O-77 Monday, October 8, 2018 11:45 AM

VALIDATION OF SIMULTANEOUS DIAGNOSIS OF SINGLE GENE DISORDER (SGD) AND NEXT GENERATION SEQUENCING (NGS) - BASED COMPREHENSIVE CHROMOSOMAL ANEUPLOIDY SCREENING (CCS) FROM A SINGLE TROPHECTODERM (TE) BIOPSY.

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OBJECTIVE: We previously established a concurrent methodology of SGD pre-implantation genetic diagnosis (PGD) and CCS using quantitative real-time (q)PCR from the same TE biopsies, which resulted in excellent clinical outcomes. To improve the accuracy of CCS and reduce the cost, we switched the CCS platform from qPCR to NGS. This study sought to validate simultaneously testing SGD and CCS based on NGS from a single TE biopsy.

DESIGN: Blinded. e34 ASRM Abstracts Vol. 110, No. 4, Supplement, September 2018

MATERIALS AND METHODS: Phase I-Reliability Analysis: Fibroblasts were isolated as 5-cell samples to mimic TE biopsies, and followed by multiplex- amplification with primers of NGS CCS and 40 SNPs with high minor allele frequencies. The allele drop out (ADO) and amplification failure (AF) rates were assessed by comparing to genotypes of isolated genomic DNA using Taqman genotyping assays. Phase II-Analysis of TE biopsies: Two TE biopsies were obtained from 10 aneuploid embryos, which were contributed by four patients with previous SGD and qPCR CCS results. Workups involved identifying informative SNPs in the parents using SNP arrays and phasing the markers using qPCR on family members.

RESULTS: Phase I: Twenty four 5-cell samples showed 0.74% ADO rate (8/1080), and 0% AF rate (0/1920), which demonstrated the reliability of the targeted amplification of the 40 SNPs with NGS CCS amplicons. Phase II: TE biopsies of 10 embryos from 4 cases, including autosomal or X-linked, recessive or dominant disorders, were tested with mutation and linkage assays with 0% ADO rate (0/176) and 0% AF rate (0/348). The SGD results were consistent with the previous PGD diagnosis.

CONCLUSIONS: This approach to combined CCS and SGD PGD provides the ability to reliably produce accurate SGD PGD results in parallel with NGS based CCS from the same biopsy.