Cytogenomic Microarray, Products of Conception

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) and/or intrauterine fetal demise or stillbirth. Microarray testing is more likely to yield diagnostic results in products of conception (POC) and formalin-fixed, paraffin-embedded (FFPE) tissue specimens compared to other cytogenetic testing methods because it does not require living cells and offers increased resolution for the detection of copy number variants (CNVs).

Featured ARUP Testing

Genomic SNP Microarray, Products of Conception 2005633

Method: Genomic Microarray (Oligo-SNP Array)

- Detects small CNVs and further characterizes chromosomal abnormalities identified by conventional cytogenetic methods on fresh tissues from a fetal demise
- Preferred test for POC specimens that fail to grow in culture

Chromosome Analysis, Products of Conception, with Reflex to Genomic Microarray 2005762

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

- Preferred test strategy with highest diagnostic yield for fresh tissue specimens from a fetal demise
- When tissue culture is unsuccessful or if results of chromosome analysis are normal, testing reflexes to genomic microarray

Cytogenomic Molecular Inversion Probe Array FFPE Tissue - Products of Conception 3004273

Method: Molecular Inversion Probe Array

- Preferred test for FFPE tissue specimens from a fetal demise

Disease Overview

Diagnostic Issues

- Many abnormal phenotypes are associated with chromosomal imbalances.
- Chromosome analysis has limited ability to detect copy number abnormalities less than approximately 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

- Chromosomal abnormalities are present in approximately half of early (<20 weeks) fetal losses:
  - Autosomal trisomies: 60-70%
  - Monosomy X: 10-15%
  - Triploidy: 10-15%
  - Other chromosomal abnormalities: 10-15%
- Genomic microarray identifies abnormal results in 6-13% of fetal losses.

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.
- 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.

Result	Description
Normal	No clinically significant CNV or ROH detected
Abnormal	One or more pathogenic or likely pathogenic finding 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 >3-5 Mb are considered for this estimate, depending on platform utilized.
- Single terminal ROH >3-5 Mb or single interstitial ROH >10-20 Mb are generally reported, dependent upon chromosomal location and likelihood of imprinting disorder, as well as platform utilized.
- 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

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