Preimplantation Genetic Testing (PGT) For *De Novo* Variants: Embryo Whole Genome Sequencing goes Beyond Carrier Screening Risks

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PURPOSE & OBJECTIVES

Whole genome preimplantation genetic testing (PGT-WGS) performed on a trophectoderm biopsy demonstrated high levels of concordance with the subsequently born child for *de novo* variants and variants associated with carrier status. These results present an opportunity to offer patients with a broader selection of PGT options.

MATERIALS & METHODS

Following the In-Vitro Fertilization (IVF) cycle of a couple, three embryos underwent biopsy and subsequent PGT-WGS, encompassing analysis for chromosomal and monogenic variants. Following the birth resulting from the transfer of a euploid embryo, fetal cord blood sequencing was conducted to enable comparison with the amplified embryonic DNA. Sanger sequencing was performed to confirm the presence or absence of suspected *de novo* variants in the parents and the newborn child.

Demonstrating high concordance in exome calls and accurately detecting *de novo* variants and variants linked to autosomal recessive conditions without the use of probes, PGT-WGS emerges as an invaluable tool for prospective parents.

RESULTS

Exome variant calls between amplified embryonic DNA and fetal cord blood demonstrated high levels of concordance in both sensitivity and precision. PGT-WGS successfully identified all five confirmed *de novo* variants, all of which were located in non-coding regions (see *figure 1*). Furthermore, the parents were found to be carriers of three autosomal recessive conditions: HFE c.187C>G p.H63D, PAH c.1074A>T p.L358F, and MEFV c.2084A>G p.K695R (*figure 2*). A comparison between cord blood and embryonic DNA revealed identical variants with consistent zygosity, affirming the accuracy of embryo screening.

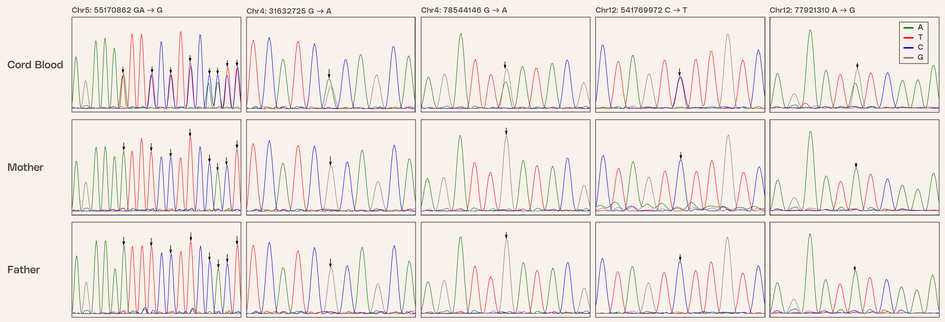


***Fig. 1**: Sanger chromatograms for confirmation of* de novo *variants in the born child and ref/ref genotype in parents*

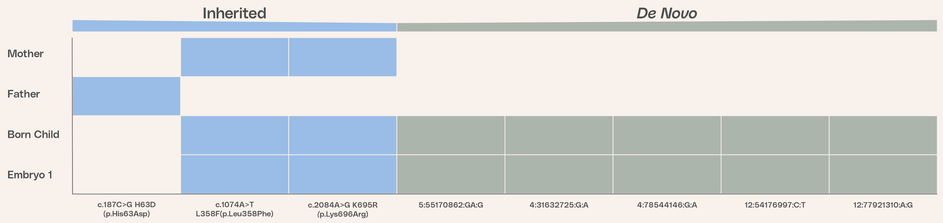


***Fig. 2**: Variants identified in parents vs. born child and embryo*

CONCLUSIONS

PGT-WGS offers the opportunity to detect genetic variants that are not explicitly targeted by monogenic screening, including *de novo* variants, which could be linked to significant phenotypes. Additionally, it can identify known monogenic conditions without requiring the development of probes necessary in traditional PGT for monogenic conditions.

CONTACT