Cytogenomic SNP Microarray, Fetal

Indications for Ordering

- Abnormal ultrasound findings
- Further characterize an abnormal fetal karyotype
- Suspicion of an imbalance in a specific genomic region that is best evaluated by microarray
- Investigate de novo, apparently balanced translocations
- Family history of a known or suspected chromosomal abnormality best evaluated by microarray
- Patients undergoing invasive prenatal testing (instead of, or in addition to, chromosome analysis)

Test Description

- DNA extraction, amplification, purification, labeling, hybridization, washing, array scanning, analysis, and interpretation
  - Fetal DNA is extracted from amniotic fluid and/or chorionic villus sampling (CVS) cell cultures
- Microarray platform contains over 2.6 million copy number markers, including 750,000 SNP probes

Tests to Consider

Primary tests

Cytogenomic SNP Microarray – Fetal 2002366
- Identifies genomic abnormalities (eg, aneuploidy and microdeletions) in fetus
- Performed on cultured and direct amniotic fluid and CVS specimens

Chromosome FISH, Amniotic Fluid with Reflex to Chromosome Analysis or Genomic Microarray 2011130
- If results of aneuploidy FISH panel are normal, genomic microarray 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
- If results of aneuploidy FISH panel are normal, genomic microarray 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
- If results of chromosome analysis are normal, genomic microarray will be performed

Related tests

Other fetal testing for cytogenetic abnormalities

Chromosome FISH, Prenatal 2002297
- Rapid detection of aneuploidy involving chromosomes 13, 18, 21, X, and Y
- Specimen – uncultured amniotic fluid

Chromosome Analysis, Amniotic Fluid 2002293
- Use for prenatal chromosome analysis after 14 weeks gestation

Chorionic Villus, FISH 0040203
- Rapid detection of aneuploidy involving chromosomes 13, 18, 21, X, and Y
- Specimen – uncultured CVS

Chromosome Analysis, Chorionic Villus 2002291
- Use for prenatal chromosome analysis at 10-13 weeks gestation

Disease Overview

Diagnostic issues

- Many abnormal phenotypes are associated with chromosomal imbalances
- SNP microarray can detect many chromosomal variants that conventional cytogenetics cannot
  - Submicroscopic abnormalities
  - Absence of heterozygosity (AOH) that may suggest uniparental disomy or an increased risk of recessive condition
- Identification of specific abnormalities may be helpful in medical management and planning for special needs

Genetics

- Whole genome coverage, including subtelomeric and pericentromeric regions
- Detects >50 known microdeletion/microduplication syndromes
- Detects loss of heterozygosity (LOH) throughout the genome

Test Interpretation

Clinical sensitivity

- 100% for non-mosaic aneuploidy that is detectable by karyotype
- In cases with a normal karyotype, microarray studies reveal clinically relevant copy number variations (CNV)
  - ~6% of fetuses with a structural anomaly
  - ~2% whose indication is advanced maternal age or positive aneuploidy screen
- Test results are often complex, and a CNV of uncertain clinical significance may be detected
- A written summary and an interpretation of the microarray findings are provided

Results

- Abnormal
  - Deletion/duplication involves a clinically significant gene or region
  - Abnormal allele distribution consistent with triploidy
  - AOH
  - Regions of homozygosity may be reported when
    - A single region of AOH is >15 MB
    - When the total autosomal AOH proportion is >10% of the genome
    - Only autosomal AOH >3 MB is considered for this estimate
- Normal
  - No clinically significant abnormality detected
- Clinical significance unknown
  - CNV detected at or above the reportable criteria, but clinical significance is unknown
  - Deletions/duplications that confer carrier status for recessive conditions

Limitations

- Does not detect
  - Base pair mutations
  - Very small deletions/duplications
  - Tetraploidy
  - Balanced rearrangements (translocations, inversions, and balanced insertions)
  - Low-level mosaicism
  - Imbalances of the mitochondrial genome
- To minimize variations of undetermined significance, duplications smaller than 2 MB and deletions smaller than 1 MB may not be reported if they contain only a few genes that have no compelling association with disease
- May reveal a biological relationship, including a close blood relationship (consanguinity or incest) between the mother and the father of the fetus
- Failure of the array to detect an imbalance at any specific locus does not exclude the diagnosis of any disorder associated with that locus