Prenatal Microarray:
Structural fetal abnormalities identified by ultrasound scan (including NT>3.5mm)

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Samples required
- 15-20ml amniotic fluid or 12mg chorionic villus biopsy in transport medium.
- A completed request card should accompany all samples. Ultrasound findings including NT measurement and gestation must be provided in order to allow clinical interpretation of the microarray.

Patient details
To facilitate accurate testing and reporting please provide patient demographic details (full name, date of birth, address and ethnic origin), details of any relevant family history and full contact details for the referring clinician.

Introduction
Genome-wide chromosomal microarray (CMA) detects pathogenic copy number variants (pCNV) in 4-10% of prenatal samples (amniotic fluid or chorionic villus samples).
CMA may also detect copy number variants of uncertain clinical significance which may require parental follow up testing to aid interpretation.
CMA may also detect pCNV which are not associated with the presenting phenotype (incidental findings).

Referrals
- Samples from pregnancies that have structural abnormalities identified by ultrasound scan where rapid trisomy testing is negative. Note that absent nasal bone and isolated IUGR are not classified as structural fetal abnormalities.
- NT>3.5mm (before 14 weeks gestation) where rapid trisomy testing is negative.

Prenatal reporting
pCNV identified by the microarray are reported as pathogenic if they are associated with fetal scan abnormalities or with fully penetrant intellectual disability.
In line with RCPath guidelines, CNV which are associated with susceptibility to neurodevelopmental disorders (variable penetrance) are reported only if there is a published risk of fetal structural abnormality.
CNV of uncertain clinical significance are reviewed by a panel of Clinical Geneticists and Clinical Scientists and will only be reported if they require segregation analysis (parental carrier status) to aid interpretation of the clinical significance.
pCNV identified by microarray are confirmed using karyotype, qPCR or Fluorescence In Situ Hybridisation (FISH). These targeted tests are then applied to family members for carrier testing and for prenatal analysis in future pregnancies. Please contact the laboratory for further details.

Service offered
Whole genome microarray analysis at a practical resolution of 200kb for copy number variants (chromosomal deletions and duplications) and additional SNP based identification of uniparental isodisomy and ploidy level changes.

Technical
Whole genome chromosomal microarray analysis using the Affymetrix 750K microarray is performed on DNA extracted from uncultured amniotic fluid or chorionic villus samples. The microarray design uses both single nucleotide polymorphic (SNP) probes and non-polymorphic probes to enable consistent genomic coverage. Copy number variations (CNV) and regions with absence of heterozygosity (AOH) are identified using infoQuant Fusion software. The estimated practical resolution is 200kb; CNV below this threshold may not be identified. The microarray will not detect balanced structural chromosome anomalies and may not detect mosaicism. AOH may indicate uniparental isodisomy or regions identical by descent. The CNV identified by the CMA are compared to databases of known genetic variation and to reports of known pathogenic changes. Variants which are not known to have a pathogenic effect or do not have a high risk of pathogenicity may not be reported. AOH of non-imprinted chromosome regions will not be reported.
If pCNV or variants of uncertain significance are reported, further samples may be requested (EDTA venous blood and/or lithium heparin venous blood from parents) to aid clinical interpretation and provide a recurrence risk for the family.

Target reporting time
Routine analysis – 14 days