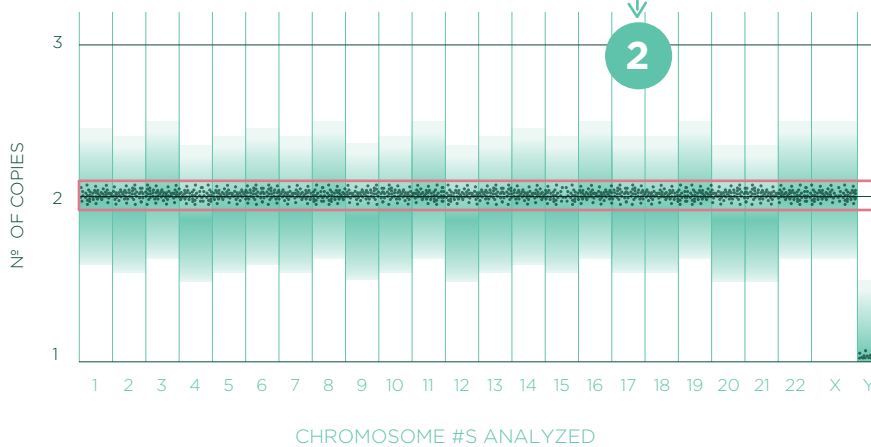
## WHEN IS THE TEST PERFORMED?



## NGS

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

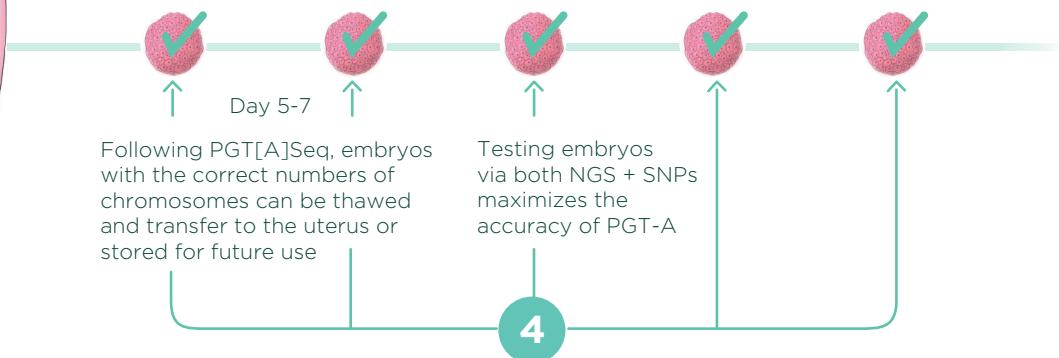
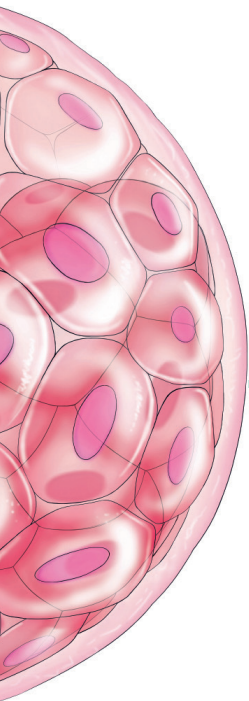
Juno uses next-generation sequencing to measure the amount of DNA at thousands of sites on each chromosome. This allows the number of copies of the chromosome to be calculated with high accuracy.



## NGS + SNPs

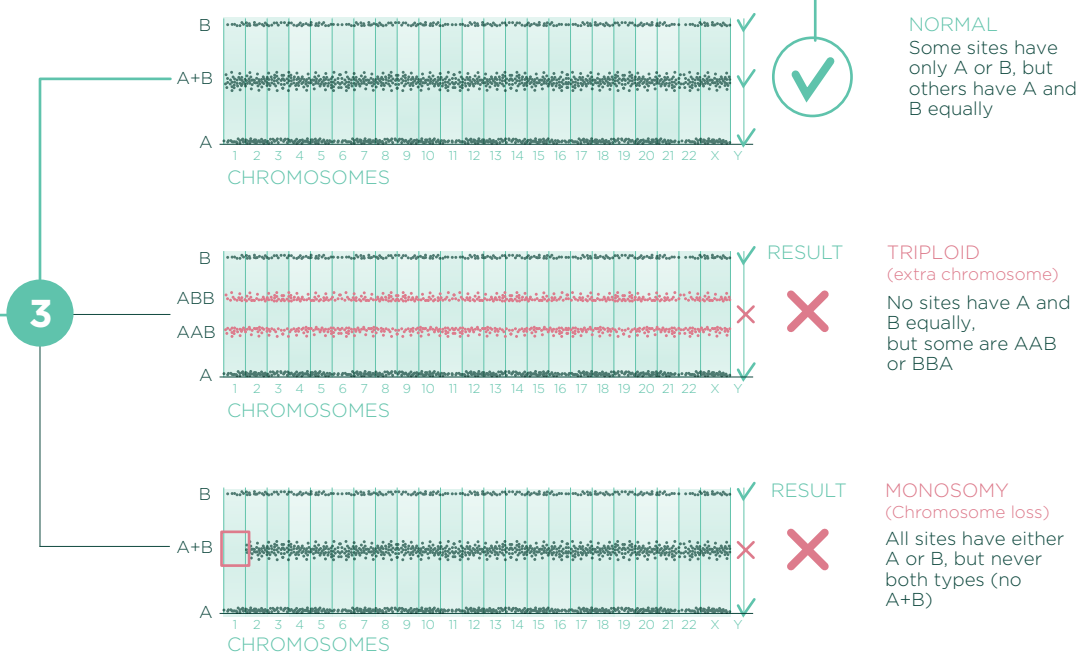
Together, the measurement of the amount of DNA and the analysis of the DNA sequence greatly increases the accuracy of PGT[A]Seq.

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



## 4000 SNPs (Points where the DNA sequence between individuals can differ)

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



# PGT **M** Seq

## PGT for monogenic conditions

Juno Genetics has performed PGT-M for thousands of different genes and variants of autosomal and X-linked inheritance.

Our custom PGT-M technologies enable us to provide testing of the highest accuracy.

We can often accept challenging cases including de novo variants in a prior offspring, mosaic variants in a patient or partner, and some microdeletions/duplications.

Our experienced team of genetic counselors works with each patient to guide them through the PGT-M process and provide support.

In combination with our fully validated PGT[A]Seq platform, Juno is able to provide PGT-M patients with the best chance for a successful IVF outcome while also dramatically reducing the risk for the genetic condition in the next generation.





# PGT SR Seq

## PGT for structural rearrangements

June offers PGT-SR for a variety of inherited chromosome rearrangements including reciprocal and Robertsonian translocations and inversions.

June is typically able to offer PGT-SR without need for additional probes or fees.



## 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

**+350**

scientific publications

**4**

research centers

**UK**

**USA**

**SPAIN**

**ITALY**

state-of-the-art laboratories

**Juno Genetics is a state-of-the-art laboratory specializing** in preimplantation genetic testing (PGT). Our mission is to provide rigorously validated, evidence-based PGT of the highest clinical quality to IVF clinics and patients. We are also passionate about research and advancement of knowledge in embryo genetics; collaboration and transparency with our clinical partners and patients; and education at all professional levels to promote understanding and applications of embryonic diagnostics. .

**The innovative tests offered by Juno are the result of world-class research carried out by an internationally renowned team of scientists and are amongst the most technologically advanced and accurate available anywhere in the world.**



# Online Brochures

**Juno Genetics is  
a paperless company**

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specialist in reproductive genetics

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