MAYO CLINIC LABORATORIES

Test Definition: CMACB

Chromosomal Microarray, Congenital, Blood

Overview

Useful For

First-tier, postnatal testing for individuals with multiple anomalies that are not specific to well-delineated genetic syndromes, apparently nonsyndromic developmental delay or intellectual disability, or autism spectrum disorders as recommended by the American College of Medical Genetics and Genomics

Follow-up testing for individuals with unexplained developmental delay or intellectual disability, autism spectrum disorders, or congenital anomalies with a previously normal conventional chromosome study

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, 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

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

Testing Algorithm

The following algorithms are available:

-Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm

-Prader-Willi and Angelman Syndromes: Laboratory Approach to Diagnosis

Special Instructions

- Informed Consent for Genetic Testing
- Prader-Willi and Angelman Syndromes: Laboratory Approach to Diagnosis
- Chromosomal Microarray Patient Information
- GenomeConnect Patient Portal
- Family Member Phenotype Information for Genomic Testing
- Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm
- Informed Consent for Genetic Testing (Spanish)

Method Name

Chromosomal Microarray

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

This test is **not appropriate** for detecting acquired copy number changes and excessive homozygosity. If this test is ordered with a reason for testing indicating a hematological disorder, the test will be canceled and CMAH / Chromosomal Microarray, Hematologic Disorders, Varies will be ordered and performed as the appropriate test.

Necessary Information

The reason for testing is required.

Specimen Required

This test requires 2 blood specimens: 1 sodium heparin and 1 EDTA. Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube: Green top (sodium heparin) **and** lavender top (EDTA)
Specimen Volume: 3-mL EDTA tube **and** 4-mL sodium heparin tube
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimens in original tubes. **Do not aliquot.**

Specimen Type: Cord blood
Container/Tube: Green top (sodium heparin) **and** lavender top (EDTA)
Specimen Volume: 3-mL EDTA tube **and** 4-mL sodium heparin tube
Note: The lab will attempt testing on a minimum of 1-mL whole blood, EDTA preferred.
Collection Instructions:
1. Invert several times to mix blood.
2. Send cord blood specimens in original tubes. **Do not aliquot.**
3. Label specimen as cord blood.

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 Patient Information (T665)
3. Family Member Phenotype Information for Genomic Testing
4. If not ordering electronically, complete, print, and send a Neurology Specialty Testing Client Test Request (T732) with the specimen.

Specimen Minimum Volume

2 mL

Reject Due To

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

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)		
	Refrigerated		

Clinical & Interpretive

Clinical Information

Aneuploidy or unbalanced chromosome rearrangements are often found in patients with intellectual disability, developmental delay, autism, dysmorphic features, or congenital anomalies. Some chromosomal abnormalities are large enough to be detected with conventional chromosome analysis. However, many pathogenic rearrangements are below the resolution limits of chromosome analysis (approximately 5 megabases). 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.

This CMA test utilizes greater than 1.9 million copy number probes and approximately 750,000 single nucleotide polymorphism probes for the detection of copy number changes and regions of excessive homozygosity. Identification of regions of excessive homozygosity on a single chromosome could suggest uniparental disomy (UPD), which may warrant further clinical investigation when observed on chromosomes with known imprinting disorders associated with UPD. In addition, the detection of excessive homozygosity on multiple chromosomes may suggest consanguinity and, therefore, could be useful in determining candidate genes for further testing for autosomal recessive disorders.

An online research opportunity called GenomeConnect (genomeconnect.org) is available for the recipients of genetic test results. This patient registry collects deidentified genetic and health information to advance knowledge of genetic variants. For more information see GenomeConnect Patient Portal.

Reference Values

An interpretive report will be provided.

Interpretation

When interpreting results, the following factors need to be considered:
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/or 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 (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 200 kilobases (kb) or a duplication greater than 1 megabase (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. Interstitial regions with absence of heterozygosity (AOH) of unknown significance will be reported when greater than 10 Mb on UPD-associated chromosomes, and greater than 15 Mb on non-imprinted chromosomes. Terminal AOH will be reported when greater than 5 Mb. Whole genome AOH will be reported when greater than 2% 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.

Families benefit from hearing genetic information multiple times and in multiple ways. A referral to a clinical genetics professional is appropriate for individuals and families to discuss the results of chromosomal microarray testing.

Cautions

This test is not approved by the US Food and Drug Administration and it is best used as an adjunct to existing clinical and pathologic information.

Chromosomal microarray data alone does not provide information about the structural nature of an imbalance.

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 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.

Families benefit from hearing genetic information multiple times and in multiple ways. A referral to a clinical genetics professional is appropriate for individuals and families to discuss the results of chromosomal microarray testing.

Interfering factors:
-Use of an improper anticoagulant (sodium heparin is best) or improperly mixing the blood with the anticoagulant
-Excessive transport time
-Inadequate amount of blood
-Improper packaging may result in broken, leaky, and contaminated specimen during transport

Supportive Data

The array was validated by testing 113 specimens previously tested using another array platform, chromosome analysis,

fluorescence in situ hybridization (FISH) analysis, or a polymerase chain reaction (PCR)-based assay. The study set included specimens from phenotypically normal individuals, and patients identified with a gain or loss of an autosome or sex chromosome or identified with uniparental disomy. All abnormalities were confirmed.

Clinical Reference

1. Kalia SS, Adelman K, Bale SJ, 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 Feb;19(2):249-255. doi: 10.1038/gim.2016.190
2. Manning M, Hudgins L, Professional Practice and Guidelines Committee: Array-based technology and recommendations for utilization in medical genetics practice for detection of chromosomal abnormalities. Genet Med. 2010 Nov;12(11):742-745. doi: 10.1097/GIM.0b013e3181f8baad
3. Miller DT, Adam MP, Aradhya S, et al: Consensus statement: Chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies. Am J Hum Genet. 2010 May;86(5):749-764. doi: 10.1016/j.ajhg.2010.04.006
4. Kearney HM, Thorland EC, Brown KK, et al: American College of Medical Genetics standards and guidelines for interpretation and reporting of postnatal constitutional copy number variants. Genet Med. 2011 Jul;13(7)680-685. doi: 10.1097/GIM.0b013e3182217a3a
5. Kearney HM, Kearney JB, Conlin LK: Diagnostic implications of excessive homozygosity detected by SNP-based microarrays: consanguinity, uniparental disomy, and recessive single-gene mutations. Clin Lab Med. 2011 Dec;31(4):595-613. doi: 10.1016/j.cll.2011.08.003
6. Marcou CA, Pitel B, Hagen CE, et al: Limited diagnostic impact of duplications <1 Mb of uncertain clinical significance: a 10-year retrospective analysis of reporting practices at the Mayo Clinic. Genet Med. 2020 Dec;22(12):2120-2124. doi: 10.1038/s41436-020-0932-0

Performance

Method Description

DNA extracted from the patient's peripheral blood 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 (FISH), limited chromosome analysis, or additional techniques.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

8 to 21 days

Specimen Retention Time

Four weeks

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
CMACB	Chromosomal Microarray, Blood	62343-9

Result ID	Test Result Name	Result LOINC® Value
52399	Result Summary	50397-9
52400	Result	82939-0
54643	Nomenclature	62378-5
52401	Interpretation	69965-2
CG779	Reason For Referral	42349-1
54713	Specimen	31208-2
52402	Source	31208-2
52403	Method	85069-3
52404	Released By	18771-6
55128	Additional Information	48767-8