Chromosomal Microarray: EmArray Cyto Prenatal

Test Code: CMPRE
Turnaround time: 10 days - 14 days  (All abnormal findings are called out immediately.)
CPT Codes: 81228 x1, 81265 x1

Condition Description

What is Prenatal EmArray Cyto?
The EmArray Cyto chromosomal microarray utilizes 60,000 (60K) oligonucleotides to achieve whole genome coverage at a 75 kilobase (kb) spacing. It additionally covers more than 400 targeted regions, including known recurrent microdeletion/microduplication syndromes, centromere and telomere regions and disease-causing genes.

Why Choose Prenatal EmArray Cyto?
Since the 1970's couples have presented for prenatal genetic testing to learn medical information about their unborn baby. Genetic imbalances such as chromosomal deletions and duplications have long been known to be the leading cause of intellectual disability, birth defects and developmental disorders. Traditional methods for prenatal testing consist of G-banded chromosome analysis, which yields low resolution structural analysis of the chromosomes. Unlike the traditional analysis, the EmArray Cyto array allows for objective high-definition copy number analysis using the most current methods and software. The EmArray Cyto array has been used in the pediatric population resulting in much greater detection of genetic imbalances leading to the disruption of normal development.

Couples choosing prenatal diagnosis for any reason now have the option of microarray analysis to optimize detection of submicroscopic genetic imbalances. These couples may be assured that utmost care and consideration is employed in the interpretation of the array. 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 board certified cytogeneticists, molecular geneticists and genetic counselors work in unison with the submitting clinician to assist in phenotypic correlations with any significant finding(s).

To reduce unnecessary parental concern during the testing process, we request parental blood to be submitted along with the fetal sample. This allows for determination of inheritance (de novo or inherited) for the clinical interpretation of fetal findings that are of uncertain significance without having to arrange for parental blood draws and thus, reduces the wait time for the final interpretation of an abnormal result.

Genetic counseling is recommended prior to the ordering of prenatal chromosomal microarray. To assist in counseling EGL Genetics provides a consent form specific to 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. 1 This statistic rises to 6.0% for those pregnancies with structural fetal anomalies identified by ultrasound. 1 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 2009:2

- 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 anomalies 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 EmArray Cyto 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
- 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 a custom array containing oligonucleotide probes across the genome to detect copy number imbalances. FISH analysis or another method, such as G-banding, is used to confirm any abnormal findings. (Additional information is also provided above.)

### Detection

The detection of deletions and duplications of 400 kb or greater is expected to be very high. Detection is limited to gain of copy number (duplication), loss of copy number (deletion) or normal copy number. Deletions and duplications of 400 kb or greater are reported. Smaller deletions or duplications in regions of known microdeletion/microduplication syndromes or in clinically relevant genes will also be reported.

The clinical sensitivity for known microdeletion or microduplication syndromes is available in our detection rate chart. The clinical sensitivity for other disorders is dependent on the proportion of cases caused by deletions/duplications compared with other mutations not detectable by array analysis. Microarray analysis will not detect balanced translocations, balanced inversions, imbalances smaller than the resolution of this array, triploidy, point mutations. Low level mosaicism (usually less than 25%) may not be detected by array, however in some cases the array will detect mosaic cell lines that fail to grow in culture.

### Reference Range

Consecutive abnormal oligonucleotide probes are used to identify regions of imbalance. Log2 ratios less than 0.32 are indicative of a deletion or loss of genetic material, while those greater than 0.26 are indicative of a duplication or gain of genetic material.

### 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)
- Targeted testing by FISH is available to family members of an individual with a deletion or duplication detected by microarray.
- Prenatal chromosome analysis (CV, AD)
- Alpha-Fetoprotein, Amniotic Fluid (PAFP1)
- Acetylcholinesterase (PACHE)