MAYO CLINIC LABORATORIES

Test Definition: CMAP

Chromosomal Microarray, Prenatal, Amniotic Fluid/Chorionic Villus Sampling

Overview

Useful For

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

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 identity 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 if a maternal blood sample is received to rule out the presence of maternal cells in the prenatal sample, see Additional Testing Requirements.

If an insufficient sample is received or MCC is identified in the prenatal sample, microarray testing will be performed on cultured material.

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 (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. These abnormalities may be identified by chromosome analysis; see CHRAF / Chromosome Analysis, Amniotic Fluid or CHRCV / Chromosome Analysis, Chorionic Villus Sampling.

If the reason for testing or specimen type received indicates a fetal demise, this test will be canceled and CMAPC / Chromosomal Microarray, Autopsy, Products of Conception, or Stillbirth will be added and performed as the appropriate test.

Additional Testing Requirements

A maternal blood sample is requested when ordering this test (see PPAP / Parental Sample Prep for Prenatal Microarray Testing, Blood); 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).

Portions of the specimen may be used for other tests such as measuring markers for neural tube defects (eg, AFPA / Alpha-Fetoprotein, Amniotic Fluid), molecular genetic testing, biochemical testing, and chromosome and fluorescence in situ hybridization (FISH) testing (including CHRAF / Chromosome Analysis, Amniotic Fluid; CHRCV / Chromosome Analysis, Chorionic Villus Sampling; and PADF / Prenatal Aneuploidy Detection, FISH).

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: Chorionic villi
Supplies: CVS Media (RPMI) and Small Dish (T095)
Container/Tube: 15-mL tube containing 15 mL of transport media
Specimen Volume: 20 to 30 mg
Collection Instructions:
1. Collect specimen by the transabdominal or transcervical method.
2. Transfer chorionic villi 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 the villi and remove any blood clots and maternal decidua.

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.

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

Amniotic fluid: 12 mL; Chorionic villi: 12 mg; If ordering in conjunction with other testing: With PADF: 14 mL or 14 mg; with CHRAF: 24 mL; with CHRCV: 24 mg; with PADF and CHRAF/CHRCV: 26 mL or 26 mg

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	Refrigerated (preferred)		
	Ambient		

Clinical & Interpretive

Clinical Information

Chromosomal abnormalities cause a wide range of disorders associated with birth defects and intellectual disability. Many of these disorders can be diagnosed prenatally by analysis of chorionic villi or amniocytes.

The most common reasons for performing cytogenetic studies for prenatal diagnosis include advanced maternal age, abnormal prenatal screen, a previous child with a chromosome abnormality, abnormal fetal ultrasound, or a family history of a chromosome abnormality. Chromosomal microarray (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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine

recommend the chromosomal microarray as a replacement for the fetal karyotype in patients with a pregnancy demonstrating one or more major structural abnormalities on ultrasound when undergoing invasive prenatal diagnosis.(1)

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 excessive homozygosity on a single chromosome could suggest uniparental disomy, which may warrant further clinical investigation when observed on chromosomes with known imprinting disorders. In addition, the detection of excessive 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.

When interpreting results, it is important to realize that copy number variation is found in all individuals, including patients with abnormal phenotypes and normal populations. Therefore, determining the clinical significance of a rare or novel copy number change can be challenging. Parental testing may be necessary to further assess the potential pathogenicity of a copy number change.

While most 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. In these situations, a number of considerations are taken into account to help interpret results including the size and gene content of the imbalance, whether the change is a deletion or duplication, the inheritance pattern, and the clinical and developmental history of a transmitting parent.

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.(2) 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 not related to the original reason for referral. In such cases, studies of additional family members may be required to help interpret the results.

Clinical Reference

1. 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
2. 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
3. Wapner RJ, Martin CL, Levy B, et al. Chromosomal microarray versus karyotyping for prenatal diagnosis. N Engl J Med. 2012;367(23):2175-2184. doi:10.1056/NEJMoa1203382
4. Armengol L, Nevado J, Serra-Juhe C, et al. Clinical utility of chromosomal microarray analysis in invasive prenatal diagnosis. Hum Genet. 2012;131(3):513-523. doi:10.1007/s00439-011-1095-5
5. Breman A, Pursley AN, Hixson P, et al. Prenatal chromosomal microarray analysis in a diagnostic laboratory; experience with >1000 cases and review of the literature. Prenat Diagn. 2012;32(4):351-361. doi:10.1002/pd.3861
6. South ST, Lee C, Lamb AN, et al. ACMG Standards and Guidelines for constitutional cytogenomic microarray analysis, including postnatal and prenatal applications: Revision 2013. Genet Med. 2013;15(11):903-909. doi:10.1038/gim.2013.129

Performance

Method Description

DNA extracted from either amniotic fluid or chorionic villus sample 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

6 to 21 days

Specimen Retention Time

Amniotic fluid: Discarded 14 days after results reported. Chorionic villi: Not retained.

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
CMAP	Chromosomal Microarray, Prenatal	86611-1

Result ID	Test Result Name	Result LOINC® Value
54714	Result Summary	50397-9
54715	Result	62356-1
54716	Nomenclature	62356-1
54717	Interpretation	69965-2
CG900	Reason for Referral	42349-1
CG780	Specimen	31208-2
54718	Source	31208-2
54719	Method	85069-3
53422	Additional Information	48767-8
54720	Released By	18771-6