MAYO CLINIC LABORATORIES

Test Definition: CMAMT

Chromosomal Microarray, Autopsy/Products of Conception/Stillbirth, Tissue

Overview

Useful For

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

Diagnosing 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 fluorescence in situ hybridization (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.

Special Instructions

- Informed Consent for Genetic Testing
- Chromosomal Microarray Prenatal and Products of Conception Information
- Informed Consent for Genetic Testing (Spanish)

Method Name

Chromosomal Microarray

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

If a fresh tissue specimen is submitted, this test will be cancelled and CMAPC / Chromosomal Microarray, Autopsy,

Products of Conception, or Stillborn, Varies will be added and performed as the appropriate test.

For answers to frequently asked questions and more information, see Pregnancy loss on MayoClinicLabs.com.

Additional Testing Requirements

A maternal blood sample is requested when ordering this test; order PPAP / Parental Sample Prep for Prenatal Microarray Testing, Blood under a different order number than the prenatal specimen. Maternal cell contamination 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, Blood).

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:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Chromosomal Microarray Prenatal and Products of Conception Information (T716)

Specimen Minimum Volume

Formalin-fixed, paraffin-embedded tissue block
5 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

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Refrigerated		

Clinical & 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. The detection of excess homozygosity on multiple chromosomes may suggest consanguinity. Homozygosity involving the entire genome is indicative of a complete molar pregnancy.

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.

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.

All copy number variants within the limit of detection classified as pathogenic or likely pathogenic will be reported regardless of size. This includes, but is not limited to, incidental findings currently recommended for reporting by the American College of Medical Genetics and Genomics (ACMG).(1) Copy number changes with unknown significance will be reported when at least one protein-coding gene is involved in a deletion greater than 1 megabase (Mb) or a

duplication greater than 2 Mb.

The detection of excessive homozygosity may suggest the need to test for variants in genes associated with autosomal recessive disorders consistent with the patient's clinical presentation that are present in regions of homozygosity. Homozygosity will be reported when involving greater than 20% of the genome. Homozygosity involving the entire genome is indicative of a complete molar pregnancy.
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.

Cautions

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

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

This test does not detect point alterations, small deletions, or insertions below the resolution of this assay, or other types of variants 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 fluorescence in situ hybridization analysis. All abnormalities previously identified by another methodology were confirmed.

Clinical Reference

1. Kalia S, Adelman K, Bale S, et al: Recommendations for reporting of secondary findings in clinical exome and genome sequencing. 2016 update (ACMG SF v2.0): a policy statement of the American College of Medical Genetics and Genomics. Genet Med. 2017;19:249-255
2. American College of Obstetricians and Gynecologists Committee on Genetics: Committee opinion No. 581: the use of chromosomal microarray analysis in prenatal diagnosis. Obstet Gynecol. 2013;122:1374-1377
3. Wapner RJ, Martin CL, Levy B, et al: Chromosomal microarray versus karyotyping for prenatal diagnosis. N Engl J Med. 2012;367:2175-2184
4. Armengol L, Nevado J, Serra-Juhe C, et al: Clinical utility of chromosomal microarray analysis in invasive prenatal diagnosis. Hum Genet. 2012;131:513-523
5. Laurino MY, Bennett RL, Saraiya DS, et al: Genetic evaluation and counseling of couples with recurrent miscarriage: recommendations of the National Society of Genetic Counselors. J Genet Couns. 2005;14:165-181
6. Reddy UM, Page GP, Saade GR, et al: Karyotype versus microarray testing for genetic abnormalities after stillbirth. N Engl J Med. 2012;367:2185-2193

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) Performed
Monday through Friday

Report Available
21 to 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 & 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 account representative. 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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
81229

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CMAMT	Chromosomal Microarray, POC, FFPE	94087-4

Test Definition: CMAMT

Chromosomal Microarray, Autopsy/Products of Conception/Stillbirth, Tissue

Result ID	Test Result Name	Result LOINC® Value
44005	Result Summary	50397-9
44006	Result	62356-1
44007	Nomenclature	62356-1
44008	Interpretation	69965-2
44009	Reason for Referral	42349-1
44010	Specimen	31208-2
44011	Source	31208-2
44012	Tissue ID	80398-1
44013	Method	85069-3
44014	Additional Information	48767-8
44016	Released By	18771-6