Transformational technologies drive the next generation of PGT-A

Christopher Weier, PhD

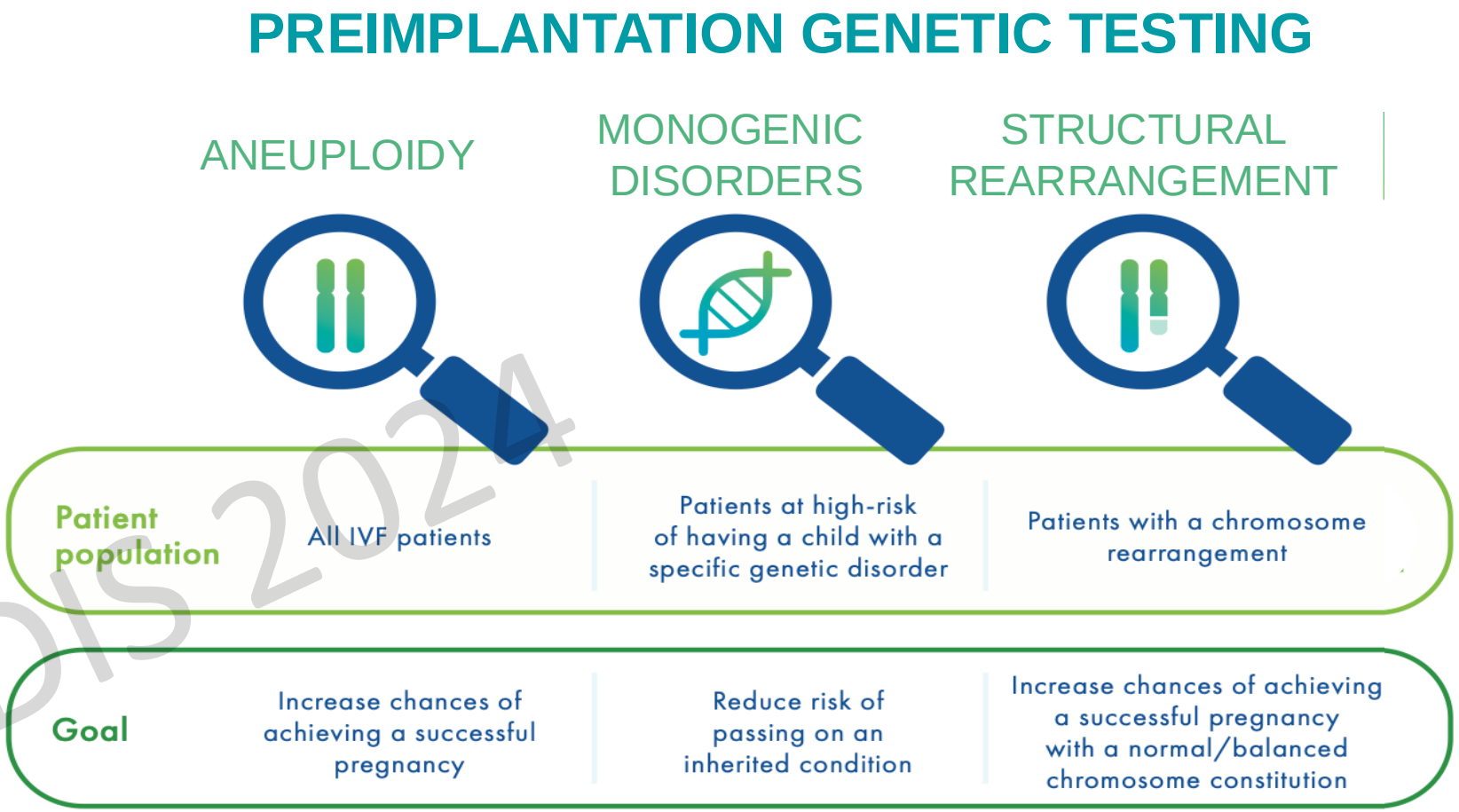
CooperSurgical Research and Development
Senior Scientist

GENOMICS

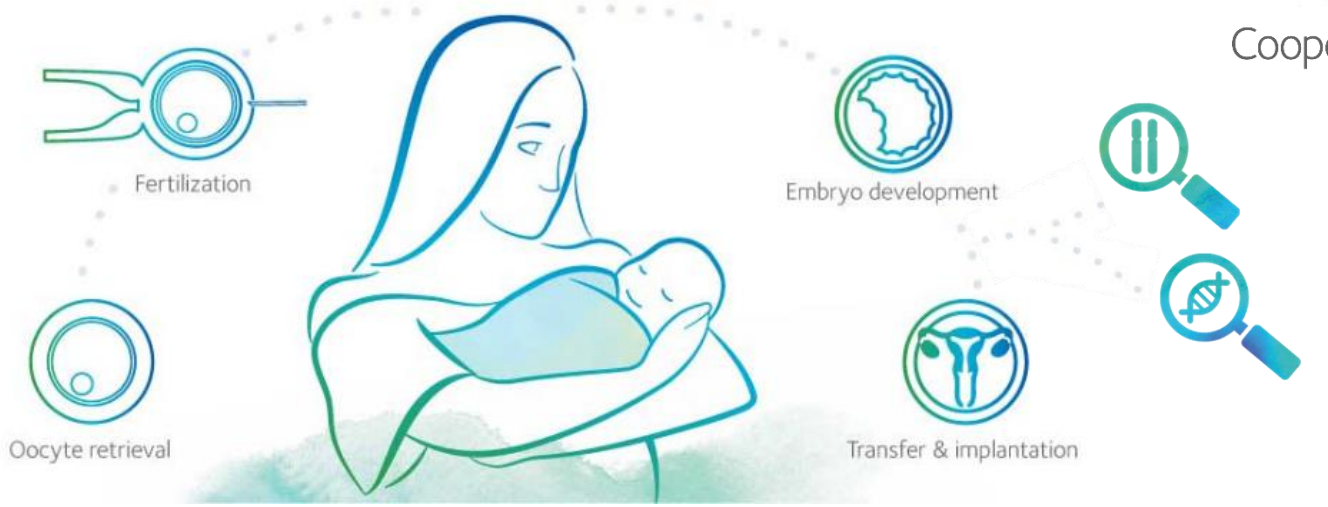
Preimplantation Genetic Testing – PGT

Laboratory tests to look at the health of the developing embryo

CooperSurgical®



PGT during IVF



Biopsy

Genomic Amplification

Library Prep.

Sequencing

Data Analysis

Report

Amplification is the first (*and most important*) step

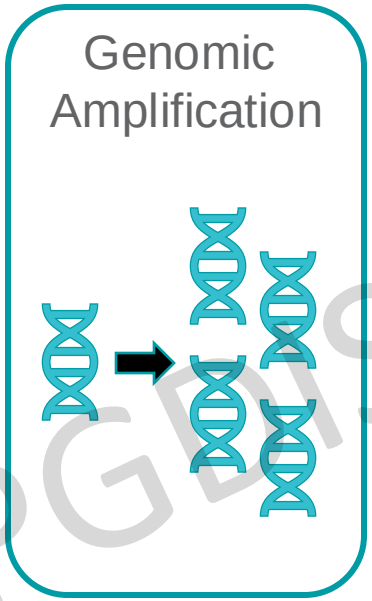
CooperSurgical®

20,000 X

5-6 Trophectoderm Cells
~50 picograms genomic DNA

~1000 ng Amplified Product

PGT-A
PGT-M
STR
Sanger
Other
Assays



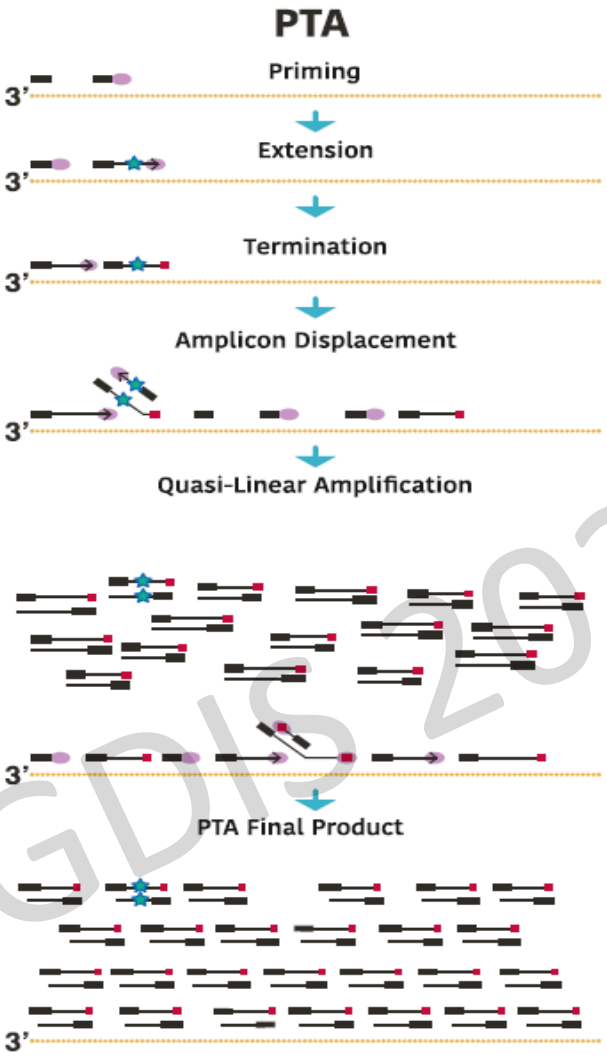
- ✓ Robust
  high consistency of producing results
- ✓ Accurate
  high fidelity = very few errors
- ✓ Complete
  low bias = nearly whole genome & both alleles

CooperSurgical internal data

True whole genome amplification

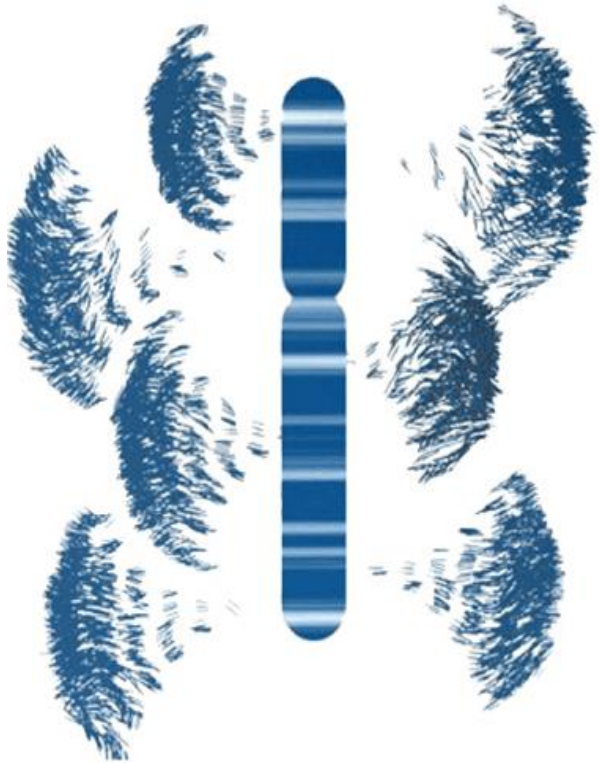
Accurate, unbiased distribution of data across the entire genome

CooperSurgical®



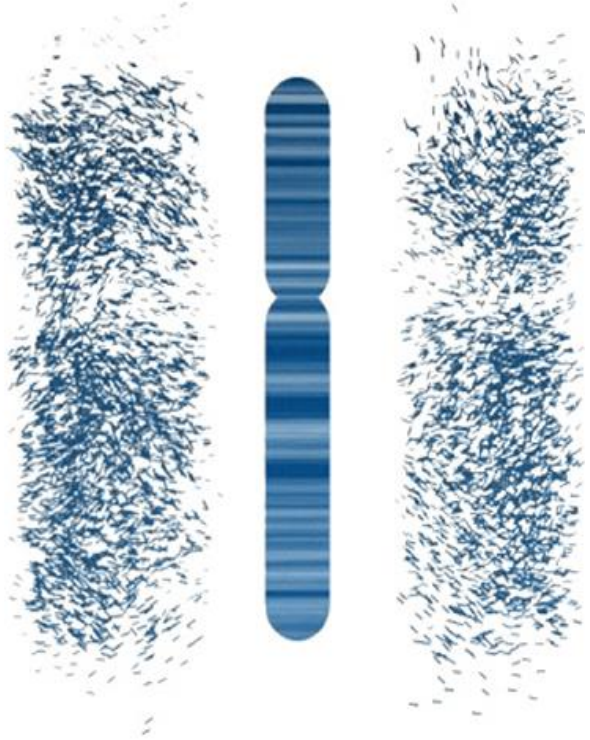
Non-PTA

Random Priming Amplification Methods



PTA

Primary Template Directed Amplification

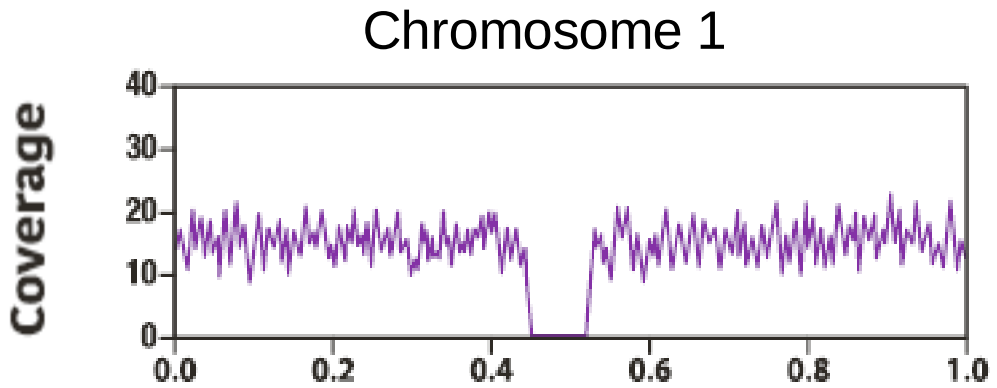


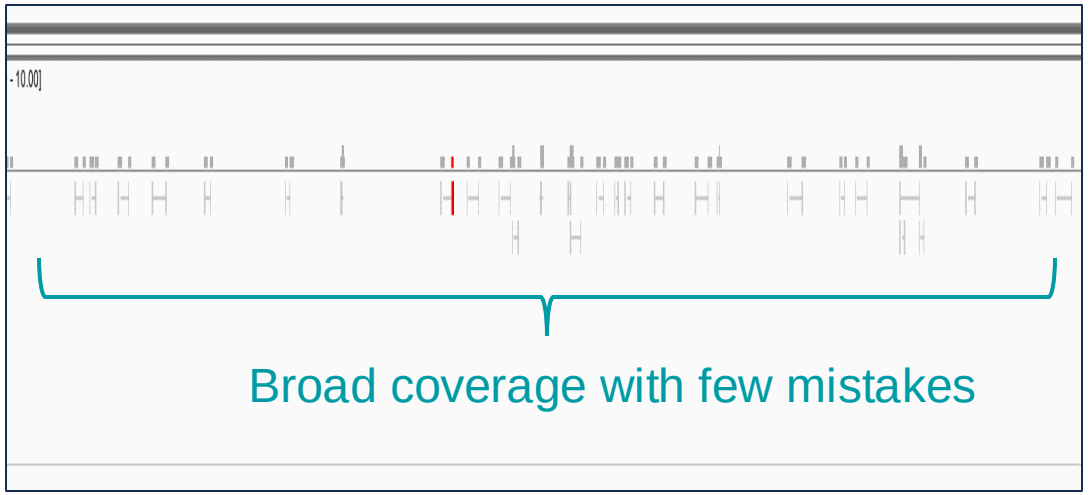
True whole genome amplification

Accurate, unbiased distribution of data across the entire genome

CooperSurgical®

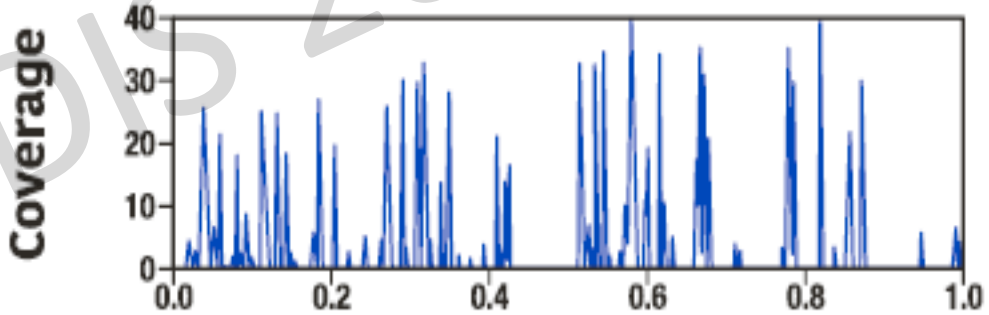
PTA





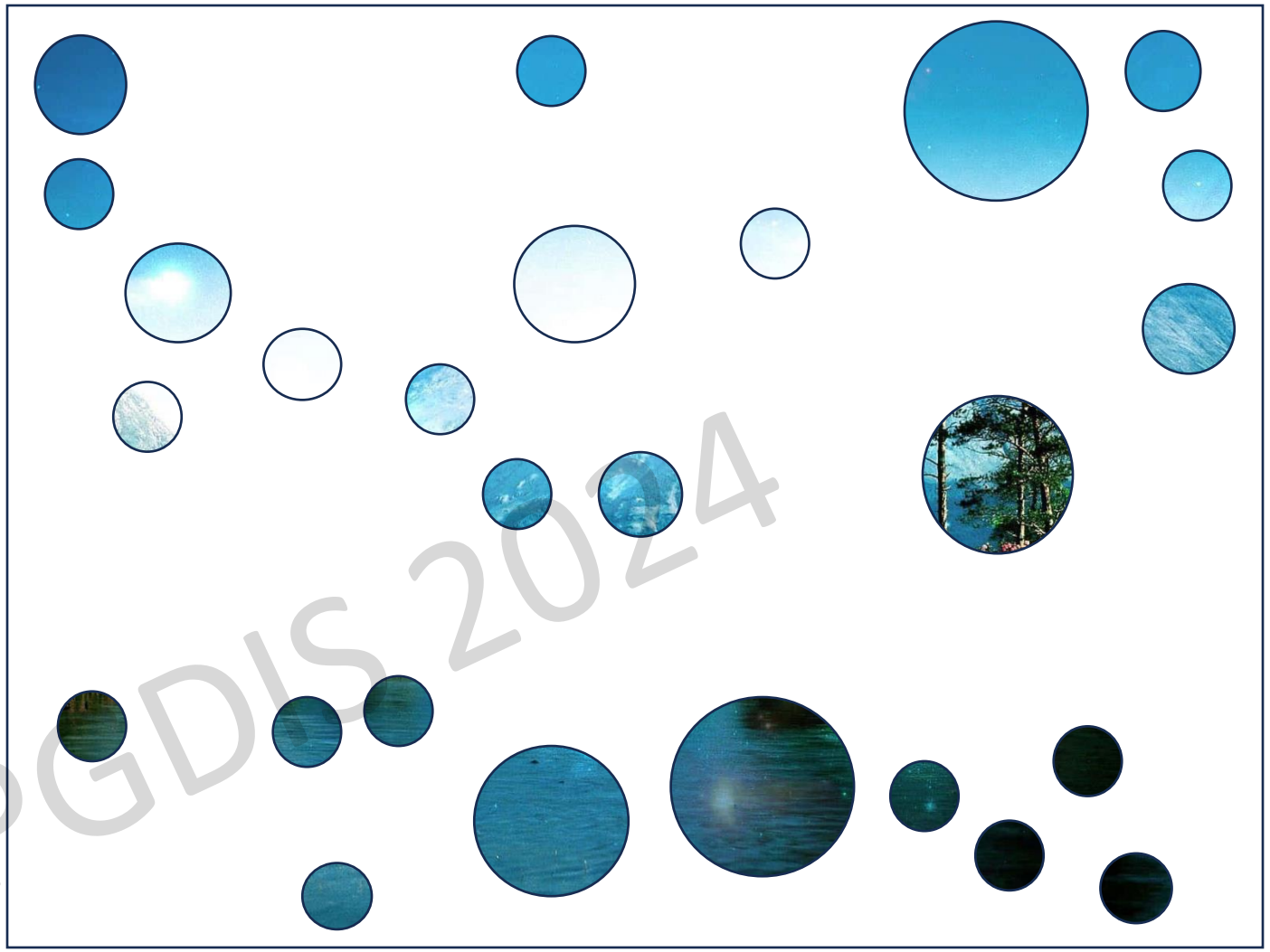
- ✓ 97% of the genome
- ✓ ADO < 1 %
- ✓ Error Rates < 0.1%

Non-PTA



Filling in the gaps with PTA

Our most complete and accurate basis for PGT



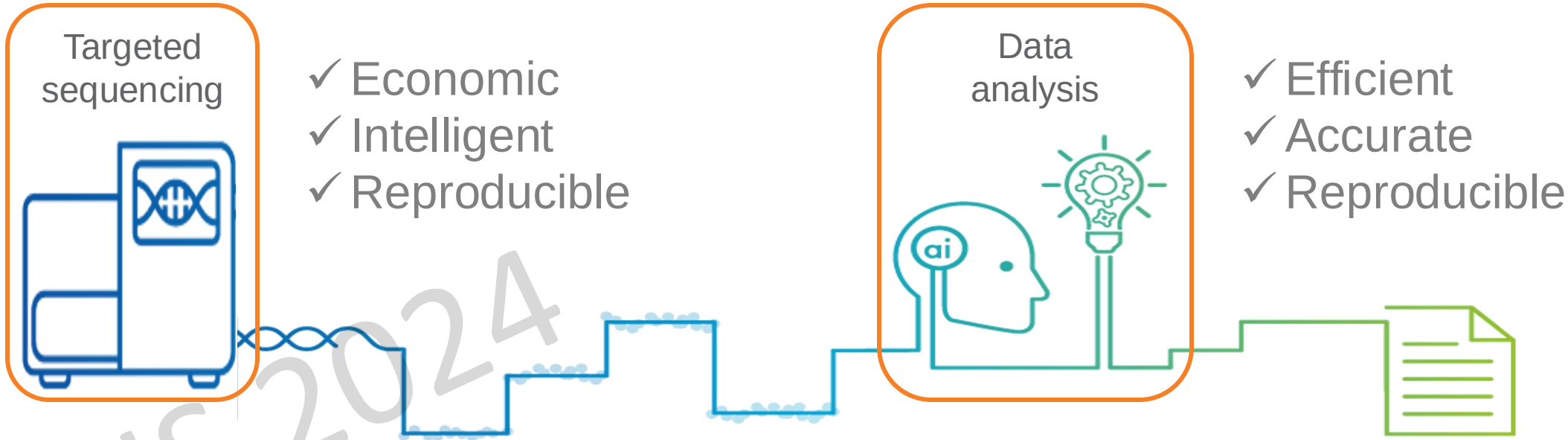
How do we *most responsibly* use this technology to the benefit of patients?

GENOMICS

CooperSurgical®

Accurate and actionable testing

Precision-based approaches deliver utility and confidence



Remove error,
Reduce noise and
Eliminate subjectivity

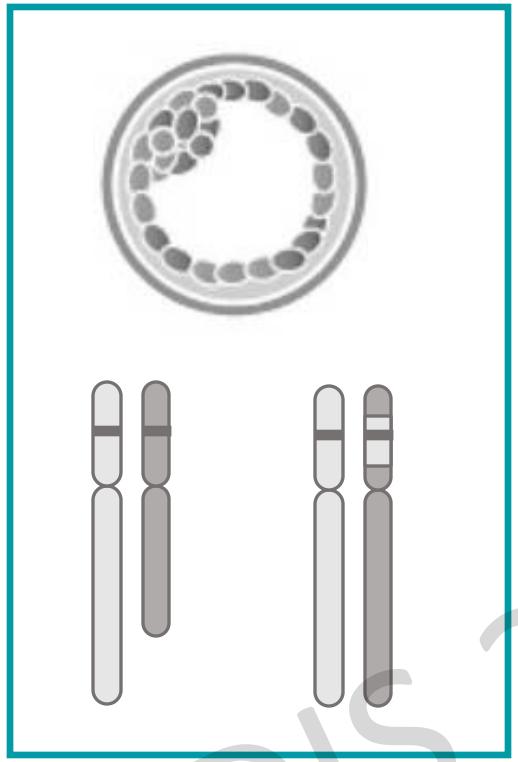
Integrate, Analyze and
Interpret complexity

GENOMICS

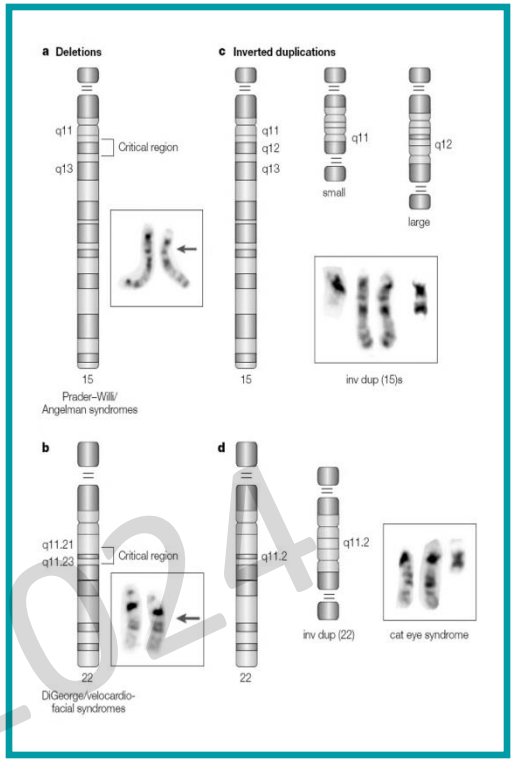
Accurate and actionable testing

Precision-based approaches deliver utility and confidence

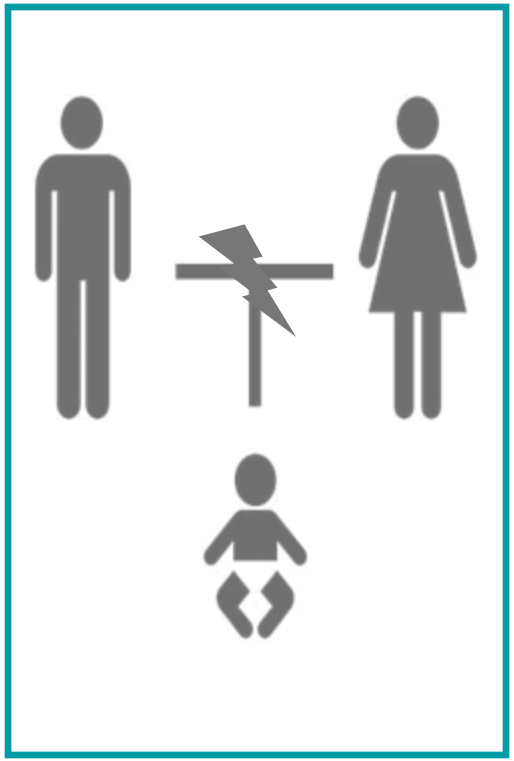
CooperSurgical®



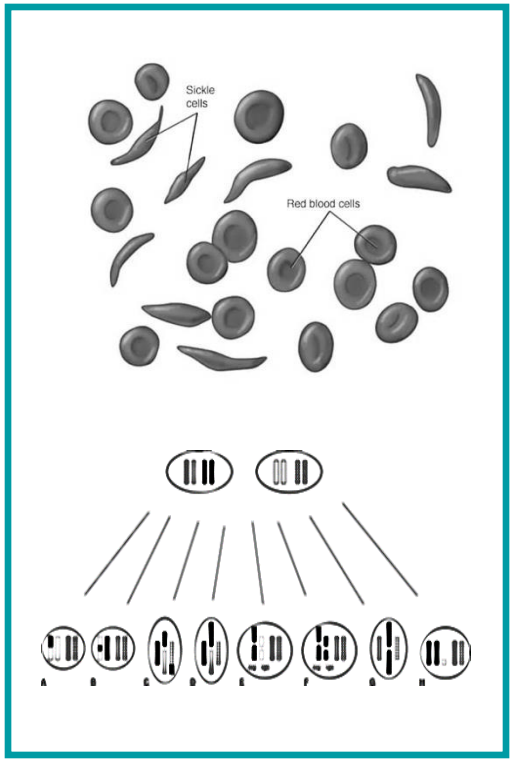
Segmental resolution, Mosaicism, and Loss of Heterozygosity (LoH)



Deletion and Duplication Syndromes



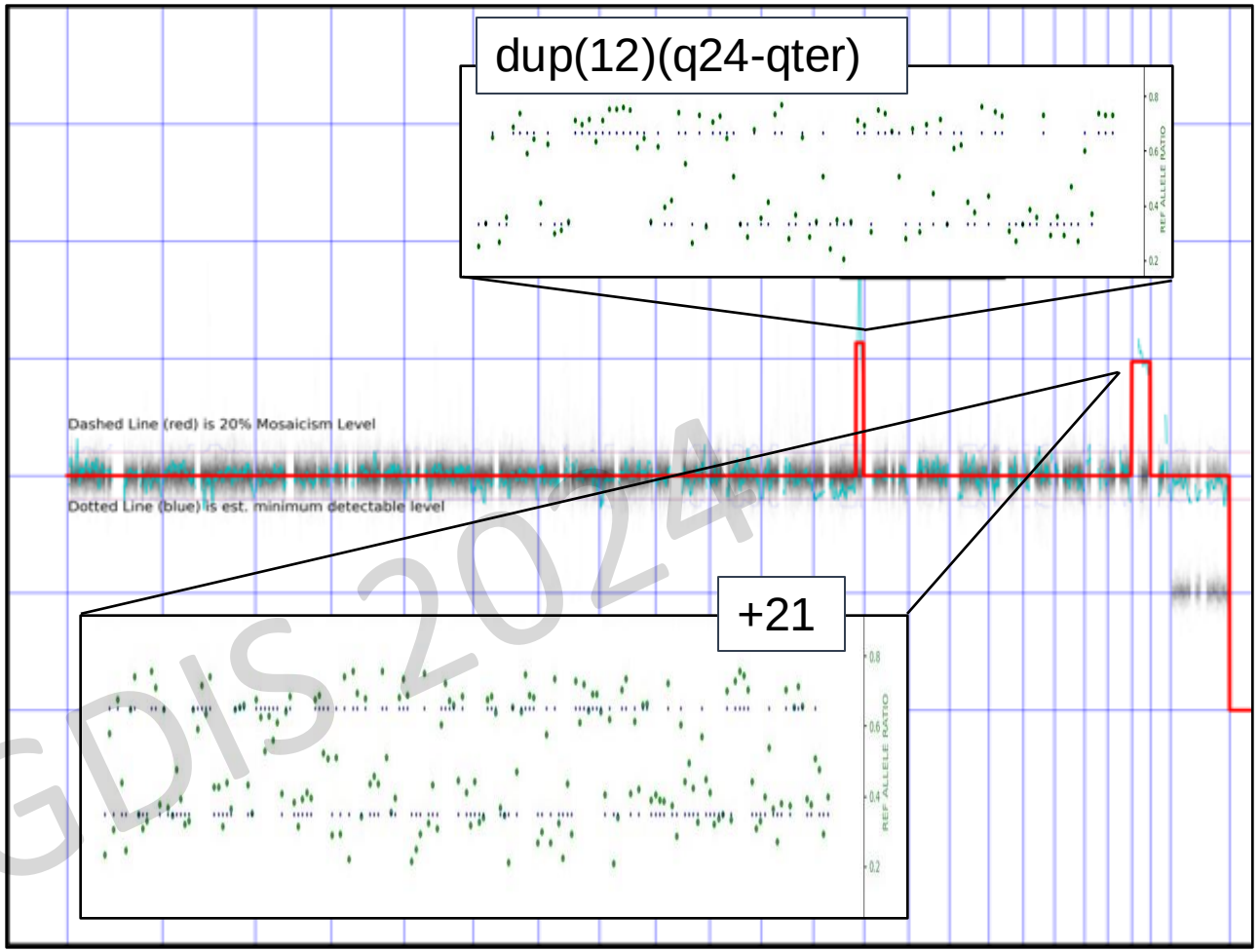
Screening for *de novo* mutations and predisposition genes



Precision testing for common disorders and rare conditions

Whole chromosome and segmental CNV

High resolution copy number variation + allele analysis



TWO-FACTOR "AUTHENTICATION"

Tiered copy number and SNPs –
High confidence reporting through new levels of data analysis

- Locus specific,
  high depth sequencing
- 10x reduction in noise
- Up to 150,000 SNPs

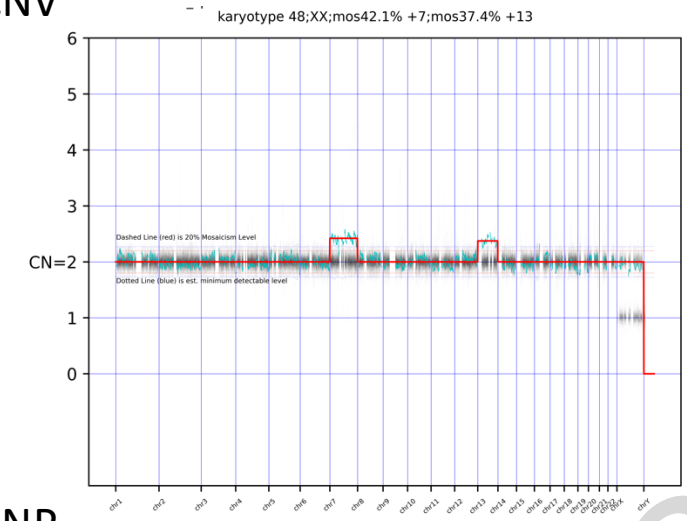
Clarifying mosaic embryos

CNV + SNP + Analysis

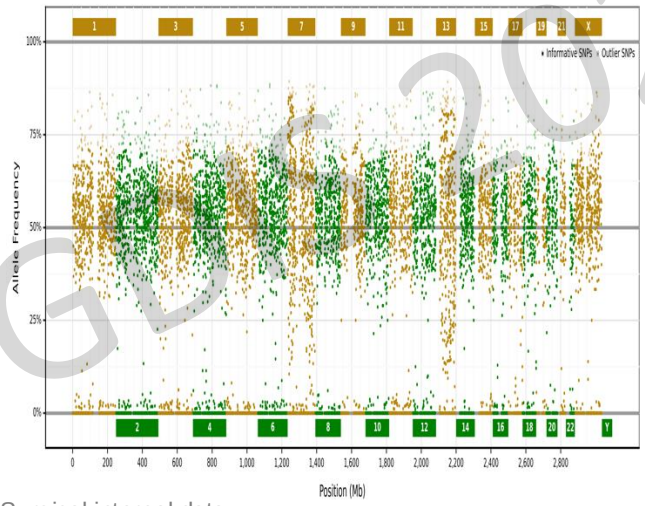
CooperSurgical®

GENOMICS

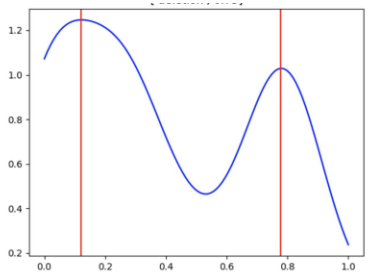
CNV



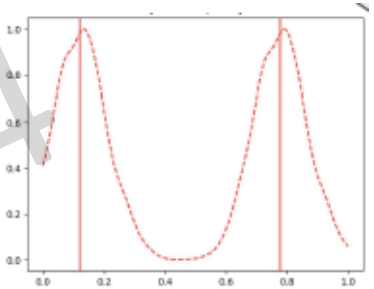
SNP

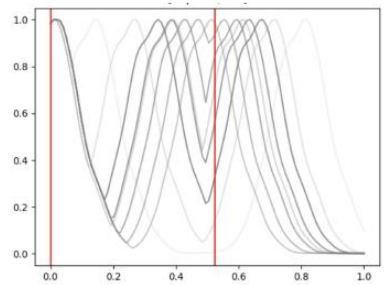


Mosaic Resolution by Decomposition

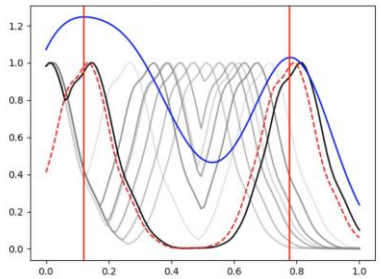


Allele Clusters estimated from SNP density

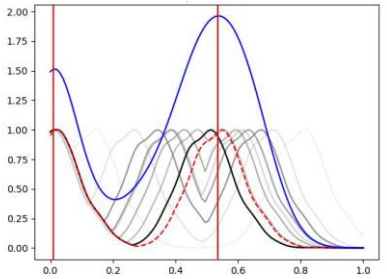




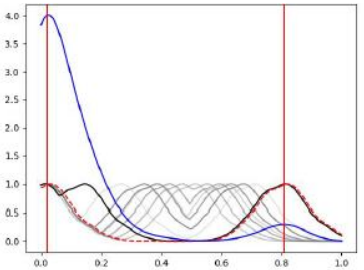
Clinical and Theoretical Decomposition to estimate mosaicism



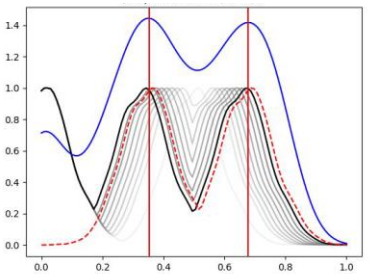
Diploid



Haploid

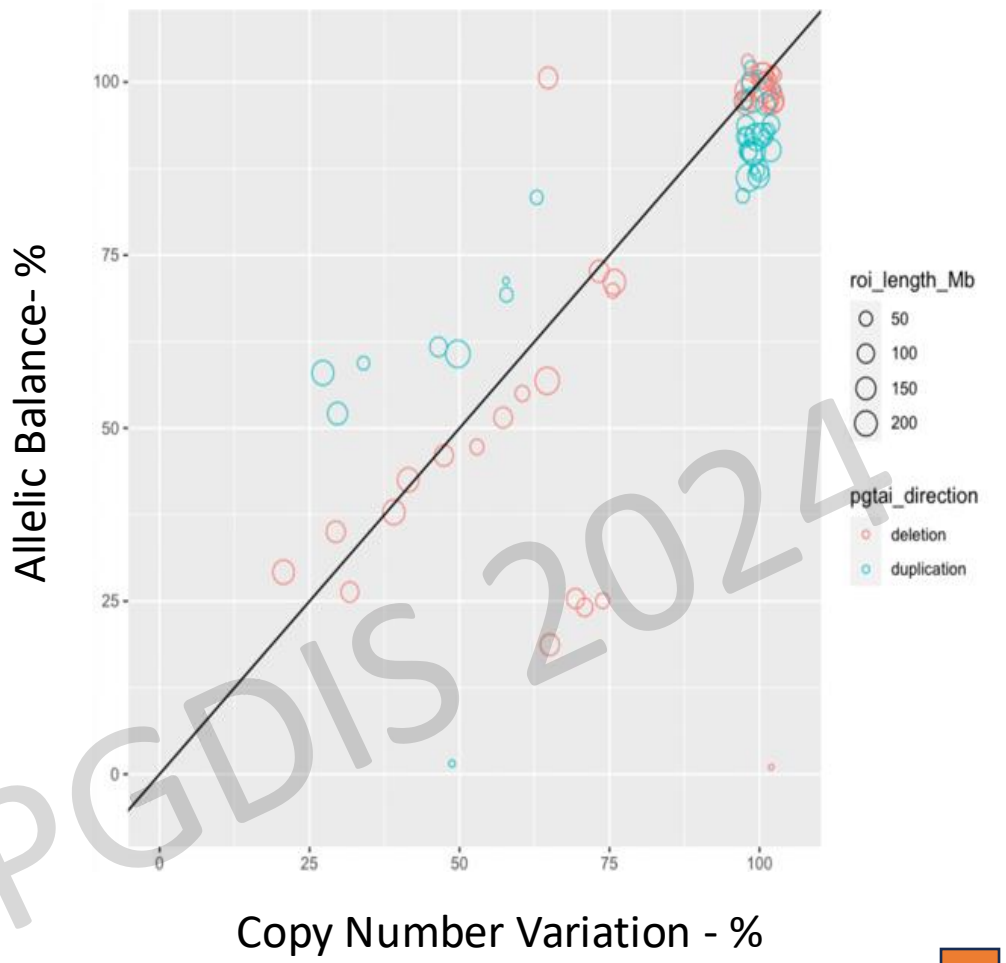


Triploid



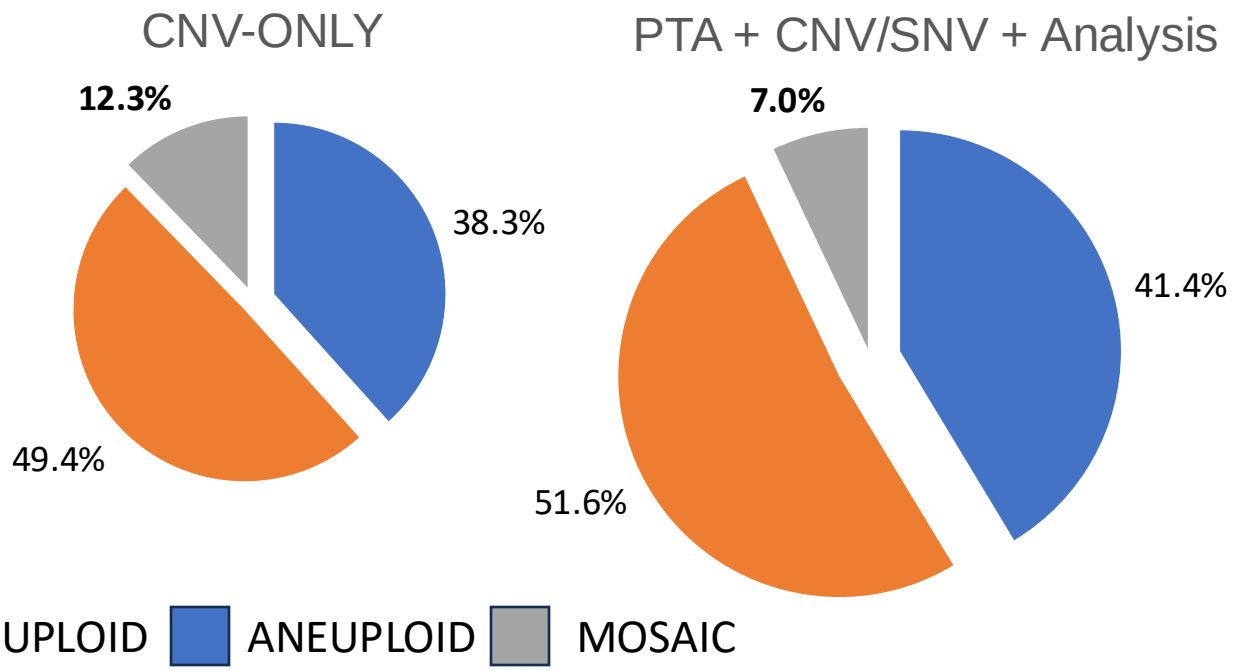
Clarifying mosaic embryos

CNV + SNP + Analysis



Integrated CNV/SNV analysis of 327 mosaics:

- ✓ 67.6% mosaics are confirmed
- ✓ 19% of low-level mosaics revert to euploid
- ✓ 13% of high-level mosaics are aneuploid

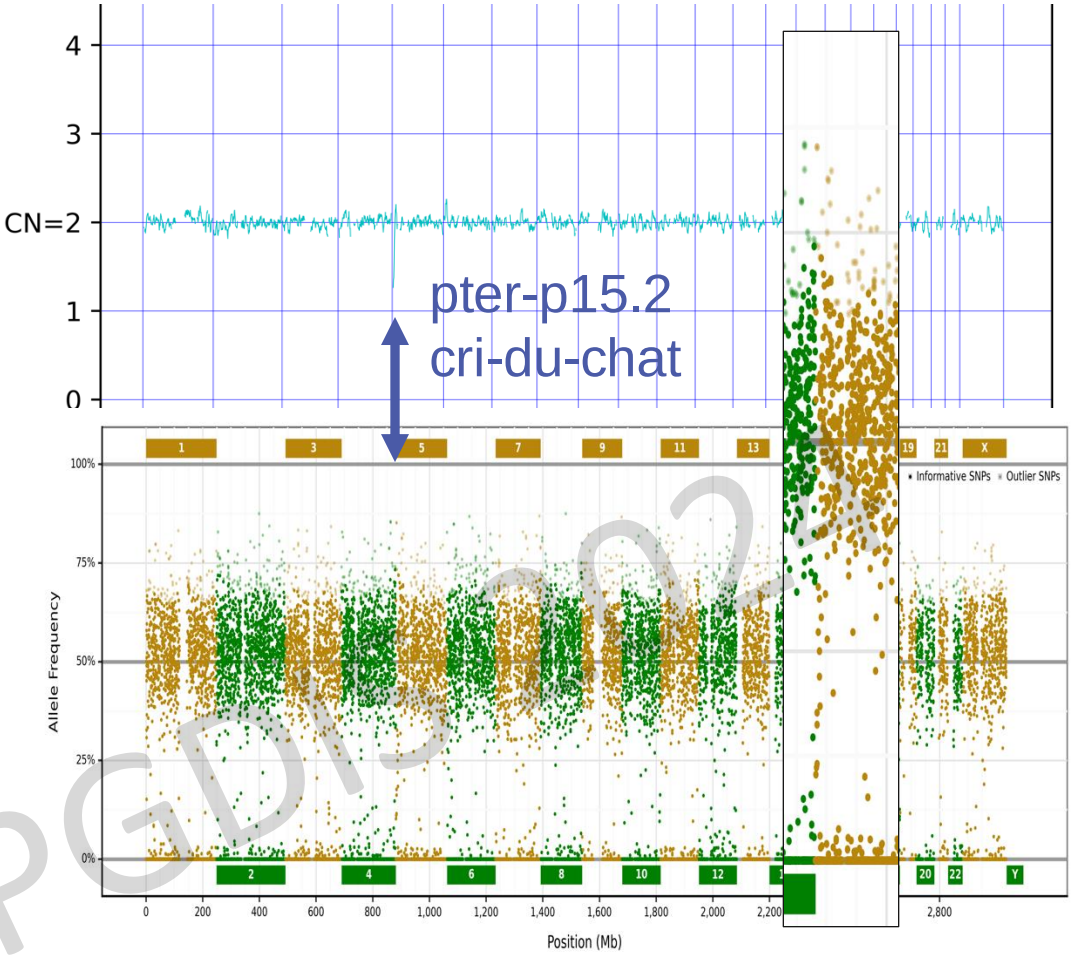


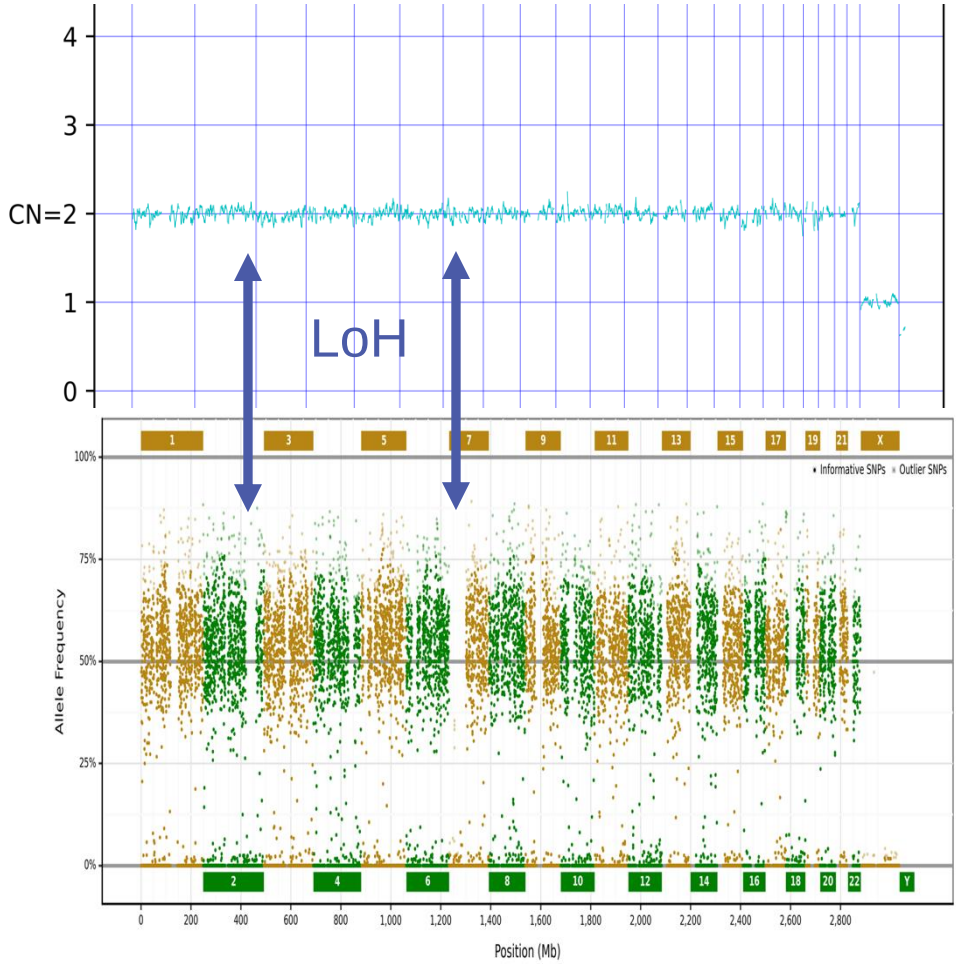
GENOMICS

Minor variation with major clinical impact

Deletions/Duplication syndromes and Loss of Heterozygosity

CooperSurgical®





GENOMICS

Direct mutation analysis

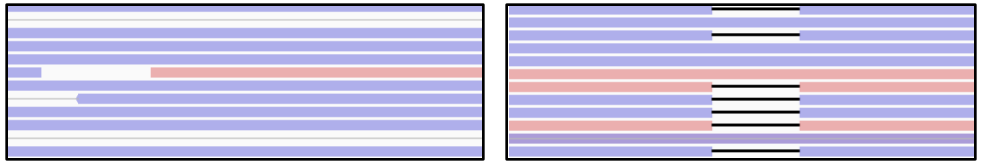
Screening embryos for *de novo* and inherited mutations

CooperSurgical®

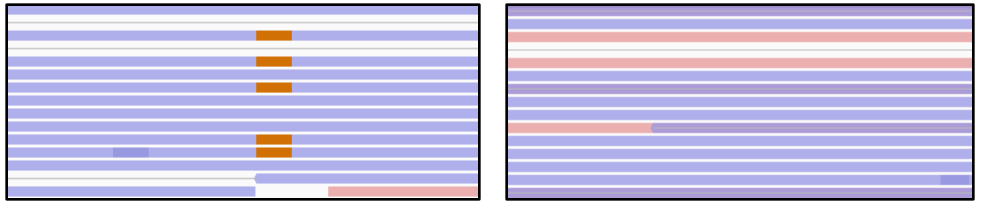
Gene	Condition	Concordant / Embryos Tested
BRCA 1/2	Hereditary Breast and Ovarian Cancer	44 / 44
CFTR	Cystic Fibrosis	21 / 21
GJB2	Non-Syndromic Hearing Loss	21 / 21
HBB	Sickle Cell Anemia	16 / 16
SDHB	Her. Paraganglioma-Pheochromocytoma	12 / 12
APC	Familial Adenomatous Polyposis	9 / 9
TP53	Li-Fraumeni syndrome	6 / 6
PMM2	Congenital Disorder of Glycosylation, T1a	6 / 6
MEFV	Familial Mediterranean Fever	6 / 6
GALC	Krabbe Disease	6 / 6
ATM	ATM-Associated Cancer Susceptibility	6 / 6
GAA	Glycogen Storage Disease, Type 2	5 / 5
HBA1/HBA2	Alpha-Thalassemia	5 / 5

Total Concordant 200 / 200

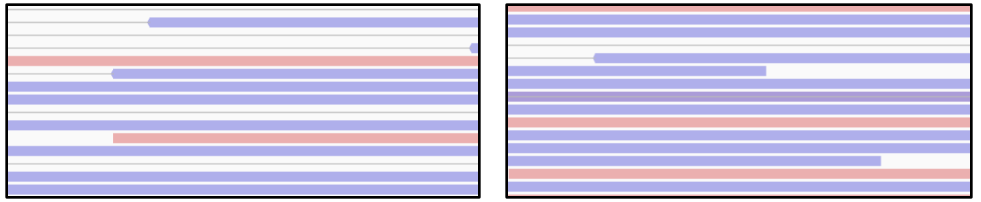
Embryo 1 – Paternal Carrier



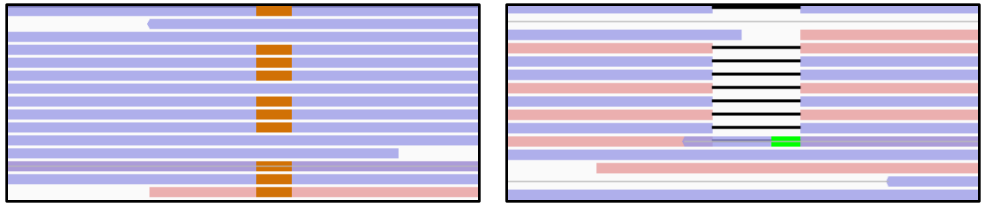
Embryo 2 – Maternal Carrier



Embryo 3 – Unaffected



Embryo 3 – Affected



c.3041 A > G **c.1521_1523 del CTT**

CooperSurgical®

Thank you!

Christopher Weier, PhD

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Senior Scientist