MAYO CLINIC LABORATORIES

Test Definition: CMAPC

Chromosomal Microarray, Autopsy, Products of Conception, or Stillbirth

Overview

Useful For

Prenatal diagnosis of copy number changes (gains or losses) across the entire genome

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 by other methods, such as conventional chromosome and fluorescence in situ hybridization studies

Determining if apparently balanced abnormalities identified by previous conventional chromosome studies have cryptic imbalances, as 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

Assessing regions of homozygosity related to uniparental disomy or identical by descent

Genetics Test Information

Cultures from this specimen will be discarded 10 days after all cytogenetic test results have been reported. If additional testing is desired, call the laboratory at 800-533-1710.

Testing Algorithm

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. For more information see Additional Testing Requirements. If an insufficient specimen is received or MCC is identified in the prenatal specimen, microarray testing will be performed on cultured material.

Special Instructions

- Final Disposition of Fetal/Stillborn Remains
- Informed Consent for Genetic Testing
- Chromosomal Microarray Prenatal and Products of Conception Information
- Informed Consent for Genetic Testing (Spanish)

Method Name

Chromosomal Microarray (CMA)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

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

If a formalin-fixed, paraffin-embedded specimen is submitted, the test will be canceled and CMAMT / Chromosomal Microarray, Autopsy/Products of Conception/Stillbirth, Tissue 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 (see PPAP / Parental Sample Prep for Prenatal Microarray Testing, Blood). 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, Blood.

If additional molecular genetic or biochemical genetic testing is needed, order CULAF / Culture for Genetic Testing, Amniotic Fluid or CULFB / Fibroblast Culture for Biochemical or Molecular Testing, Chorionic Villi/Products of Conception/Tissue so that cultures may be set up specifically for use in these tests.

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. Provide a reason for testing 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.
2. Notify the laboratory if the pregnancy involves an egg donor or gestational carrier.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Products of conception or stillbirth
Supplies: Hank's Solution (T132)
Container/Tube: Sterile container with sterile Hank's solution, Ringer's solution, or normal saline
Specimen Volume: 1 cm(3) of placenta (including 50-mg chorionic villi) **and** 1 cm(3) biopsy specimen of muscle/fascia from the thigh
Collection Instructions:
1. Attempt to identify and send only fetal tissue for analysis.
2. If a fetus cannot be specifically identified, collect 50-mg villus material or tissue that appears to be of fetal origin.
3. If multiple specimen types are sent, send each specimen in a separate container. Multiple specimens received (eg,

placenta and fetal thigh) will be ordered under 1 test. All specimens will be processed separately.

Additional Information:

1. **Do not** send entire fetus.
2. **Do not** send the container from a dilation and curettage (D and C) procedure.
3. **Do not** send other containers with large volumes of tissue.
4. While fresher specimens prepared as described above are preferred, we can attempt analysis on specimens that have been in less-than-ideal conditions.

Specimen Type: Autopsy
Supplies: Hank's Solution (T132)
Container/Tube: Sterile container with sterile Hank's solution, Ringer's solution, or normal saline
Specimen Volume: 1 cm(3) biopsy specimen of muscle/fascia from the thigh
Collection Instructions:

1. Wash biopsy site with an antiseptic soap.
2. Thoroughly rinse area with sterile water.
3. Do not use alcohol or iodine preparations.
4. Biopsy specimens are best taken by punch biopsy to include full thickness of dermis.

Specimen Type: Amniotic fluid
Container/Tube: Amniotic fluid container
Specimen Volume: 20 to 30 mL
Collection Instructions:

1. Optimal timing for specimen collection is during 14 to 18 weeks of gestation, but specimens collected at other weeks of gestation are also accepted. Provide gestational age at the time of amniocentesis.
2. Discard the first 2 mL of amniotic fluid.

Additional Information:

1. Unavoidably, about 1% to 2% of mailed-in specimens are not viable.
2. Bloody specimens are undesirable.
3. Results will be reported and telephoned or faxed if requested.

Specimen Type: Chorionic villus
Supplies: CVS Media (RPMI) and Small Dish (T095)
Container/Tube: 15-mL tube containing 15 mL of transport media
Specimen Volume: 50 mg
Collection Instructions:

1. Collect chorionic villus specimen (CVS) by transabdominal or transcervical method.
2. Transfer CVS to a Petri dish containing transport medium (such as CVS Media [RPMI] and Small Dish).
3. Using a stereomicroscope and sterile forceps, assess the quality and quantity of villi and remove any blood clots and maternal decidua.

Acceptable
Specimen Type: Cultured cells
Container/Tube: T25 flasks with culture media
Specimen Volume: 2 T25 flasks

Specimen Type: Tissue
Supplies: Hank's Solution (T132)
Container/Tube: In sterile Hank's solution

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. Final Disposition of Fetal/Stillborn Remains if fetal specimen is sent. Only for products of conception or stillbirth specimens.
3. Chromosomal Microarray Prenatal and Products of Conception Information (T716)

Specimen Minimum Volume

Chorionic villus: 10 mg; Muscle-fascia: 1 cm(3); Other specimen types: See Specimen Required

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, a stillborn infant, or neonate (autopsy) may provide useful information concerning the cause of 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.

Chromosomal microarray 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 greater than 2 million copy number probes and approximately 750,000 single nucleotide polymorphism probes 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.

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.(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 for additional clinical testing to confirm uniparental disomy (UPD) or 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. Regions with absence of heterozygosity (AOH) of unknown significance will be reported when greater than 5 Mb (terminal) and 10 Mb (interstitial) on UPD-associated chromosomes. Whole genome AOH will be reported when greater than 5% of the genome.

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 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 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 30 direct and cultured samples previously tested using chromosome analysis or 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(2):249-255. doi:10.1038/gim.2016.190
2. Shao L, Akkari Y, Cooley LD, et al. Chromosomal microarray analysis, including constitutional and neoplastic disease applications, 2021 revision: a technical standard of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2021;23(10):1818-1829. doi:10.1038/s41436-021-01214-w
3. Society for Maternal-Fetal Medicine (SMFM), Dugoff L, Norton ME, Kuller JA: The use of chromosomal microarray for prenatal diagnosis. Am J Obstet Gynecol. 2016;215(4):B2-B9. doi:10.1016/j.ajog.2016.07.016
4. Sahoo T, Dzidic N, Strecker MN, et al: Comprehensive genetic analysis of pregnancy loss by chromosomal microarrays: Outcomes, benefits, and challenges. Genet Med. 2017;19(1):83-89. doi:10.1038/gim.2016.69
5. Rosenfeld JA, Tucker ME, Escobar LF, et al: Diagnostic utility of microarray testing in pregnancy loss. Ultrasound Obstet Gynecol. 2015;46(4):478-486. doi:10.1002/uog.14866

Performance

Method Description

DNA extracted from either 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, and some abnormal results may be characterized by fluorescence in situ hybridization, limited chromosome analysis, or additional techniques.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

10 to 25 days

Specimen Retention Time

Any identifiable fetal tissue (eg, skin, muscle) is held until the completion of testing and is eventually cremated on a quarterly basis. All other tissue (eg, placenta, chorionic villus) is discarded at the time results are reported.

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

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
CMAPC	Chromosomal Microarray, POC	94087-4

Result ID	Test Result Name	Result LOINC® Value
55253	Result Summary	86611-1
55254	Result	62356-1
55255	Nomenclature	62378-5
55256	Interpretation	62357-9
CG945	Reason for Referral	42349-1
CG946	Specimen	31208-2
55257	Source	48002-0
55259	Additional Information	48767-8
55260	Released By	18771-6
55258	Method	85069-3