Overview

Useful For
Diagnosis of congenital copy number changes in products of conception, including aneuploidy (ie, trisomy or monosomy) and structural abnormalities

Determining chromosomal causes for fetal death

Determining recurrence risk of future pregnancy losses

Determining the size, precise breakpoints, gene content, and any unappreciated complexity of abnormalities detected previously by other methods such as conventional chromosome and FISH studies

Determining if apparently balanced abnormalities identified by previous conventional chromosome studies have cryptic imbalances, since a proportion of such rearrangements that appear balanced at the resolution of a chromosome study are actually unbalanced when analyzed by higher-resolution chromosomal microarray

Testing Algorithm
Hematoxylin and eosin stain review of the paraffin-embedded sample is performed to identify the area of fetal tissue prior to DNA extraction and microarray analysis. If additional FISH testing is requested, it will be performed at an additional charge.

A maternal blood sample is requested when ordering this test, see PPAP / Parental Sample Prep for Prenatal Microarray Testing. The PPAP test must be ordered under a different order number than the prenatal specimen.

Maternal cell contamination (MCC) testing will be performed at no additional charge on the maternal blood and fetal tissue to rule out the presence of maternal cells in the product of conception sample. Testing will not be rejected if maternal blood is not received; however, the possibility of maternal cell contamination cannot be excluded.

A paternal blood sample is desired but not required, see PPAP / Parental Sample Prep for Prenatal Microarray Testing.

If a fresh specimen is submitted, the test will be cancelled and CMAPC / Chromosomal Microarray, Autopsy, Products of Conception, or Stillborn will be added and performed as the appropriate test.

See Frequently Asked Questions: Cytogenetic Testing of Products of Conception by Chromosomal Microarray Analysis in Special Instructions.

Special Instructions

- Informed Consent for Genetic Testing
- Chromosomal Microarray Prenatal Patient Information
- Frequently Asked Questions: Cytogenetic Testing of Products of Conception by Chromosomal Microarray Analysis
- Informed Consent for Genetic Testing (Spanish)

Method Name
Chromosomal Microarray (CMA) Using Applied Biosystems (Affymetrix) Oncoscan

NY State Available
Yes
Specimen

Specimen Type

Varies

Advisory Information

If a specimen in fixative is submitted, ANPAT / Anatomic Pathology Consultation, Wet Tissue will be added by the laboratory, at an additional charge, to facilitate the performance of this test.

Additional Testing Requirements

A maternal blood sample is requested when ordering this test (see PPAP / Parental Sample Prep for Prenatal Microarray Testing). Testing will not be rejected if maternal blood is not received; however, the possibility of maternal cell contamination cannot be excluded. The PPAP test must be ordered under a different order number than the prenatal specimen.

A paternal blood sample is desired but not required (see PPAP / Parental Sample Prep for Prenatal Microarray Testing).

Necessary Information

A reason for referral and pathology report are required in order for testing to be performed. Send information with specimen. Acceptable pathology reports include working drafts, preliminary pathology or surgical pathology reports.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Tissue

Container/Tube: Formalin-fixed, paraffin-embedded block containing fetal or placental (including chorionic villi) tissue.

Additional Information: A pathology report and reason for referral must be submitted with each specimen. The laboratory will not reject testing if this information is not provided, but appropriate testing and interpretation may be compromised or delayed.

Specimen Type: Slides

Specimen Volume: 6 consecutive, unstained, 5-micron-thick sections placed on positively charged slides and 1 hematoxylin and eosin-stained slide.

Forms

1. New York Clients-Informed consent is required. Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

   - Informed Consent for Genetic Testing (T576)

   - Informed Consent for Genetic Testing-Spanish (T826)

2. Chromosomal Microarray Prenatal Patient Information (T716) in Special Instructions.
Test Definition: CMAMT
Chromosomal Microarray, POC, FFPE

Specimen Minimum Volume
Formalin-fixed, paraffin-embedded tissue block
Five consecutive, unstained slides and 1 hematoxylin and eosin-stained slide

Reject Due To
All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

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<tr>
<th>Specimen Type</th>
<th>Temperature</th>
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<tr>
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Clinical and Interpretive

Clinical Information
Chromosomal abnormalities may result in malformed fetuses, spontaneous abortions, or neonatal deaths. Estimates of the frequency of chromosome abnormalities in spontaneously aborted fetuses range from 15% to 60%.

Chromosomal microarray (CMA) studies of products of conception (POC), a stillborn infant, or a neonate (autopsy) may provide useful information concerning the cause of miscarriage or fetal loss. In addition, CMA may provide information regarding the recurrence risk for future pregnancy loss and risk of having subsequent children with chromosome anomalies. This is particularly useful information if there is a family history of 2 or more miscarriages or when fetal malformations are evident.

CMA is a high-resolution method for detecting copy number changes (gains or losses) across the entire genome in a single assay and is sometimes called a molecular karyotype. This CMA test utilizes over 220,000 markers for the detection of copy number changes and regions with absence of heterozygosity. Identification of regions of excess homozygosity on a single chromosome could suggest uniparental disomy that may warrant further clinical investigation when observed on chromosomes with known imprinting disorders. In addition, the detection of excess homozygosity on multiple chromosomes may suggest consanguinity.

Reference Values
An interpretive report will be provided.

Interpretation
Copy number variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. A normal result will be reported as arr(1-22,X)x2 or arr(1-22)x2,(XY)x1. A copy number change known to be of clinical significance will be reported as pathogenic. Copy number changes with unknown significance will be reported as either likely benign, uncertain, or likely pathogenic. Absence of heterozygosity will be reported.

While many copy number changes observed by chromosomal microarray testing can readily be characterized as pathogenic or benign, there are limited data available to support definitive classification of a subset into either of these categories, making interpretation of these variants challenging. In these situations, a number of considerations are taken into account to help interpret results including the size and gene content of the imbalance, as well as whether the change is a deletion or duplication. Parental testing may also be necessary to further assess the
potential pathogenicity of a copy number change. In such situations, the inheritance pattern and clinical and developmental history of the transmitting parent will be taken into consideration.

The continual discovery of novel copy number variation and published clinical reports means that the interpretation of any given copy number change may evolve with increased scientific understanding.

The detection of excess homozygosity may suggest the need for additional clinical testing to confirm uniparental disomy or to test for mutations in genes associated with autosomal recessive disorders present in regions of homozygosity.

Cautions
This test does not detect balanced chromosome rearrangements such as Robertsonian or other reciprocal translocations, inversions, or balanced insertions.

This test does not detect all types and instances of uniparental disomy.

This test is not designed to detect low-level mosaicism, although it can be detected in some cases.

This test does not detect point mutations, small deletions, or insertions below the resolution of this assay, or other types of mutations such as epigenetic changes.

The results of this test may reveal incidental findings unrelated to the original reason for referral. In such cases, studies of additional family members may be required to help interpret the results.

Supportive Data
The array was validated by testing 25 formalin-fixed, paraffin-embedded products of conception specimens previously tested using FISH analysis. All abnormalities previously identified by another methodology were confirmed.

Clinical Reference


Performance

Method Description
DNA extracted from paraffin-embedded autopsy, products of conception, or stillbirth samples is labeled and hybridized to the microarray. Following hybridization, the microarray is scanned and the intensity of signals is measured and compared to a reference data set. These data are used to determine copy number changes and
regions of excess homozygosity. Chromosomal microarray data alone does not provide information about the structural nature of an imbalance.(Unpublished Mayo method)

PDF Report
No

Day(s) and Time(s) Test Performed
Specimens are processed Monday through Sunday.

Results reported Monday through Friday, 8 a.m.-5 p.m.

Analytic Time
21 days

Maximum Laboratory Time
30 days

Specimen Retention Time
Slides and H and E-stained slide used for analysis are retained by the laboratory. Client provided paraffin blocks and extra unstained slides (if provided) will be returned after testing is complete.

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
81229

LOINC® Information

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### Test Definition: CMAMT
Chromosomal Microarray, POC, FFPE

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