EVALUATION OF THE INHERITANCE OF COPY NUMBER VARIATIONS (CNVS) IN THE EMBRYOS WHEN THE SAME CNV PRESENTS IN MORE THAN ONE EMBRYO AFTER PGT-A FROM IVF CYCLES

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Abstract Body

CNV involves both duplications and deletions of DNA sequences, which may cause human diseases. Some CNVs can be identified using targeted next generation sequencing (tNGS)-based preimplantation genetic testing for aneuploidy (PGT-A). When the same patterns of the CNVs are observed in more than one embryo, one of the parents may carry the CNV. In this study, we requested follow-up parental testing to confirm whether the CNVs presenting more than once in embryos are inherited.
tNGS-based PGT-A amplifies ~5000 amplicons across the human genome for PGT-A, and validations for CNVs were performed using 5-cell samples from cell lines with known CNV, and trophectoderm (TE) biopsies from embryos with a previously diagnosed structural rearrangement. Among 3489 tNGS-based PGT-A cycles from 2885 patients, 42 cycles from 29 patients showed the same CNVs in more than one embryo and 31 CNVs were observed. The size of deletions or duplications involved in CNVs ranged from 3.5 kb to 8.6 Mb, and included from 2 to 17 amplicons. Microarray testing was requested for the couples. Among the 22 results received, and 91% (20 out of 22) confirmed that one of parents carried the CNVs. For the ClinVar pathogenic category, 5 out of 20 were benign, and the euploid embryos carrying the CNVs were available for transferring. 11 out 20 had uncertain significance. Finally, 2 were likely pathogenic, and 1 was pathogenic.
The confirmation of parental CNVs further validated the diagnostic accuracy of deletions or duplications in embryo biopsies. Genetic counseling about the PGT-A and parental CNV results will help patients to decide whether they will transfer the embryos with parentally-inherited CNVs.