Cytogenomic SNP Microarray, Fetal

Last Literature Review: April 2020 Last Update: August 2023

Cytogenomic SNP microarray testing is used to identify genomic imbalances (deletions and duplications) and may be used to further characterize abnormalities identified by chromosome analysis, including unbalanced translocations, recombinant chromosomes, markers, and ring chromosomes. Regions of homozygosity (ROH) can also be identified. It is the recommended first-tier test for patients undergoing prenatal diagnosis for the indication of a fetal structural abnormality detected by ultrasound (unless the structural abnormality is strongly suggestive of a specific aneuploidy, in which case, karyotype with or without fluorescence in situ hybridization [FISH] may be offered before genomic microarray).

Disease Overview

Diagnostic Issues

- Many abnormal phenotypes are associated with chromosomal imbalances.
- Chromosome analysis has limited ability to detect copy number abnormalities less than 10-15 Mb in size.
- Genomic microarray can detect chromosomal imbalances at a much higher level of resolution than standard chromosome analysis.
- Genomic microarray can detect ROH, which may indicate an increased risk for autosomal recessive (AR) disease for genes contained within the ROH, and/or the risk of an imprinting disorder due to uniparental disomy (UPD), or molar pregnancy.
- Identification of specific abnormalities may be helpful in medical management and planning for special needs.

Test Interpretation

Diagnostic Yield

- Among cases with a normal karyotype, microarray studies reveal clinically relevant copy number variants (CNVs) in:
  - Approximately 6% of fetuses with a structural anomaly; percentage may be higher, depending on anomaly
  - Approximately 2% whose indication is advanced maternal age or positive aneuploidy screen
- The diagnostic yield varies by patient population and the presence of comorbidities.

Results

- A written summary and an interpretation of the microarray findings are provided.
- CNV evaluation is performed in accordance with recommendations by the American College of Medical Genetics and Genomics (ACMG):
  - Standard 5-tier classification terminology is used:
    - Pathogenic
    - Likely pathogenic
    - Variant of uncertain significance (VUS)
    - Likely benign
    - Benign
  - Variants that do not fall within these categories may be reported with descriptive language specific to that variant.

Featured ARUP Testing

Cytogenomic SNP Microarray - Fetal 2002366

Method: Genomic Microarray (Oligo-SNP Array)

Detects small copy number variants (CNVs) and further characterizes chromosomal abnormalities identified by conventional cytogenetic methods on direct and cultured amniotic fluid and chorionic villus sampling (CVS) specimens.

Chromosome FISH, Amniotic Fluid with Reflex to Chromosome Analysis or Genomic Microarray 2011130

Method: Fluorescence in situ Hybridization (FISH)

- Rapid detection of aneuploidy involving chromosomes 13, 18, 21, X, and Y
- If results of aneuploidy FISH panel are **normal**, genomic microarray analysis will be performed
- If results of aneuploidy FISH panel are **abnormal**, chromosome analysis will be performed
- Performed on uncultured amniotic fluid

Chromosome FISH, Chorionic Villus with Reflex to Chromosome Analysis or Genomic Microarray 2011131

Method: Fluorescence in situ Hybridization (FISH)

- Rapid detection of aneuploidy involving chromosomes 13, 18, 21, X, and Y
- If results of aneuploidy FISH panel are **normal**, genomic microarray analysis will be performed
- If results of aneuploidy FISH panel are **abnormal**, chromosome analysis will be performed
- Performed on uncultured CVS

Chromosome Analysis, Amniotic Fluid, with Reflex to Genomic Microarray 2008367

Method: Giemsa Band/Genomic Microarray (Oligo-SNP Array)

- Chromosome analysis is used for detection of aneuploidy and other chromosomal abnormalities (eg, large deletions/duplications, translocations, inversions, marker chromosomes)
- If results of chromosome analysis are normal, genomic microarray analysis will be performed

For other fetal testing to detect cytogenetic abnormalities, refer to the Laboratory Test Directory.

- For additional information regarding CNV classification, refer to the ARUP Constitutional Copy Number Variant Assertion Criteria.
  - Additional resources can be found on the ARUP Genetics Resources website.
- Submission of a maternal blood sample for maternal cell contamination studies is encouraged.

Result	Description
Normal	No clinically significant CNV or ROH detected
Abnormal	One or more pathogenic or likely pathogenic findings detected
Uncertain	One or more CNVs of uncertain clinical significance detected • Insufficient evidence for unequivocal determination of clinical significance available at the time of review • AR risk Uncertain ROH: risk for AR disease and/or imprinting disorder due to UPD • Testing may suggest relatedness between the parents of the tested individual

Reporting Criteria

- Deletions >1 Mb and duplications >2 Mb are generally reported, dependent on genomic content.
- CNVs classified as VUS are generally reported when found to have suspected clinical relevance based on information available at the time of review, or when meeting size criteria.
- Total autosomal homozygosity >5% is generally reported.
  - Only autosomal ROH >3 Mb are considered for this estimate.
- Single terminal ROH >3 Mb or single interstitial ROH >10-20 Mb are generally reported, dependent upon chromosomal location and likelihood of imprinting disorder.
- Recessive disease risk and recurrent CNVs with established reduced penetrance are generally reported.
- Known or expected pathogenic CNVs affecting genes with known clinical significance but which are unrelated to the indication for testing will generally be reported.
- CNVs classified as likely benign or benign that are devoid of relevant gene content or reported as common findings in the general population are generally not reported.

Limitations

- Does not detect:
  - CNVs below the limit of resolution of the testing platform
  - Sequence-level variants (mutations), including point mutations and small insertions/deletions
  - Balanced chromosomal rearrangements (translocations, inversions, and insertions)
  - Imbalances of the mitochondrial genome
  - Low-level mosaicism (generally <20-30%)
  - Most cases of tetraploidy

Related Information

Prenatal Testing for Chromosomal Abnormalities and Neural Tube Defects