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Chat PGT

BSRM

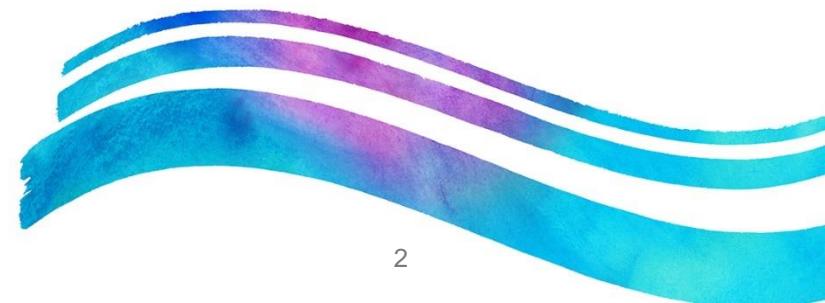
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Disclosure



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- I am full-time employee and shareholder of CooperSurgical, Inc



You may already be using machine learning AI



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E.g. AI personal assistants

Machine learning is used to help train the voice processing system from customer audio input/feedback



Hey Siri

Ok Google, order paper towels

Got it, ordering paper towels

amazon alexa

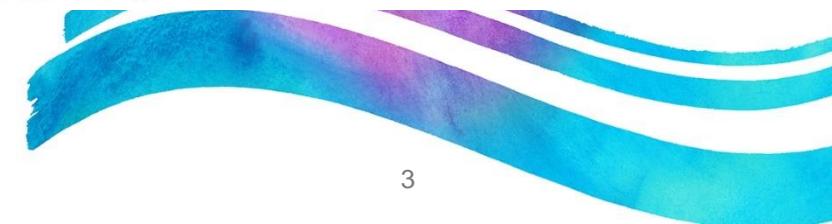
"Alexa, turn on Welcome Home"

"Alexa, turn on my Chill Time"



"Alexa, turn off my Bedroom Sonos"

"Alexa, turn on the TV"



Will AI improve IVF outcomes? Ask ChatGPT!



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ChatGPT 4o mini ▾

will AI improve IVF outcomes

 Yes, AI has the potential to significantly improve in vitro fertilization (IVF) outcomes in several ways, by enhancing both the technical and decision-making aspects of the process. Here are some key areas where AI can contribute:

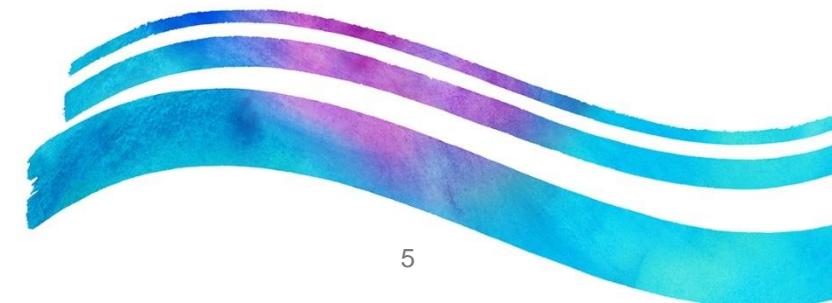


Will AI improve IVF outcomes? Ask ChatGPT!



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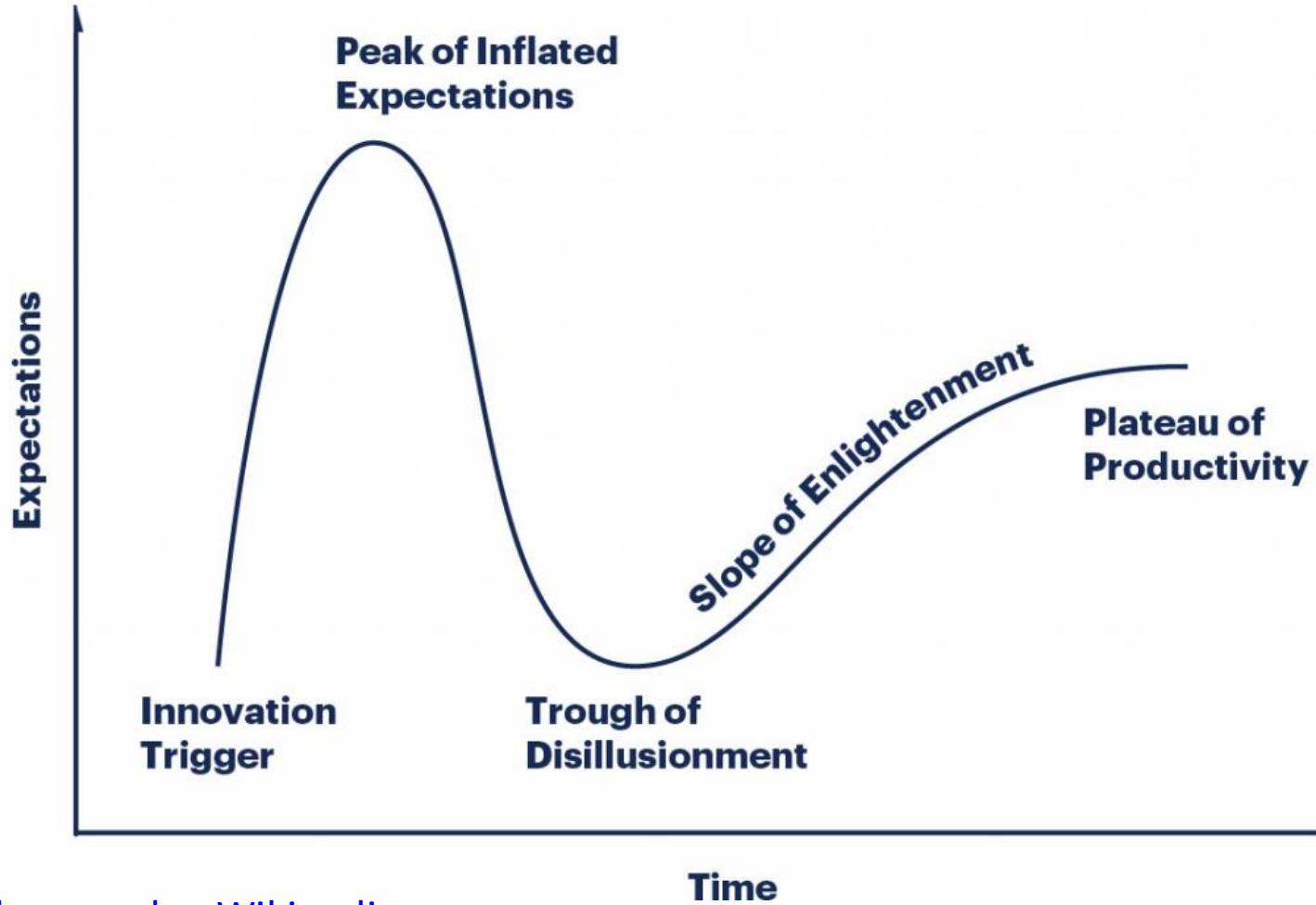
- **1. Embryo Selection**
 - Morphological features
 - Embryo development
- **2. Personalizing Treatment Plans**
- **3. Predicting Success Rates**
- **4. Improving Sperm and Egg Quality Assessment**
- **5. Optimizing Laboratory Conditions**
- **6. Genetic Screening and Preimplantation Genetic Testing (PGT)**
- **7. Reducing Human Error**
- **8. Robotics and Automation**
- **9. Data-Driven Insights**
 - Challenges and Ethical Considerations
 - Data privacy
 - Bias and fairness
 - Over-reliance on AI
- In conclusion, AI has the potential to enhance IVF outcomes by improving embryo selection, personalizing treatment plans, predicting success rates, optimizing lab conditions, and reducing human error. However, like any medical technology, it will need to be integrated carefully, with attention to ethical, legal, and social implications, to truly transform IVF practice in a positive way.



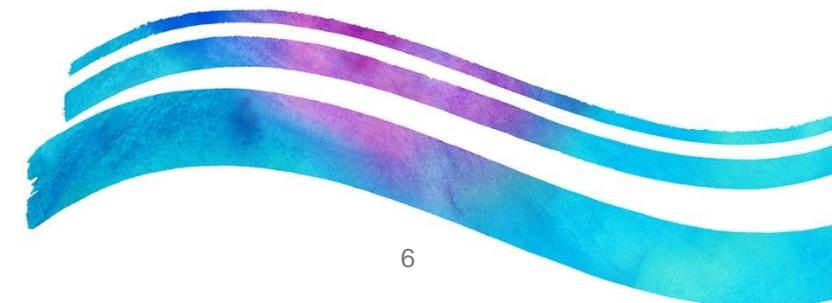


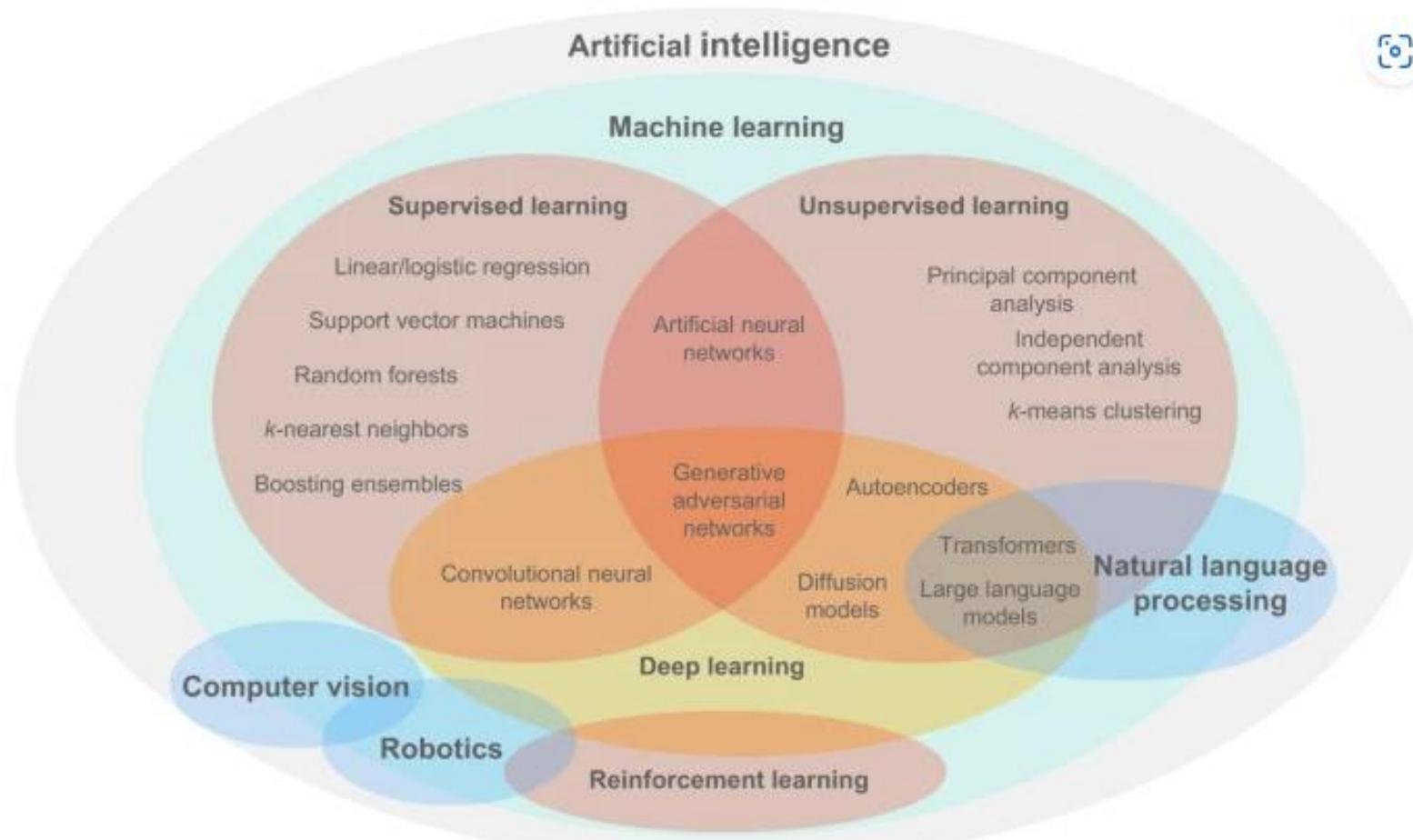
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The “Hype Cycle”



[Gartner hype cycle - Wikipedia](#)





Supervised vs unsupervised learning

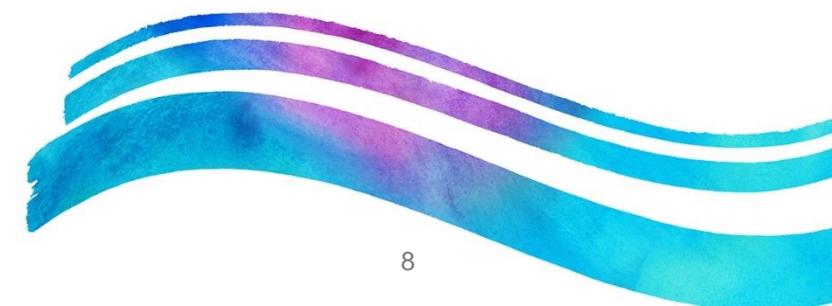


Supervised learning is a machine learning approach that's defined by its use of labeled datasets. These datasets are designed to train or "supervise" algorithms into classifying data or predicting outcomes accurately. Using labeled inputs and outputs, the model can measure its accuracy and learn over time.

- Do you need to retrospectively analyse data
- Fixed algorithms
- "labelled data" aka truth data

Unsupervised learning uses machine learning algorithms to analyze and cluster unlabeled data sets. These algorithms discover hidden patterns in data without the need for human intervention (hence, they are "unsupervised").

[Supervised vs. Unsupervised Learning: What's the Difference? - IBM Blog](#)





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Optimizing PGT-A with the PGTai technology platform



Data is generated via NGS

Data is analyzed using mathematical algorithms & machine learning technology

- The new technology uses algorithms based on a continuously growing data set (>10,000 samples)
- Removes human subjectivity
- Avoids human errors

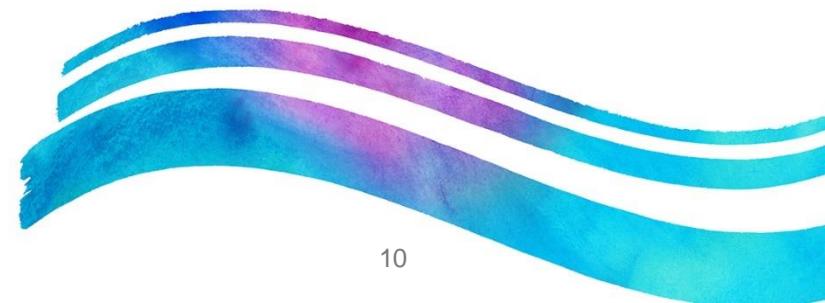
Brings the power of big data to the clinician's transfer decisions

PGT-A vs PGT-M vs PGT-SR



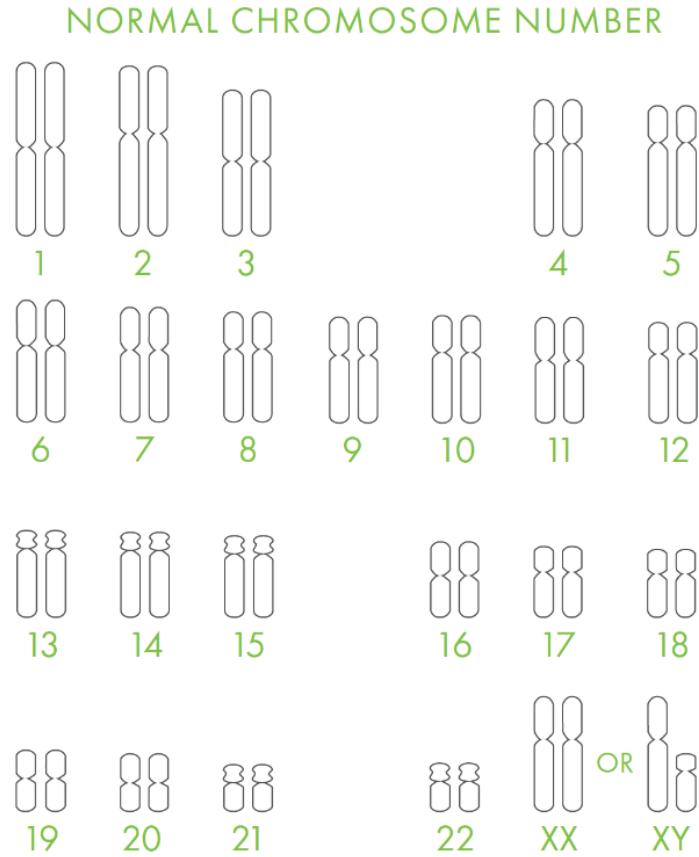
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PGT-A	PGT-M	PGT-SR
Preimplantation Genetic Testing – Aneuploidy (PGS, CCS)	Preimplantation Genetic Testing – Monogenic/Single Gene Disorders (PGD)	Preimplantation Genetic Testing – Structural Rearrangements (PGD)
Screens for chromosome abnormalities	Screens for a specific single-gene disorder	Screens for inherited chromosome rearrangements
Option for all IVF patients?	For couples at high-risk of having a child with a specific genetic disease	For carriers of translocations, inversions, and complex chromosome rearrangements
Improves IVF success rates?	Reduces risk of genetic disease	Reduces risk of pregnancy loss/developmental disorders
Does not require personalized test prep	Requires personalized test prep and design	Requires personalized review of parental karyotype(s)



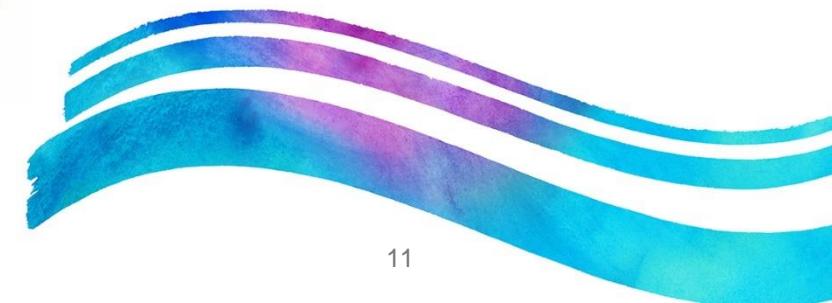


Chromosomal health of embryos



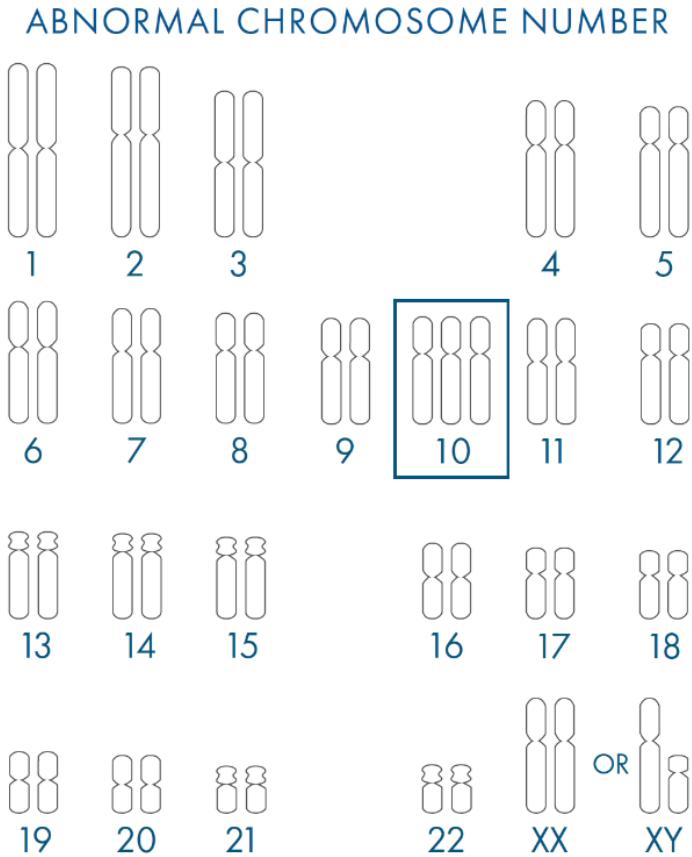
Euploid embryos

- Correct number of chromosomes
- Highest likelihood of successful pregnancy



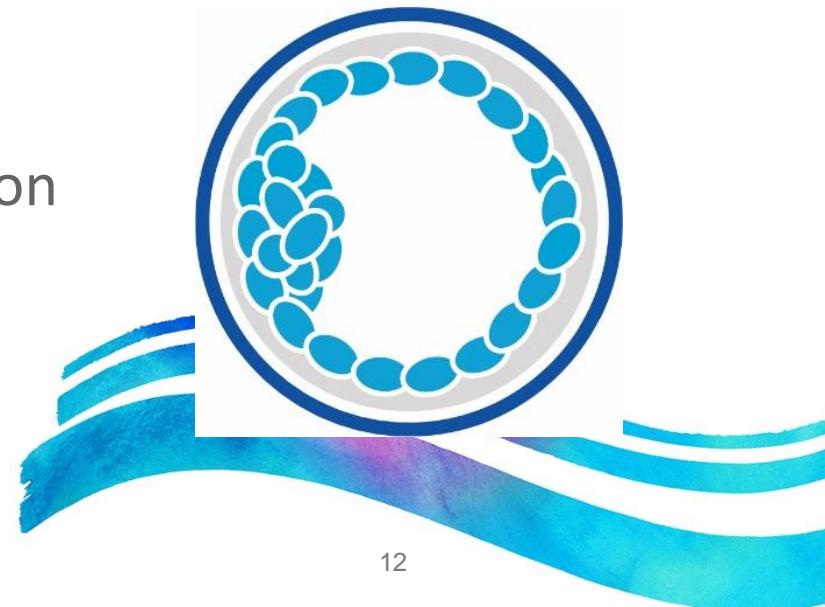


Chromosomal health of embryos



Aneuploid embryos

- Incorrect number of chromosomes
- Aneuploidy is found in embryos of IVF patients of any age, but has shown to increase with maternal age
- May result in:
 - Failed implantation
 - Miscarriage
 - Genetic disease



High throughput non-subjective PGT-A calling



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Efficiency and consistency requirements?

- High throughput – potentially 1000 embryo biopsy PGT-A results called per day
- Full automated karyotype
- No/reduced requirement for teams of laboratory analysts for calling
- Reduced requirement for associated calling competency training
- Inter-laboratory consistency
- Reduction of or no human input for interpretation and transcription to reports





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Subjective PGTA calling

Most commercial platforms rely on subjective calling to some extent^{1,2}

- Some automated and some subjective by lab analysts, typically subjective calling for smaller changes and/or mosaic calling
- End users may be required to set calling thresholds
- End users may be required to input either cell lines or small embryo datasets for normalization
- Reporting is typically manual

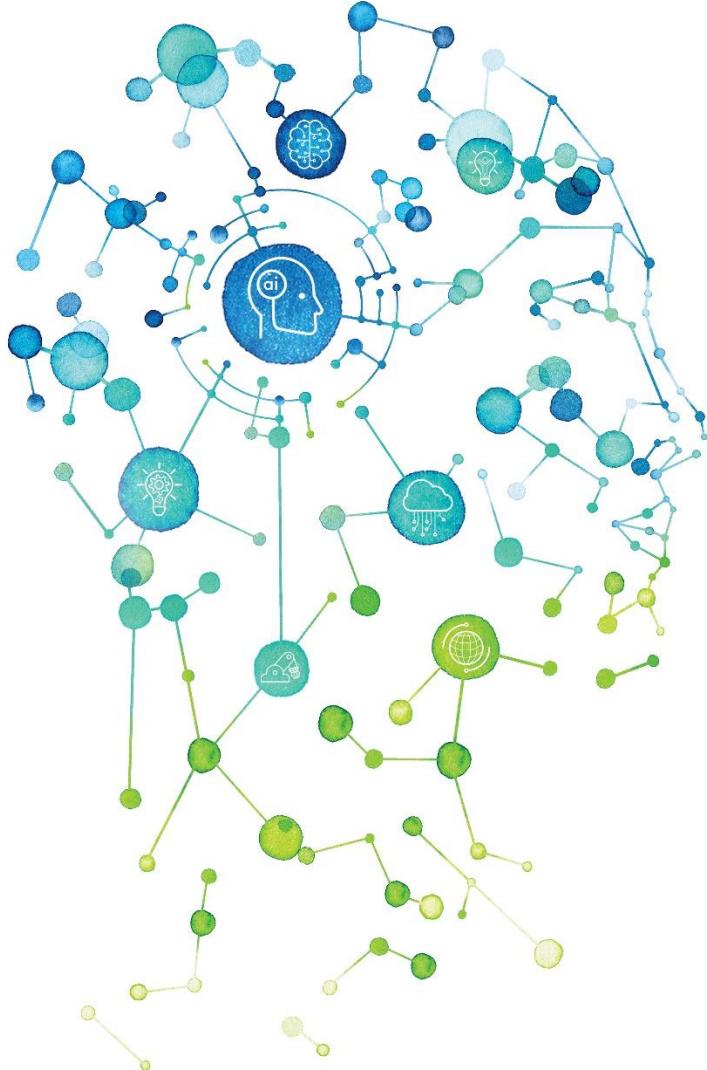


1. <https://www.vitrolife.com/products/genomics/embryomap/> 2. <https://www.thermofisher.com/document-connect/document-connect.html?url=https://assets.thermofisher.com/TFS-Assets%2FGSD%2FApplication-Notes%2Fpreseq-pgs-kits-app-note.pdf>

A leap in PGT-A analysis and reporting



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The PGTai platform is a **ground-breaking, first-of-its-kind mathematical algorithm** that harnesses the power of AI, big data, and machine learning to **maximize both sensitivity and specificity during PGT-A**

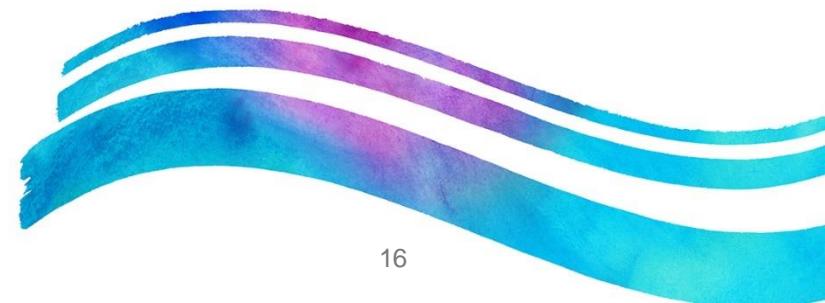




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To err is human

Alexander Pope. An Essay on Criticism

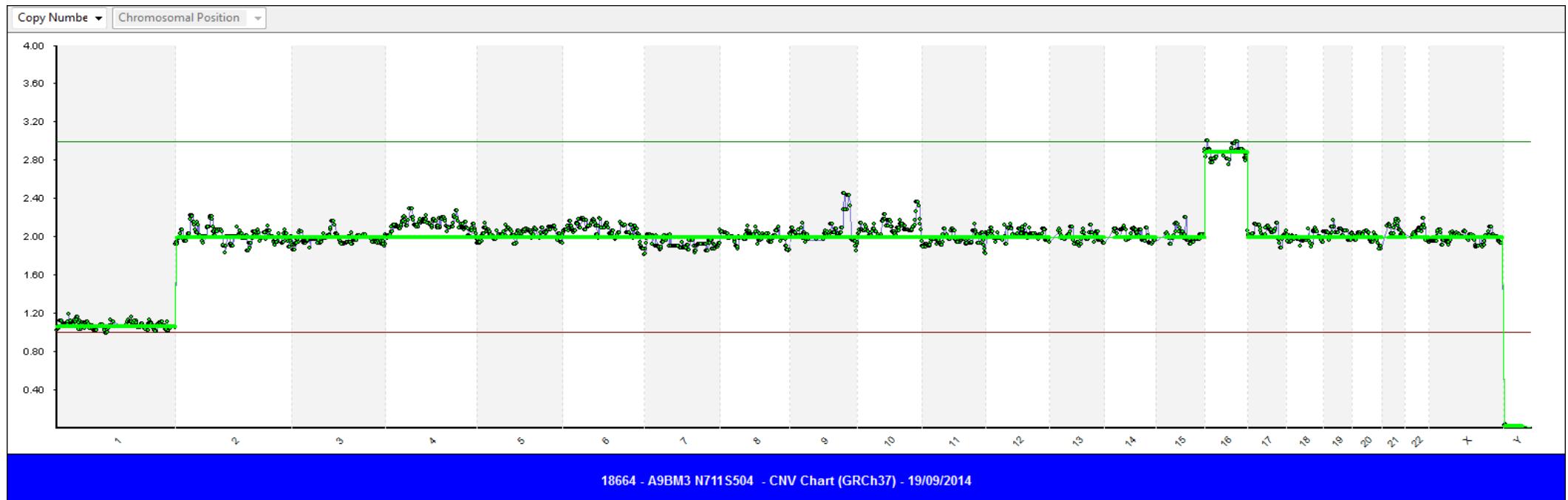


NGS 46XX,-1,+16



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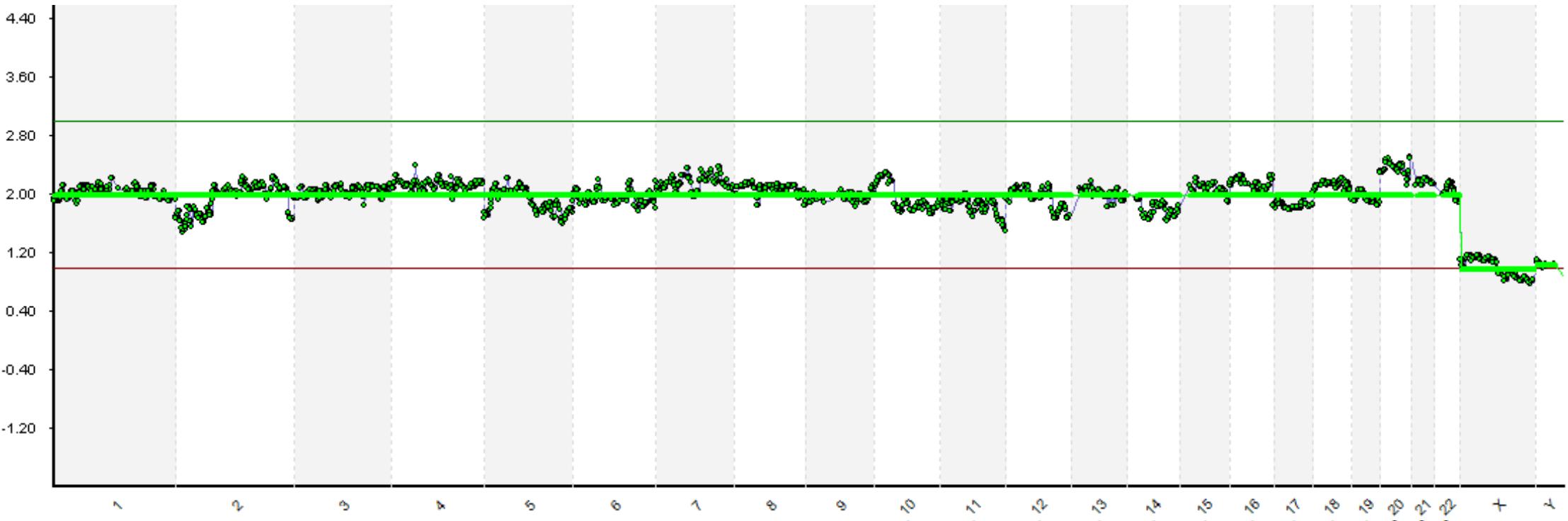
NGS





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Subjective interpretation?



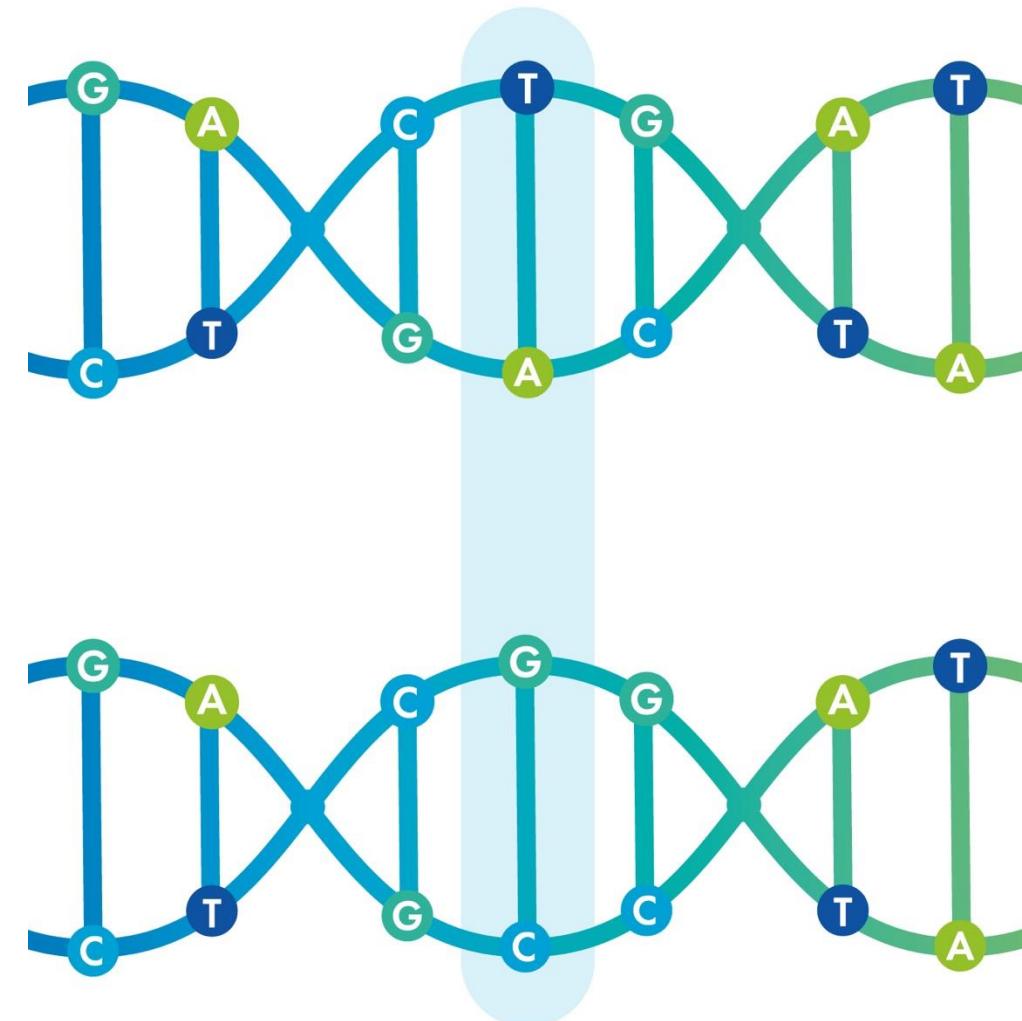
Which blips are real? How do we know?

Single nucleotide polymorphisms (SNP) are a common form of genetic variation



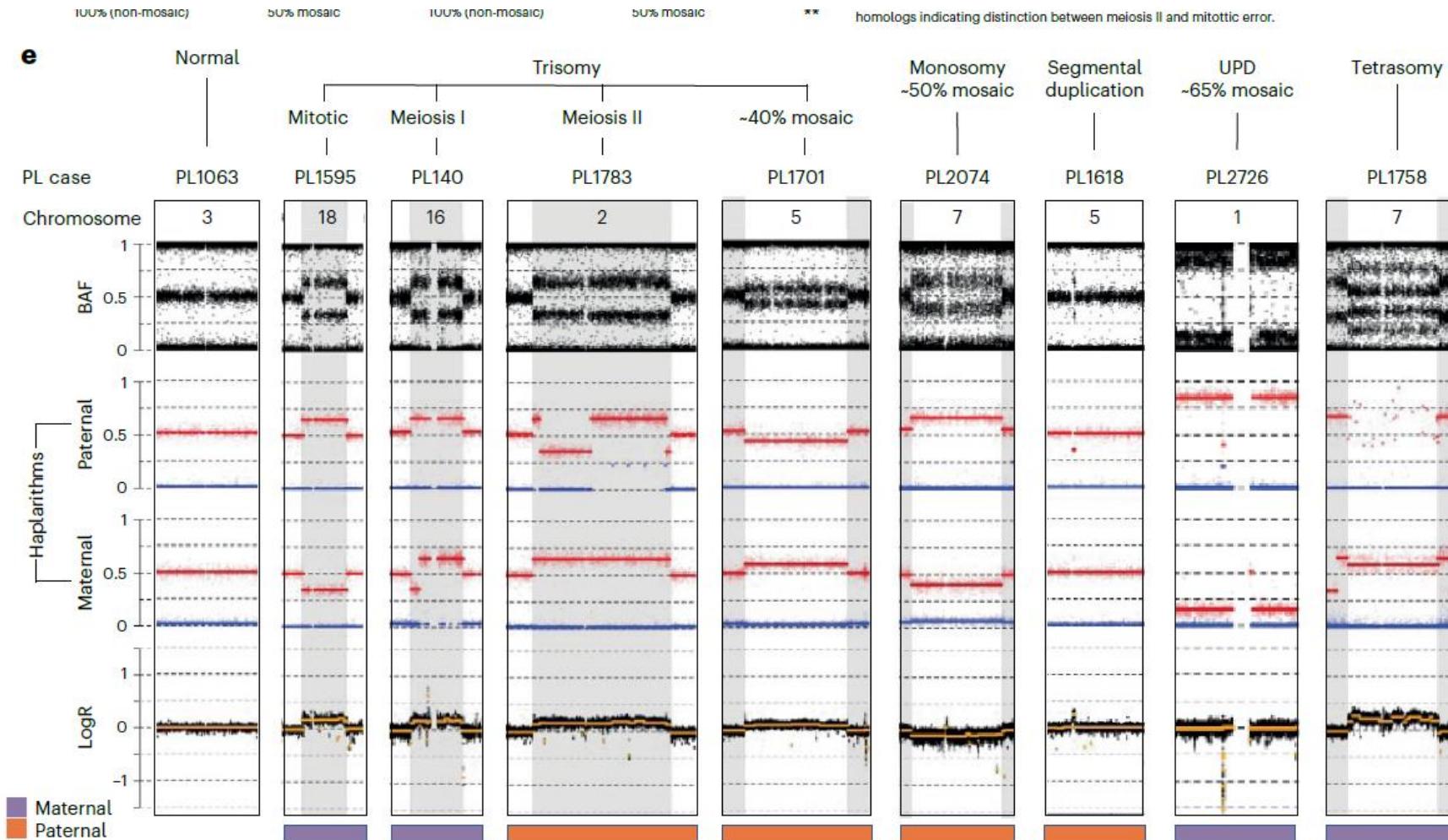
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- Each SNP is a difference in a single DNA building block, within a specific stretch of DNA
- They result from natural variation in human evolution and reproduction
- Most SNPs have no effect on health or development



Prevalence of chromosomal alterations in first-trimester spontaneous pregnancy loss

Essers et al, 23rd Nov 2023. Nature Medicine

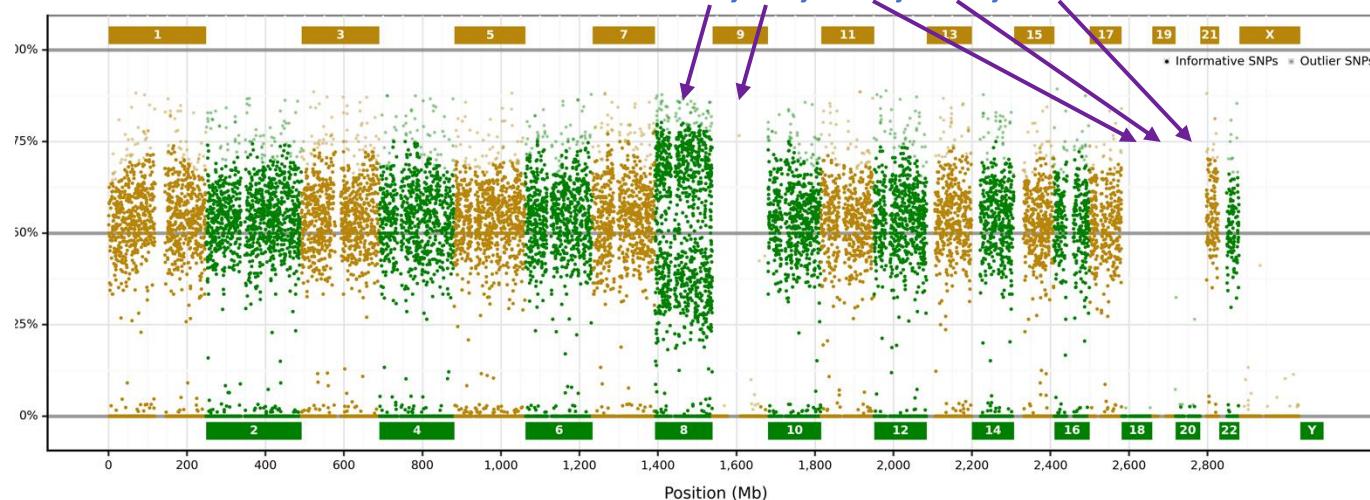
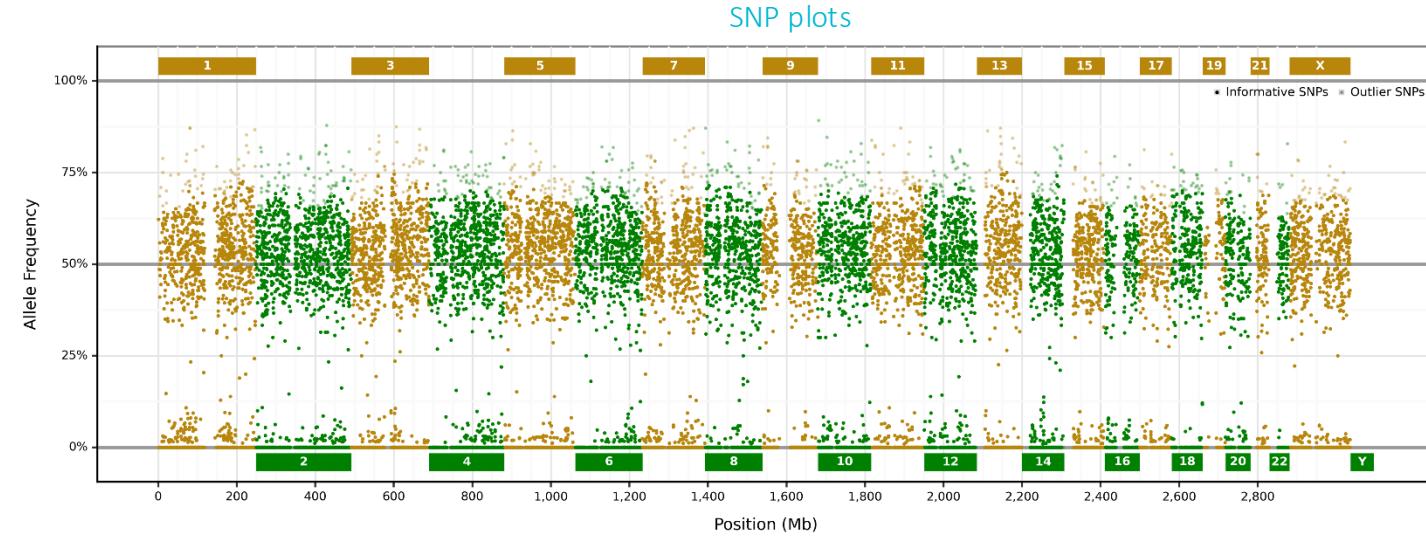
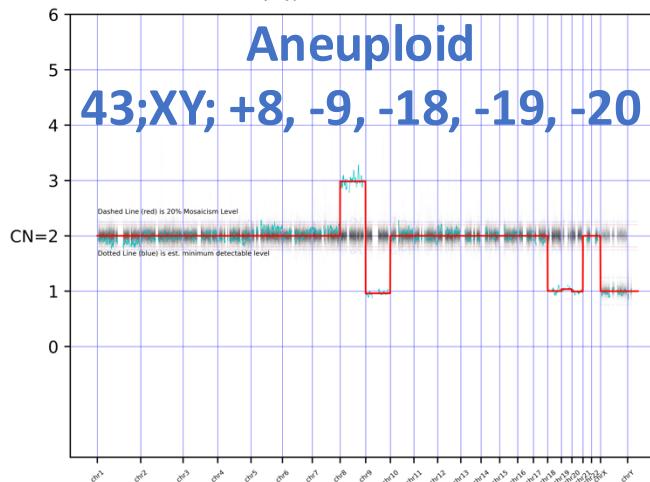
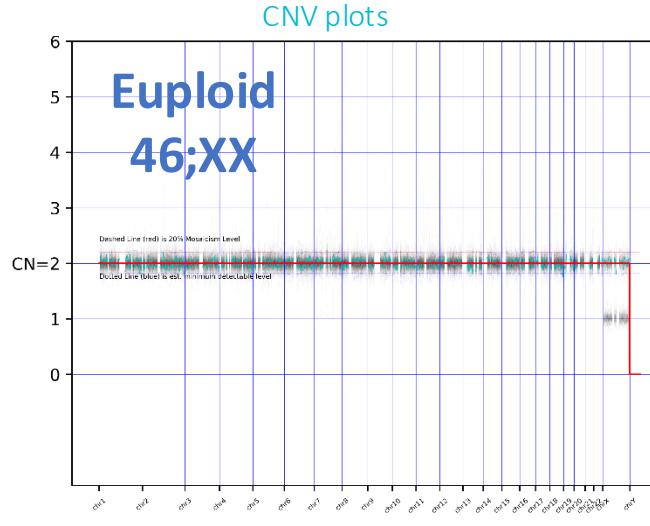


Whole chromosome and segmental CNV

High resolution copy number variation + SNP analysis



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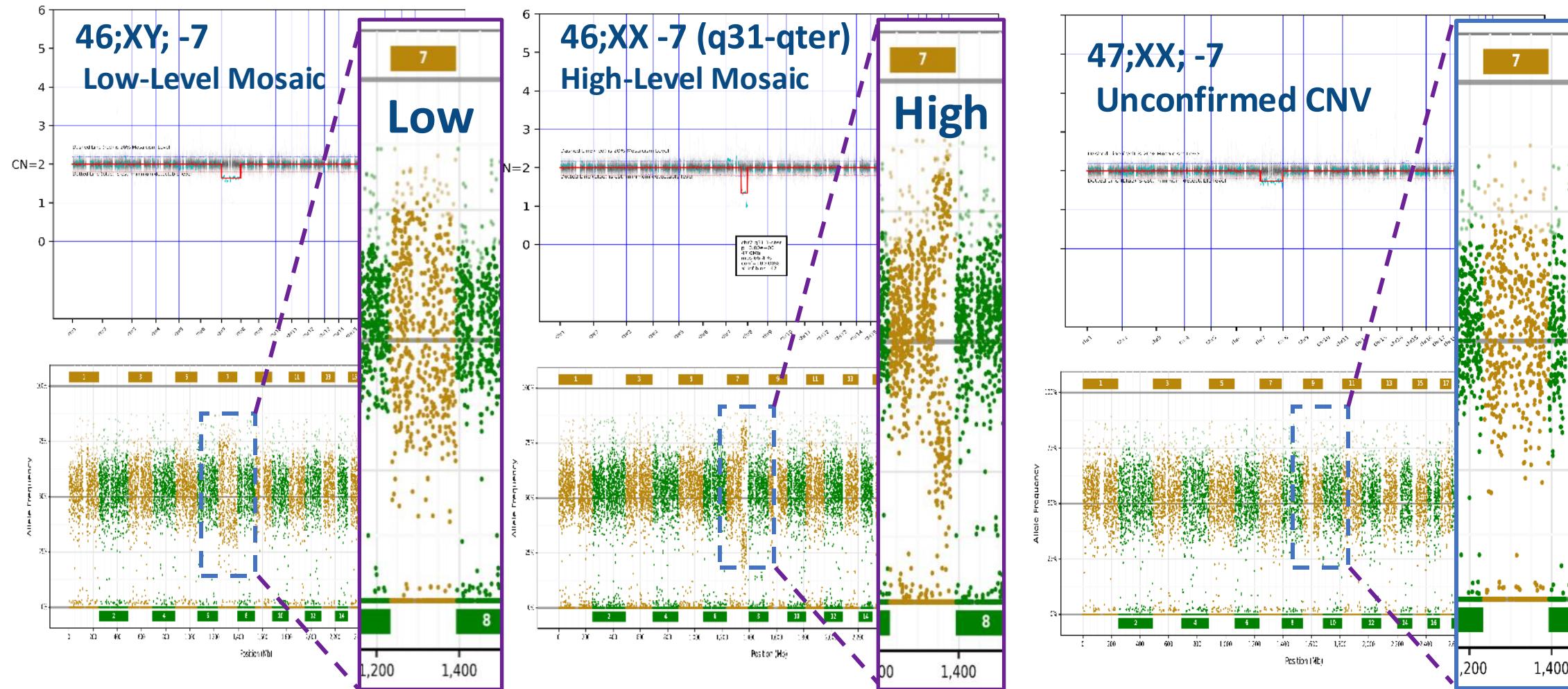


CLARIFYING MOSAIC EMBRYOS

Classification and quantification of mosaicism – *eliminating unconfirmed CNV*



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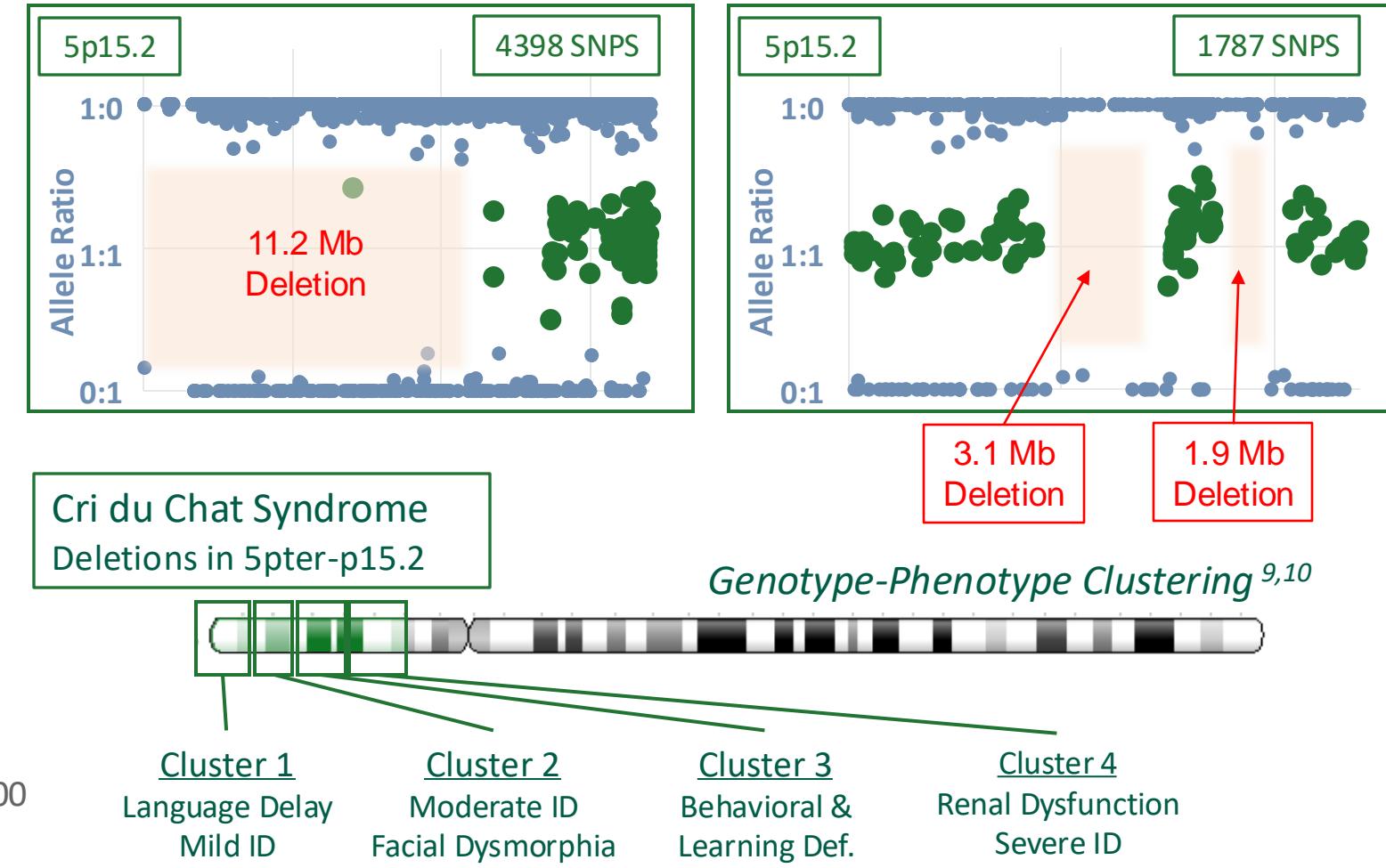
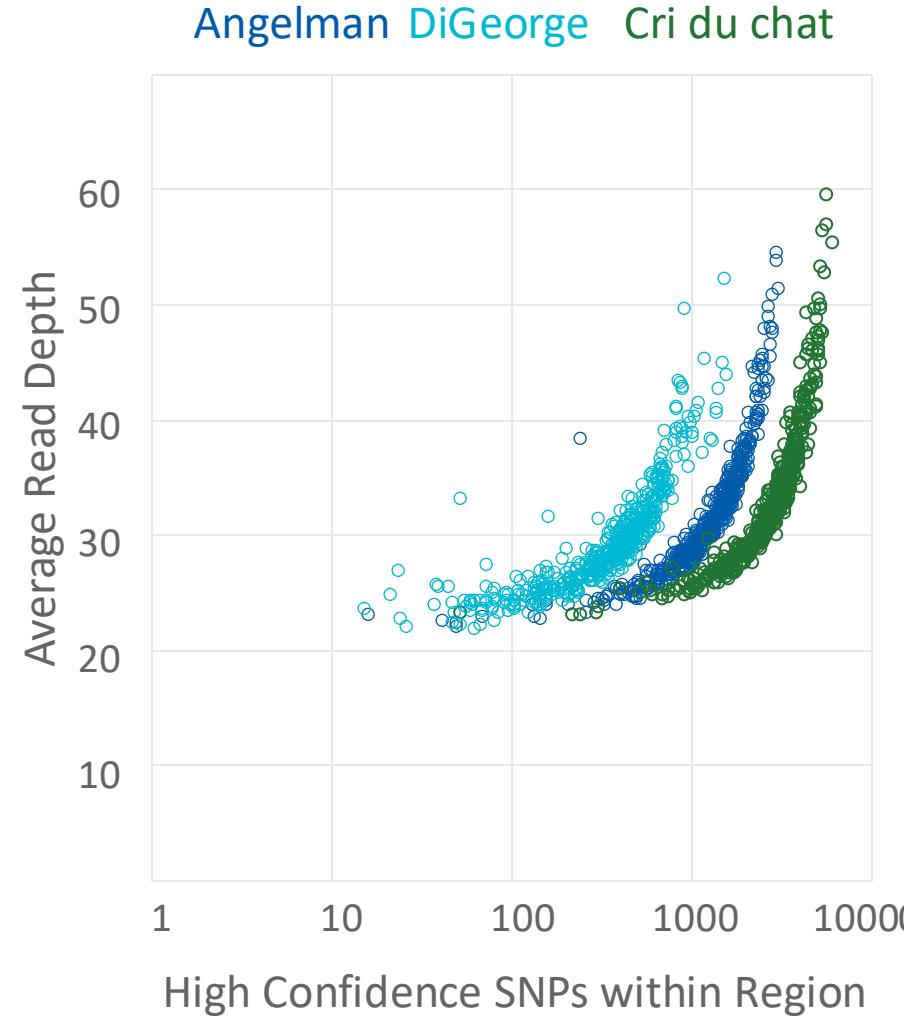


Target specific analysis to identify significant CNV

Higher resolution may identify subregions with clinical impact



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The PGT-CompleteSM test



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PGT-A featuring Parental QC, Genetic PN Check, and Origin of Aneuploidy

PGT-A (PGT^{ai} Platform)

Feature

PGT-A testing using PGT^{ai}, our artificial intelligence (AI) platform.

Benefit to you

Our PGT^{ai} is the only test available using AI that is based on clinical outcome data of live births and sustained pregnancies. Our platform has been shown to improve the odds of IVF success.²



Parental QC*

Feature

Confirms a match^{**} between embryo biopsy sample and provided patient samples.²

Benefit to you

Reassures you that the intended egg and sperm were used in your IVF process, helping to reduce the anxiety of potential mix-ups.



Genetic Fertilization ("PN") Check

Feature

Genetically confirms the visual inspection that the egg was correctly fertilized by the sperm.



Benefit to you

Depending on your clinic's protocols, this may offer you a chance of having additional transfers and possibly achieving pregnancy.⁵

Origin of Aneuploidy

Feature

Determines where the aneuploidy came from (sperm or egg).



Benefit to you

Might facilitate decision-making for you, and your care team regarding future IVF planning.



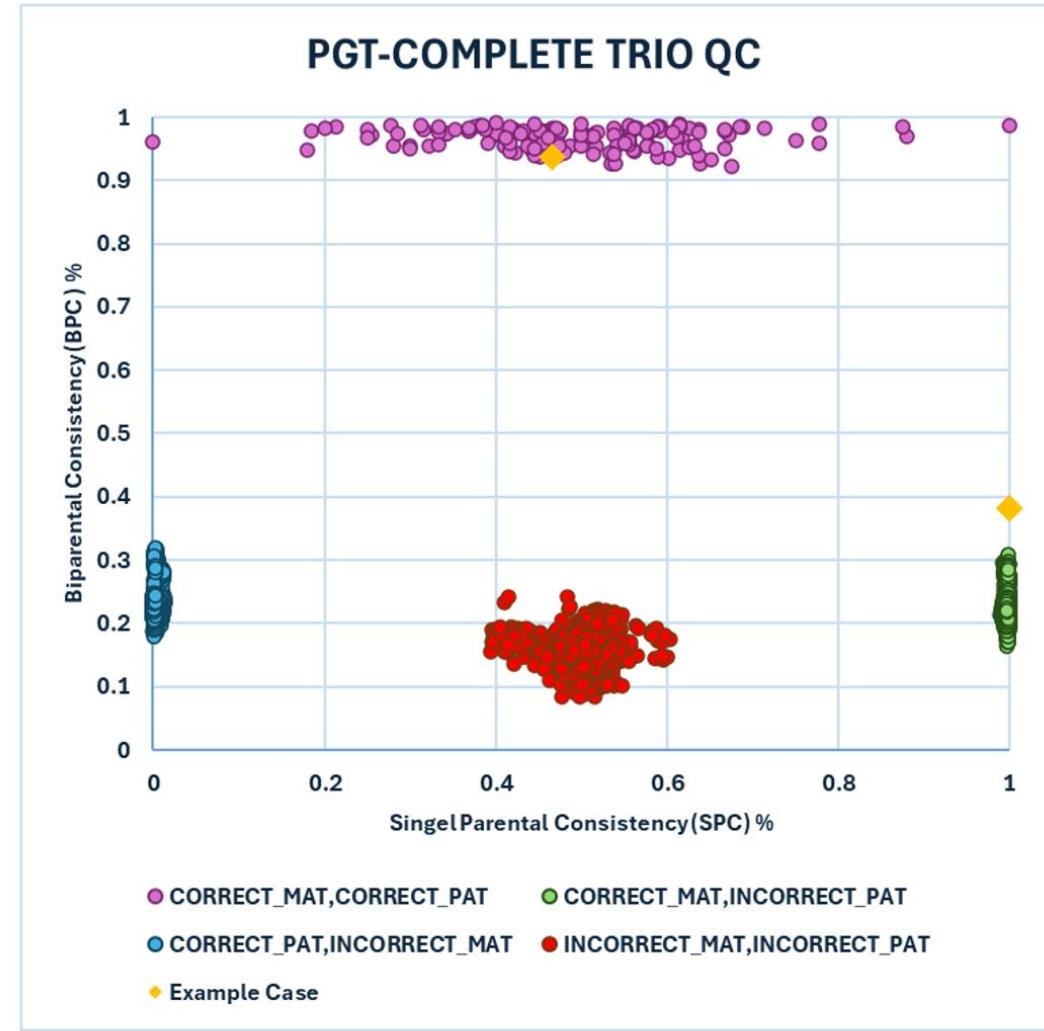
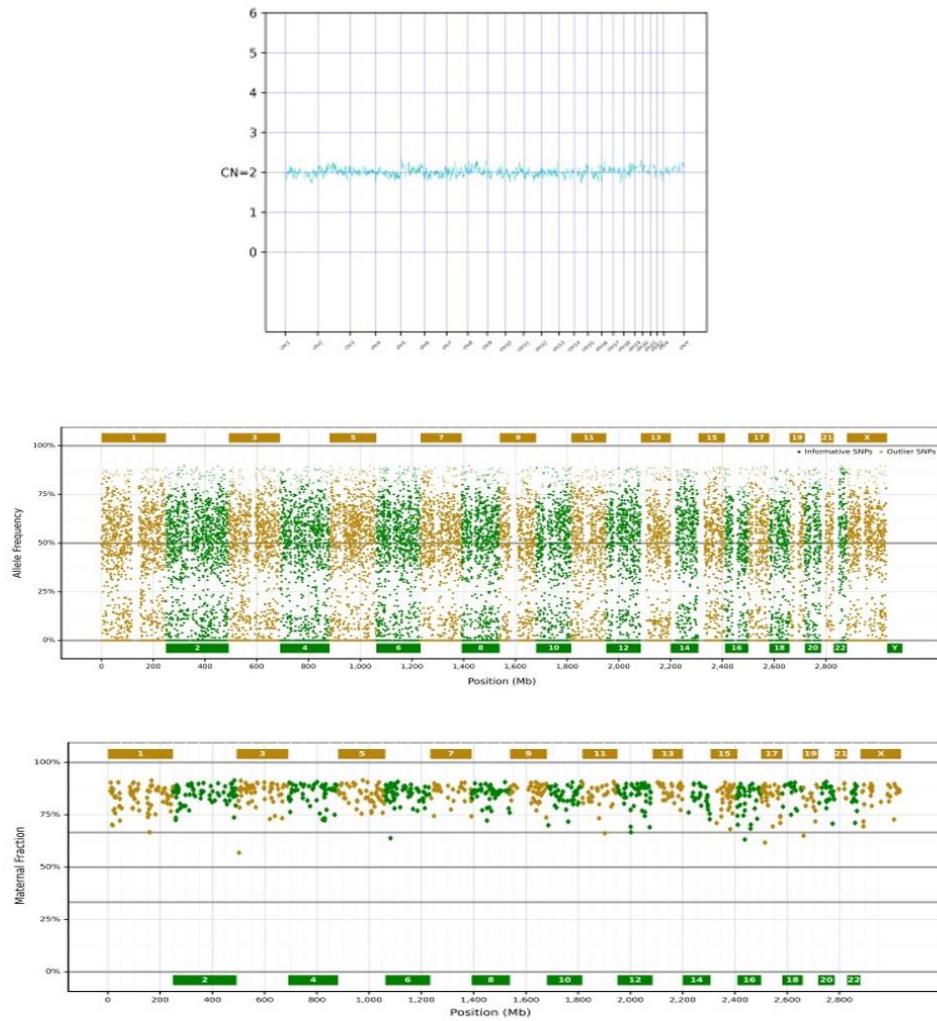
* Parental QC is not reported in countries (e.g. UK) where it is not permitted by regulatory bodies.

**A match is defined as a genotype that is consistent with a shared inheritance and familial relationship between the parental samples and the embryo biopsy sample.

2. Busto-Lliscardi J, Large, M.J., McCulloh, D.H., et al. Utilization of standardized preimplantation genetic testing for aneuploidy (PGT-A) via artificial intelligence (AI) technology is correlated with improved pregnancy outcomes in single thawed euploid embryo transfer (STEET) cycles. Journal of Assisted Reproduction and Genetics. 2023 Feb;40(2):289-99.

5. Paz MV, Chiera M, Hovanyecz P, Cicaré J, Perfumo P, Domenech L, Ventura V. Blasto cysts derived from OPN oocytes: Genetic and clinical results. JBRA Assisted Reproduction. 2020 Apr;24(2):143.

Maternal Cell Contamination





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Case 1

Sample ID	Sample Barcode	Parental QC	Result	Sex	Chromosomes Impacted	Interpretation
1		Match	EUPLOID	XY		NORMAL
2		Match	Aneuploid	XX	dup(1)(pter-p32.3)[pat] del(19)(pter-p13.2)	Abnormal
3		Match	Aneuploid	XY	dup(1)(pter-p32.3)[pat]-13 [mos], del(19)(pter-p13.12)[pat]	Complex Abnormal
4		Match	Aneuploid	XX	-3 [mos], +13[pat]	Abnormal
5		Match	Aneuploid	XX	dup(1)(pter-p32.3)[pat] del(19)(pter-p13.2)	Abnormal
6		Match	Aneuploid	XY	dup(1)(pter-p32.3)[pat] del(7)(q22.1-qter)[pat]-14 [pat] del(19)(pter-p13.2), -21 [mos]	Complex Abnormal
7		Match	Aneuploid	XX	dup(1)(pter-p32.3)[pat] del(19)(pter-p13.2)	Abnormal



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Clinical outcomes: PGTai 2.0

Single-center retrospective study observed improvements
in ongoing pregnancy and live-birth rates





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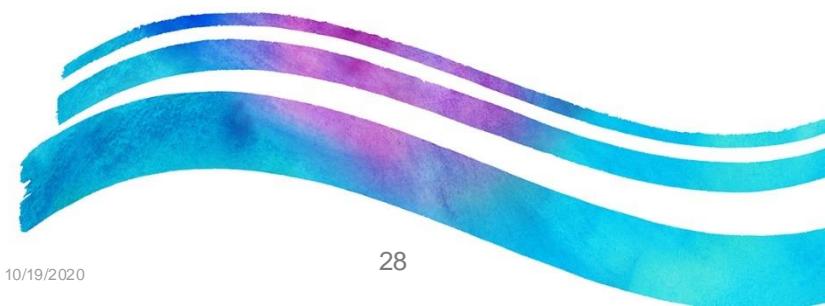
Improved IVF Clinical Outcomes

Positive obstetric outcomes observed in this study

- PGTai 2.0 clinical data demonstrates improvements in the key patient outcomes of ongoing pregnancy and live birth (OP/LBR)
- The retrospective study compares clinical outcomes achieved with the PGTai 2.0 platform to those observed with prior NGS platforms.

	NGS Subjective/Prior Methods	PGTai 2.0 Platform
Implantation Rate	80.70% (322/399)	82.96% (151/182)
Clinical Pregnancy Rate	71.17% (284/399)	79.12% (144/182)
OP/LBR*	61.65% (246/399)	70.32% (128/182)

* p < 0.05

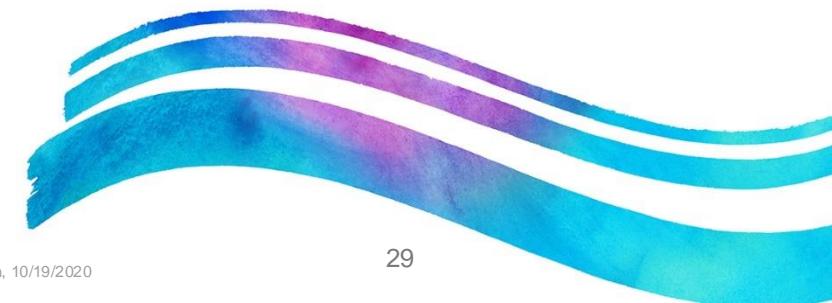
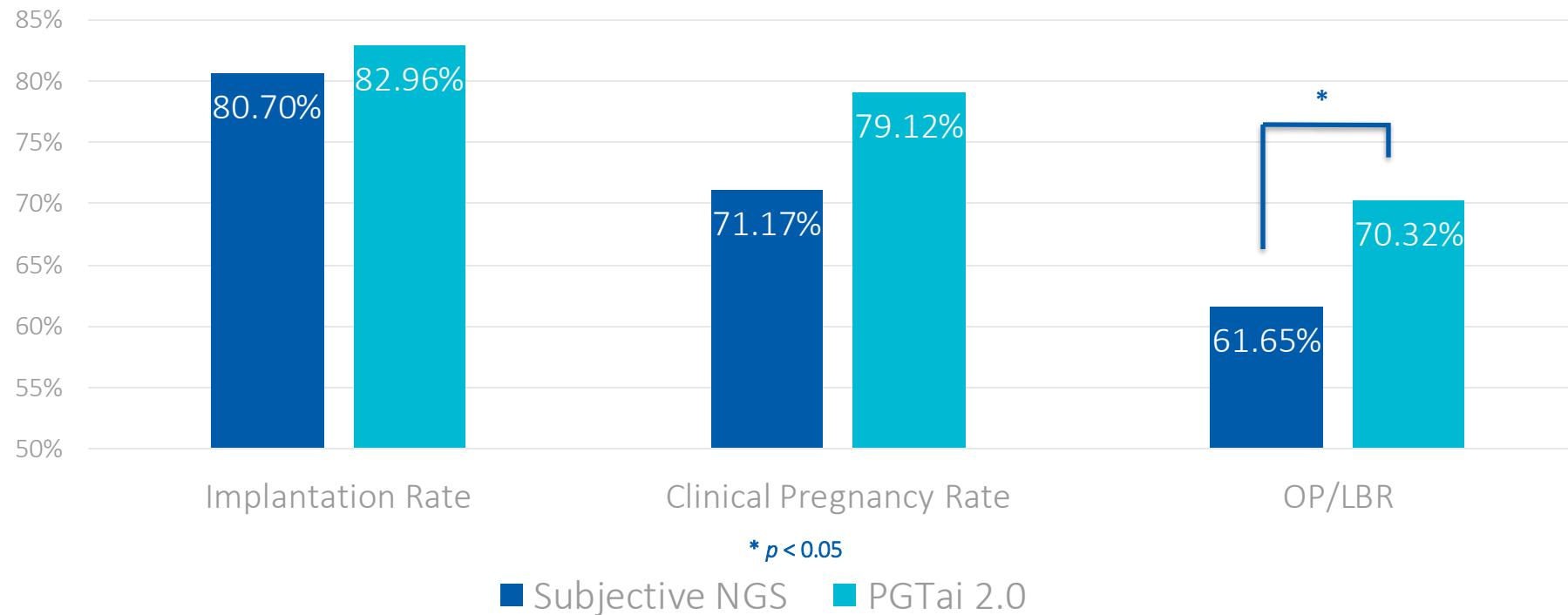




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Success rates per embryo transfer

Statistically significant increase in ongoing pregnancy and live birth rates

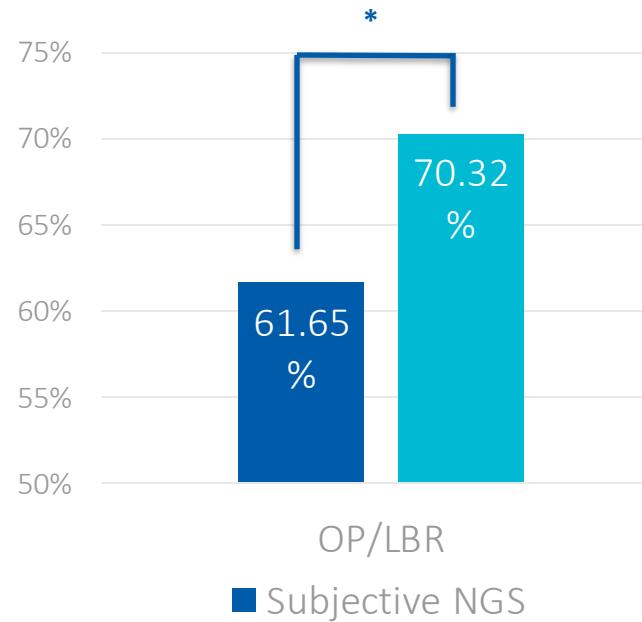


NYU Study: Patients' chances of having a baby improved with the PGTai 2.0 Platform!



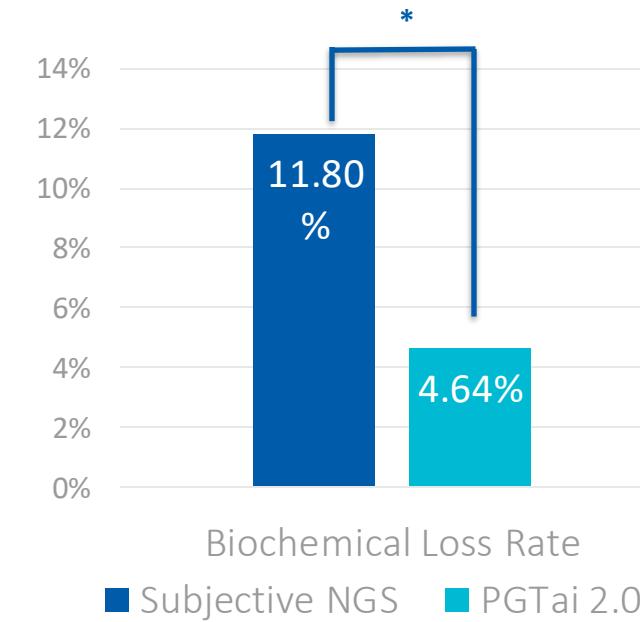
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Significant increase in ongoing pregnancy and livebirth rates



* $p < 0.05$

Early loss rates nearly halved, study shows

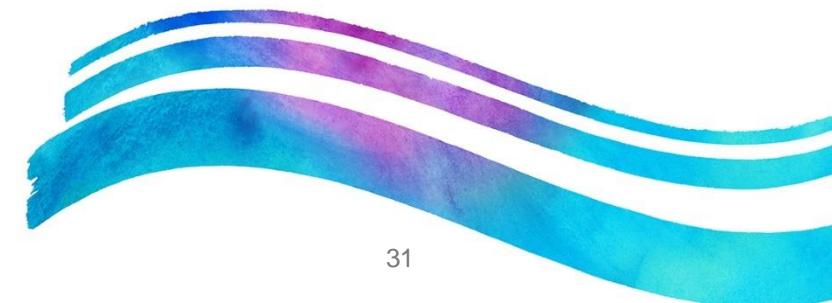


The future of AI in PGT



Increasingly we are sequencing embryos more deeply

- Research based whole genome / exome embryo sequencing^{1,2}
- Calling of smaller changes – microdeletion / microduplication
- AI for calling Variants of Unknown Significance (VUS)
- AI for interpretation of SNP / mutation calling phenotype - genotype



1. Murphy NM, Samarasekera TS, Macaskill L, Mullen J, Rombauts LJF. Genome sequencing of human in vitro fertilisation embryos for pathogenic variation screening. *Sci Rep.* 2020 Mar 2;10(1):3795. 2. Kumar A, Im K, Banjevic M, Ng PC, Tunstall T, Garcia G, Galhardo L, Sun J, Schaedel ON, Levy B, Hongo D, Kijacic D, Kiehl M, Tran ND, Klatsky PC, Rabinowitz M. Whole-genome risk prediction of common diseases in human preimplantation embryos. *Nat Med.* 2022 Mar;28(3):513-516



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