00489 Implementing Prenatal Chromosome Microarray Analysis (CMA) in KKH Cytogenetics Laboratory

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Aims: CMA will detect significant Copy Number Variations (CNVs) in an additional 1-1.7% of cases in cases with a normal karyotype and normal ultrasound, an additional 6-7% potentially CNV can be detected. As such the implementation of CMA as routine prenatal testing is valuable to the health needs of patient.

Methodology: Postnatal and prenatal samples were extracted using Puregene Blood Kit and modified Puregene Cell Kit respectively. Postnatal CMA was performed using Agilent Technologies SurePrint G3 ISCA CGH+SNP 4x180K and Affymetrix CytoScanTM 750K Assay. CMA using Affymetrix CytoScanTM 750K Assay and chromosome analysis were performed on prenatal samples.

Result: Out of 42 postnatal samples performed on SurePrint 4x180K, 37 samples previously reported as pathogenic with CNV ranging from 2kb to 26.8Mb were run on CytoScan™ 750K. Filters for gains and losses with 50 markers were set. 35 samples with pathogenic CNVs were identified.

The remaining 5 postnatal samples with known uniparental isodisomy were selected to validate the allelic differentiation potential of SNP-detecting platforms. CMA results showed 4 samples contained the expected copy-neutral Absence of Heterozygosity (AOH). Additional further testing may be required if the detection of AOH identify a concern.

Out of 27 prenatal samples with karyotype done, 22 from cultured cells and 5 from uncultured cells were validated. 24 samples showed normal karyotype with 3 showed 22q11.2 deletion by Fluorescent In Situ Hybridisation (FISH). Filters for gains and losses of 400kb or larger with 50 markers were set. CMA results showed 7 samples with pathogenic CNVs. Out of 3 samples showing abnormal karyotypes, only 1 revealed normal CMA result.

Conclusion: CMA in prenatal setting has been proven its add-on value in conjunction with conventional cytogenetics. Interpretation of pathogenic CNVs is critical and may be especially challenging in prenatal setting with limited information on the fetal phenotype, sample quality and quantity and time constraint.