PGTai℠

The most sophisticated PGT-A analysis algorithm

Highlights

First PGT-A analysis software to deliver true statistical analysis of data

- 1,000 pregnancy outcomes used to generate baseline
- Over 10,000 samples run to generate robust statistical analysis

User-Independent answers

- Optimized and validated algorithms and automated analysis provide user-independent results
- Automated analysis and interpretation

Analysis pipeline feeds directly into CooperGenomics automated reporting software ensuring seamless reporting

Introduction

Preimplantation Genetic Testing for Aneuploidy (PGT-A) of embryos has been taking place for more than 20 years, and the evolution of the technology used for PGT-A testing coupled with the significant improvements in embryo culturing, biopsy and vitrification has led to a rapid expansion in our knowledge of the genetics of embryos, consequently leading to changes in embryo and patient management.

In 2008, 24-chromosome PGT-A testing was first performed through the analysis of single cells (PB and blastocyst) using aCGH (arrayCGH) followed by a D5/6 fresh transfer of euploid embryos. In this scenario, the analysis is binary with an outcome of euploid or aneuploid (Figure 1).

With today's improvements in embryo culture and vitrification, most embryo biopsies are multicell (5-10 cells), taken from the trophectoderm. With multiple cell analysis, it became apparent that a significant number of blastocyst embryos are mosaic, ie., carrying 2 or more cell lines and the analysis solutions put in place were unable to robustly and repeatedly call such changes.

With increasing evidence of the significance of mosaicism on embryo transfer outcome[3,4,5], it is very important that measurement and reporting of embryo status is accurate and robust. Furthermore, that the analysis tools used are capable of such calls.

PGT-A and embryo testing is not always about entire chromosomes. It is important that segmental changes (partial chromosome gains and losses) are accurately and robustly called. To date, these have often been deliberately not called by the software due to the naturally conservative nature of the technology suppliers. These segmental changes are known to result in either a failure to implant or in live births where the child can have severe developmental delays[1,2].

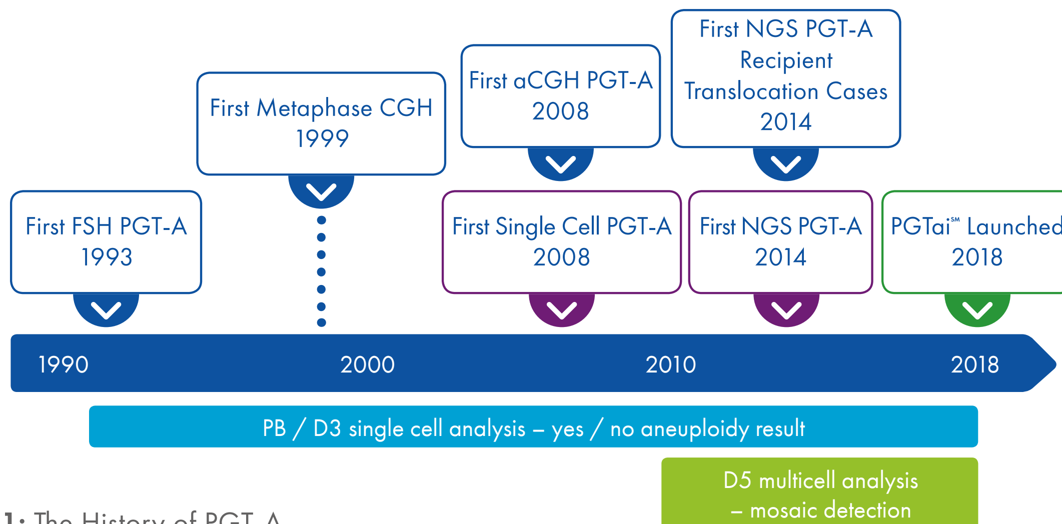


Figure 1: The History of PGT-A

Today, all the commercial "off the shelf" solutions for aneuploidy detection and reporting is to have sequencing output data turned into a highly smoothed graphical representation. These graphs are then analyzed and manually transcribed by two or more highly skilled data interpreters. However, such a process is open to subjectivity in calling and user-to-user bias in reporting which needs to be managed through careful and ongoing user competency training (Figure 2).

At CooperGenomics℠, it was understood that to have the best possible service these calls need to be automated and recorded without doubt. To this end, CooperGenomics has developed a completely new PGT-A data analysis platform - PGTai℠ - which utilizes our vast knowledge and the large amount of internal data exclusively available to us, through our many years of performing PGT.

PGTai℠

The PGTai℠ analysis platform has been developed using big data (more than 5 billion data points) and machine learning to deliver the best-in-class analysis and result for PGT-A cases. Unlike every algorithm before, which generally have used a small number of euploid samples or small number of normal cell line samples for their baseline, CooperGenomics has created an analysis based on the outcome data from 1,000 embryo transfers which had been reported as euploid and resulted in a phenotypically healthy live birth. This is a vastly larger dataset for baseline than other available PGT-A software in use today.

We now have internally run over 10,000 biopsy samples which has allowed us to build true statistical significance into the PGTai℠ calling algorithms, ensuring we provide data that is 100% repeatable, robust, and user independent, with no analyst subjectivity.

It is very important to understand that the data used to generate PGTai℠ analysis platform came from multiple centers, and multiple CooperGenomics laboratories. This allowed us to capture and model all of the aspects of the noise that can affect data outcomes including biopsy differences, embryo quality and run-to-run variables. Other analysis software packages often use single laboratory data and controls therefore they do not account for the variabilities that can affect calling.

The PGTai℠ analysis platform has been developed to accurately call mosaic chromosomes, full segmental and mosaic segmental changes, as well as full chromosome euploidy and aneuploidy, using a combination of phenotypically healthy live birth outcomes from PGT-SR cases, previous data and dilution series experiments.

The PGTai℠ analysis also produces fully automated karyotypes, meaning less chances of transcription errors (Figure 3).

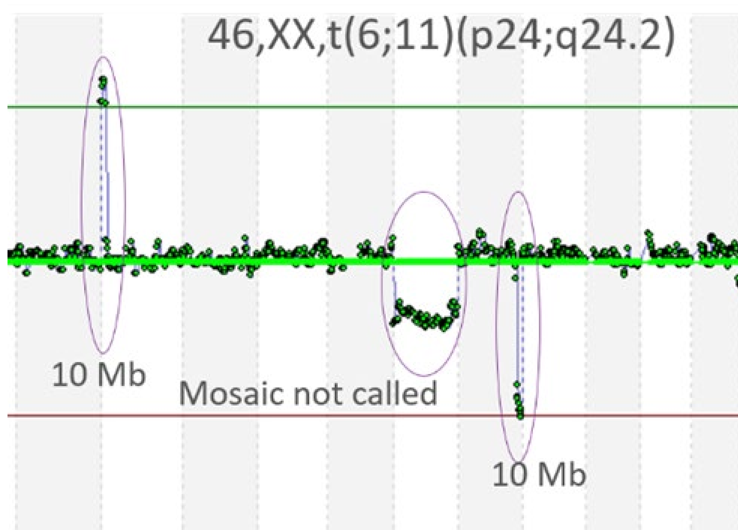
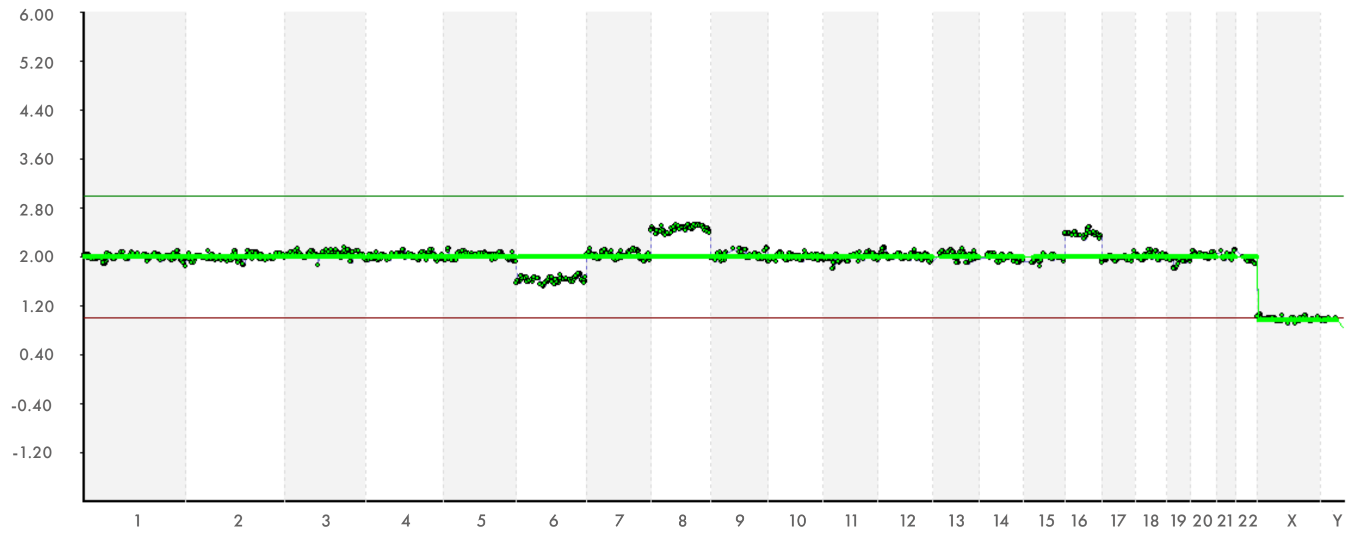
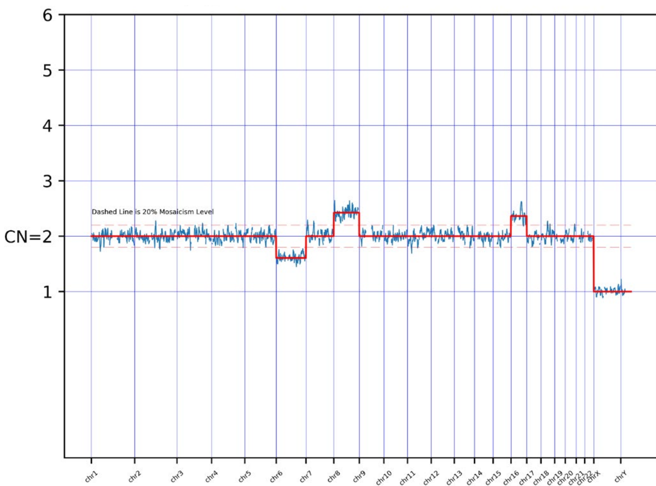
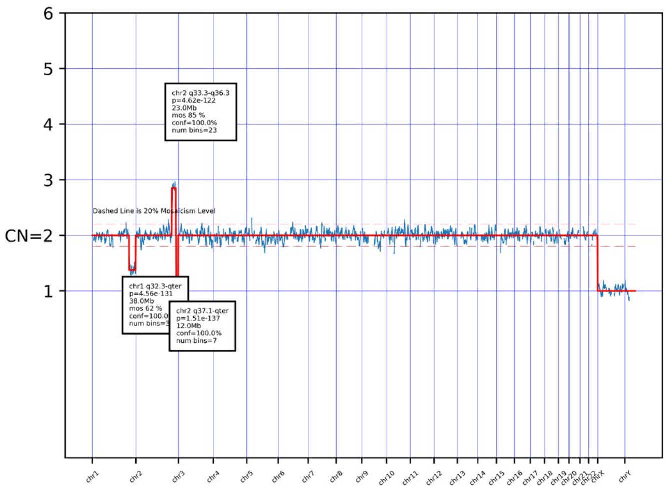


Figure 2: Chromosomal changes clearly visible but not called using BlueFuse Multi v4.4 (Illumina) due to the segmental change either being too small in size (less than 50% of a chromosome, or below 50% abnormal value threshold for aneuploidy calling. These are automatically called using the PGTai℠ analysis platform.







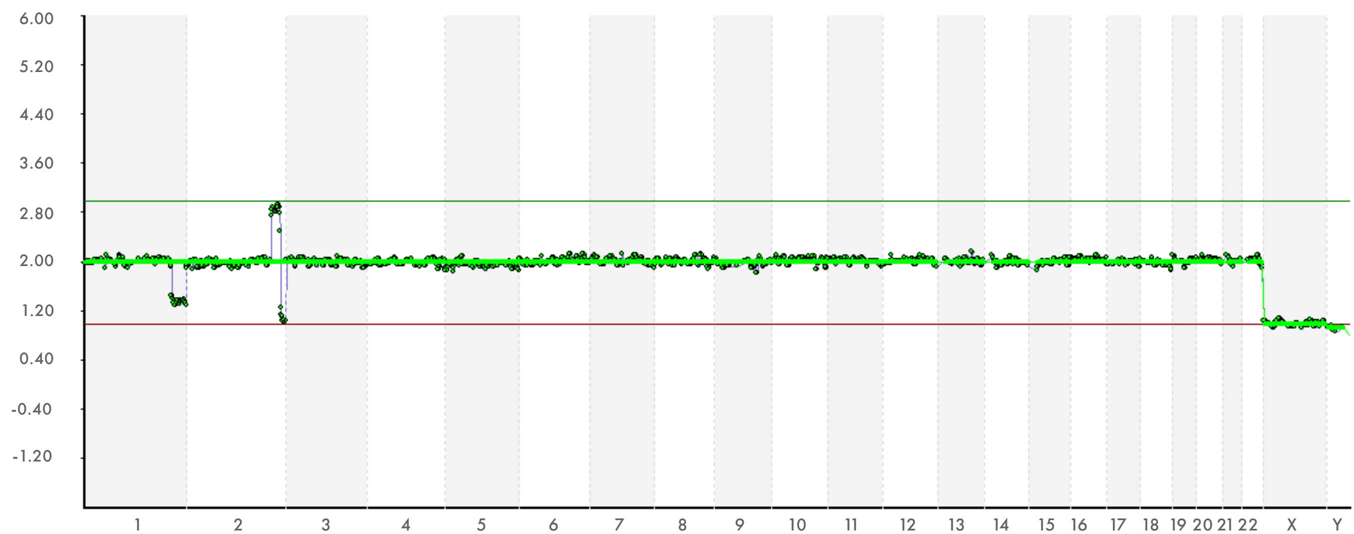
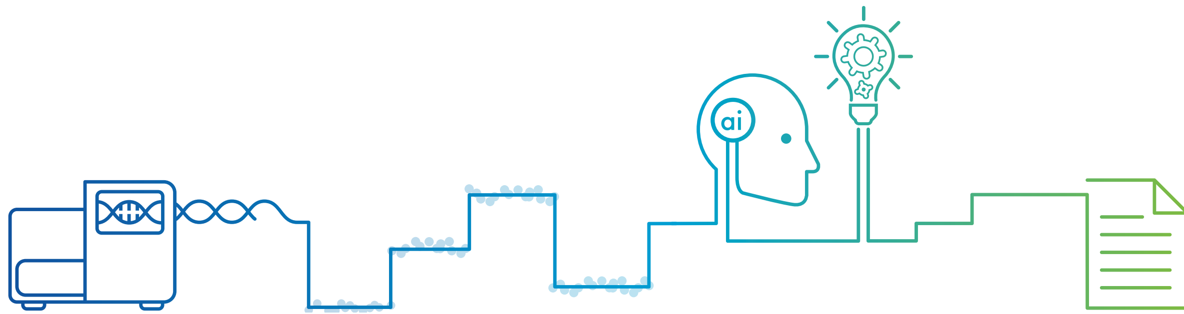


Figure 3: BlueFuse Multi v4.4 vrs PGTai^{SM} calling for low level mosaic changes and small segmental changes. BlueFuse Multi is top line, PGTai^{SM} (top and bottom images). PGTai^{SM} graphics in the center.

CooperGenomics Technology



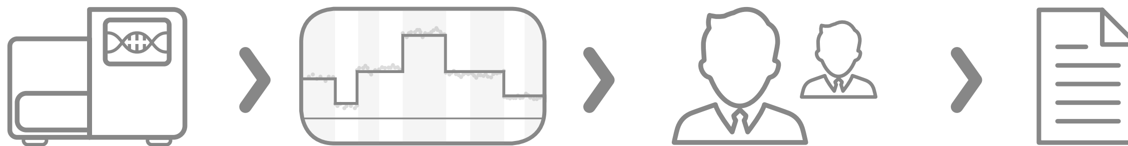
Data is generated via NGS

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

Existing Technology



Data is generated via NGS

Data is converted into an image

- Current algorithms use a small subset of data (~100 samples)

The image is analyzed by a human, making inferences based on this image

- Subjective
- Allows for human error (transcription & interpretation)

Clinicians make transfer decisions utilizing human driven data set

The CooperGenomics PGT-A Solution

The PGTai℠ analysis platform is a leap forward in the accuracy of PGT-A analysis, thus providing IVF centers with confidence in the decisions of embryo transfer.

At CooperGenomics, we are very proactive in ensuring the best overall service to our clients.

We have developed an entire sample pathway from sample receipt through report delivery, minimizing human interaction throughout the process and optimizing the fidelity of PGT-A results.

References

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