Prenatal Microarray Testing

Purpose
Prenatal microarray analysis should be considered as an adjunct to G-banded chromosome analysis in pregnancies referred for abnormal ultrasound findings, abnormal serum screen, advanced maternal age, family history or parental concern. The American College of Obstetrics and Gynecology has endorsed microarray analysis for prenatal testing and recommends its use in pregnancies with abnormal ultrasound findings and a normal G-banded chromosome analysis [Obstet Gynecol (2009) 114(5):1161-1163].

Methodology
DNA is isolated from an amniotic fluid or chorionic villi sample and is hybridized to a custom microarray containing probes across the entire genome to detect deletions and/or duplications. Fluorescence In Situ Hybridization (FISH) analysis is used to confirm any abnormal findings. The clinical sensitivity for any disorder is dependent on the proportion of cases caused by deletions/duplications compared with other mutations not detectable by microarray analysis.

Advantages of Prenatal Microarrays
• Higher diagnostic yield to identify deletions and/or duplications not visible by G-banded chromosome analysis
• Accurate detection of deletions and/or duplications of 400 kb or greater across the genome and 10-20 kb within clinically relevant targeted genes
• Objective high-definition copy number analysis using the most current methods and software

Limitations
• Prenatal microarray will not detect balanced translocations or inversions, imbalances below the resolution of the array or point mutations
• Low level mosaicism (usually less than 25%) may not be detected by microarray, however in some cases the microarray will detect mosaic cell line that fail to divide in culture
• Prenatal microarray must be performed in conjunction with G-banding analysis

Case Study
EGL received a prenatal sample for G-banding analysis which was referred for a fetal cardiac abnormality and hydronephrosis.

Results
As shown in the figure, two abnormalities, a loss and a gain, were identified by microarray. FISH studies revealed these imbalances were due to an unbalanced translocation in the fetus which was inherited from the mother who carries the balanced translocation. This abnormality was not visible by G-banding analysis.

As demonstrated by this case, new technologies offer improved diagnostic rates, which can have immediate implications for recurrence risk estimates and familial counseling.