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Validating PGS by Probing the Karyotypic Concordance Between ICM and TE

Introduction

Clinical trials have proven the validity of comprehensive chromosomal screening (CCS) in increasing implantation rates in IVF, justifying the routine use of preimplantation genetic screening (PGS). At the blastocyst stage, an embryo's karyotype is determined from a 5-10 cell biopsy collected from the trophectoderm (TE), a precursor tissue to the placenta. Interestingly, a considerable number of embryos deemed euploid do not result in pregnancies; conversely, there are spurious reports of aneuploid embryos that implant and lead to births of healthy, chromosomally normal babies. One rationale for these phenomena is that the TE biopsy collected from blastocysts is not always representative of the inner cell mass (ICM), the precursor of all tissues in the fetus. This study investigates the karyotypic concordance between ICM and TE.

Materials and methods

Aneuploid blastocysts as determined by routine PGS (Illumina's Veriseq NGS platform) were selected for re-analysis. An ICM biopsy, as well as a second TE biopsy were captured for each embryo and subjected to PGS. Three analysts blindly interpreted all resulting karyotype profiles independently.

Results

Within a sample population of 27 aneuploid embryos determined by routine PGS, two embryos (~7%) had euploid ICMs. A further three embryos (~12%) had ICMs that contained the aneuploidy detected in the initial TE biopsy, but had additional minor karyotypic discrepancies with the original profile. For these three embryos the second TE biopsy was concordant with the original profile, suggesting that the entire TE had a different karyotypic makeup than the ICM. The remaining 22 embryos (~81%) showed perfect karyotypic concordance between ICM and TE.

Conclusions

If the observed trends hold true in our currently expanding sample size we surmise that routine PGS has a ~7% 'biological false negative' rate.