Condition Description

Genetic imbalances such as chromosomal deletions and duplications have long been known to be a significant cause of intellectual disability, birth defects, developmental disorders, and pregnancy loss. Traditional prenatal G-banded chromosome testing yields low-resolution structural and numerical analysis of the chromosomes. The Chromosomal Microarray, CytoScan SNP Array Prenatal provides high-definition copy number analysis using the most current methods and software.

Couples choosing prenatal diagnosis now have the option of microarray analysis to optimize detection of submicroscopic genetic imbalances. As the founding member of the International Standard Cytogenetic Array Consortium (ISCA), Emory Genetics leads the industry in quality improvement efforts in chromosomal microarray testing as well as improved genetic healthcare for patients. Our ABMG-certified cytogeneticists, molecular geneticists, and genetic counselors work with the ordering clinician to assist in clinical correlations with significant array finding(s).

To reduce parental concern during the testing process, we request parental blood samples to be submitted with the fetal sample. This speeds parental follow-up for genetic imbalances to determine if the finding(s) are de novo or inherited. Parental inheritance is important to consider when interpreting prenatal array findings.

Genetic counseling is recommended prior to the ordering of prenatal chromosomal microarray. To assist in counseling Emory Genetics Laboratory provides a consent form that explains the benefits and limitations of prenatal chromosomal microarray.

Approximately 1.7% of women who have invasive prenatal testing due to advanced maternal age (AMA) or abnormal serum screening will have an abnormal chromosomal microarray finding that would be missed by traditional karyotype. This statistic rises to 6.0% for those pregnancies with structural fetal anomalies identified by ultrasound. In response to these new data, the American College of Obstetricians and Gynecologists (ACOG) issued a committee opinion on the use of chromosomal microarray analysis in prenatal diagnosis, which provided the following practice recommendations to replace those set in 2009:

- Chromosomal microarray analysis (CMA) is recommended for any patient undergoing an invasive diagnostic prenatal procedure because of the ultrasound indication of one or more major structural abnormalities in the fetus. CMA replaces the need for fetal karyotype.
- CMA or karyotype can be offered in those patients undergoing invasive diagnostic prenatal testing if no structural fetal abnormalities are noted on ultrasound regardless of maternal age.
- CMA is recommended for products of conception in the case of intrauterine fetal demise or stillbirth.
- Patients choosing CMA should receive both pre-test and post-test genetic counseling.
- Since most abnormalities detected by CMA are not associated with AMA, the use of this test for prenatal diagnosis should not be restricted to women aged 35 years and older.

References:

Indications

The CytoScan SNP Array Prenatal is appropriate for any woman seeking prenatal detection of chromosomal imbalance.

Common indications for prenatal diagnosis include:
- Advanced maternal age
- Abnormal maternal serum screen
- Abnormal ultrasound
- Family history of a genetic imbalance
- Parental concern

Indications specific to the need for further testing by microarray:
- Previous normal fetal karyotype with abnormal ultrasound findings
- Previous abnormal fetal karyotype showing an imbalance (excluding aneuploidies)

- For unbalanced rearrangements, microarray can be used to size the deletion or duplication and identify the genes involved.
- Previous abnormal fetal karyotype showing an apparently balanced rearrangement

- For apparently balanced rearrangements, microarray can be used to test for cryptic deletions/duplications at the breakpoints.

**Methodology**

DNA isolated from the prenatal sample is hybridized to an array containing oligonucleotide and SNP probes across the genome to detect copy number imbalances and regions of homozygosity.

The CytoScan SNP Array array consists of 2.6 million markers (including 750,000 SNPs) which allows for the detection of both copy number variation (CNV) and large stretches (>10 Megabases (Mb)) of absence of heterozygosity (AOH), which can result from uniparental disomy (UPD) or common parental descent. The design is based on recommendations from the International Standards for Cytogenomic Arrays (ISCA) Consortium (Baldwin et al. (2008) Genet Med; 10(6):415-429).

**Detection**

The CytoScan SNP Array Prenatal detects trisomy, monosomy, chromosome deletions, and duplications. This test is designed to detect whole and partial chromosome UPD, multiple long stretches of absence of heterozygosity (AOH) greater than 3 Mb, and AOH in clinically relevant regions. In addition, this test can also detect triploidy, a common cause of miscarriages. Possible UPD will be reported when a chromosome has at least one homozygous regions >10 Mb. Homozygosity due to apparent common descent will be reported when >5% of the autosomal genome is present in long stretches of AOH. These regions of AOH will be specified to consider recessive risk alleles.

Chromosomal Microarray, CytoScan SNP Array Prenatal will not detect balanced translocations, balanced inversions, imbalances smaller than the resolution of this array, point mutations, or low level mosaicism (usually less than 25%).

**Reference Range**

N/A

**Specimen Requirements**

Submit only 1 of the following specimen types

**Type: Amniotic Fluid**

Specimen Requirements:

Collect 20-30 ml of amniotic fluid (discard the first 1-2 ml). Place in sterile conical centrifuge tubes.

For cultures: 1 T75 or 2 T25 at 70% confluency.

Specimen Collection and Shipping: Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

**Type: Chorionic Villi**

Specimen Requirements:

Collect 15-30 mg of chorionic villi using sterile technique. Place in sterile tube(s) with EGL transport media or other sterile culture media.

For cultures: 1 T75 or 2 T25 at 70% confluency.

Specimen Collection and Shipping: Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

**Type: Cord Blood**

Specimen Requirements:

In sodium heparin (green top) AND EDTA (purple top) tube: 1-3 ml of fetal blood (PUBS)

Specimen Collection and Shipping: Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

**Special Instructions**

A maternal blood sample is REQUIRED to rule out maternal cell contamination (MCC). It is also recommended to send a paternal blood sample to determine the parental inheritance of microarray findings of uncertain clinical significance. This reduces the wait time for the final interpretation of a prenatal result.

Type: Whole Blood
5-10 ml collected in an EDTA (purple top) tube
Specimen Collection and Shipping: Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.
## Related Tests

- Prenatal Rapid Screen FISH (RS)
- Prenatal chromosome analysis (CV, AD)
- EmArray Cyto Prenatal (CMPRE)
- Targeted testing by FISH, aCGH, or chromosome analysis is available for at risk family members
- Alpha-Fetoprotein, Amniotic Fluid (PAFP1)
- Acetylcholinesterase (PACHE)