Pregnancy Loss
Chromosomal Microarray

Chromosomal microarray (CMA) is a technology that analyzes sample DNA to detect gains and losses of genomic material at a much more detailed resolution than traditional chromosome analysis. CGL’s Infinium® CytoSNP-850K BeadChip array provides excellent coverage, improved accuracy of breakpoint estimation for both CNVs and regions of homozygosity (ROH), and more sensitive detection of low-level mosaicism.

Pregnancy Loss

- Up to 25% of recognized pregnancies end in miscarriage.
- Approximately 50% of 1st trimester losses are chromosomally abnormal.

Indications for Testing

- Spontaneous fetal loss at any gestational age
- Induced termination due to fetal anomalies
- Fetal loss with abnormal karyotype requiring further characterization
- Fetal loss when conventional chromosome analysis cannot be obtained (due to culture failure)

Copy Number Variant (CNV)

A copy number variant (CNV) is a segment of DNA that differs in copy number, seen as a gain (duplication) or a loss (deletion), compared to the general population. The term CNV does not describe the clinical significance of the finding. The terms “benign”, “pathogenic” or “uncertain” are often used to describe the clinical significance of a CNV. Every individual carries benign CNVs that are not reported. Pathogenic and uncertain CNVs are reported.

Region of Homozygosity (ROH)

A run or region of homozygosity (ROH) is a term used to describe a continuous area of the genome that appears to be the same (homozygous) on both chromosomes. Large and/or multiple ROH may suggest uniparental disomy (UPD) or shared ancestry (consanguinity), with possible implications for recessive disorders.

Full CMA Interpretations

CMA test results can be complicated, so the Colorado Genetics Laboratory provides a full interpretation of an abnormality. Our Directors and Genetic Counselors are on hand to aid clients in understanding the interpretation of an array result, and how to discuss results with patients and their families. This includes providing clinicians with current articles, images of test results, and other helpful materials.

Advantages

- Identifies microdeletion and microduplication syndromes in one single test
- Detects gains/losses involving thousands of known disease genes
- Provides identification of ROH utilized in analysis of uniparental isodisomy and recessive disorders

Limitations

Although CMA has the ability to detect abnormalities in a significant number of samples, it does have limitations. CMA will not detect:

- Balanced chromosome rearrangements
- Very low-level mosaicism
- Single gene mutations or single nucleotide mutations/polymorphisms
- Abnormalities that are smaller than the resolution of the array

The presence of maternal cell contamination may limit the ability to fully interpret results.

Pre-test Counseling

It is important to discuss what information CMA testing provides, as well as its advantages and limitations, with the patient prior to ordering the test. Patients should also be informed of the potential testing outcomes as listed below.

<table>
<thead>
<tr>
<th>CNV Interpretation</th>
<th>Benign (Normal)</th>
<th>Pathogenic (Abnormal)</th>
<th>Uncertain</th>
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</thead>
<tbody>
<tr>
<td>- No clinically significant gains or losses of genomic material detected.</td>
<td></td>
<td>CNV is likely to have caused the observed clinical features.</td>
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<tr>
<td>- This result does not rule out the possibility of a single gene disorder or an abnormality not detected by CMA.</td>
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<td>Diagnosis of a defined genetic condition is made.</td>
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<tr>
<td>- CNV may or may not have caused clinical features.</td>
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<td>Parental studies may help clarify the clinical significance.</td>
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<td>- More information on this finding may become available in the future.</td>
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April 2016