MAYO CLINIC LABORATORIES

Test Definition: CMAH

Chromosomal Microarray, Hematologic Disorders, Varies

Overview

Useful For

Detection and characterization of clonal copy number imbalance and loss of heterozygosity associated with hematologic neoplasms

Assisting in the diagnosis and classification of certain hematologic neoplasms

Evaluating the prognosis for patients with certain hematologic neoplasms

Testing Algorithm

DNA extraction is always performed on the specimen prior to hybridization to the microarray. An unstimulated cell culture will be set up on all specimens with adequate volume and held pending additional testing. If additional testing is requested, such as karyotype analysis or fluorescence in situ hybridization, it will be performed at an additional charge.

The following algorithms are available:
-Aggressive B-cell Lymphoma Diagnostic Algorithm
-B-Lymphoblastic Leukemia/Lymphoma Algorithm

Special Instructions

- Aggressive B-cell Lymphoma Diagnostic Algorithm
- B-Lymphoblastic Leukemia/Lymphoma Algorithm

Method Name

Chromosomal Microarray (CMA) Using Applied Biosystems (Affymetrix) Cytoscan HD

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test is not appropriate for detecting constitutional/congenital copy number changes or regions of excessive homozygosity. If this test is ordered with a reason for testing indicating a constitutional/congenital disorder, the test will be canceled and CMACB / Chromosomal Microarray, Congenital, Blood will be performed as the appropriate test.

Necessary Information

1. **A reason for testing must be provided for testing to be performed.**
2. A pathology report should accompany the specimen. If this information is not available at the time of order, submit as soon as possible for appropriateness of testing and to aid in interpretation of results.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Bone marrow
Container/Tube:
Preferred: Green top (sodium heparin)
Acceptable: Lavender top (EDTA)
Specimen Volume: 1-2 mL
Collection Instructions:
1. Invert several times to mix bone marrow.
2. Send bone marrow specimen in original tube. **Do not aliquot**.

Specimen Type: Whole blood
Container/Tube:
Preferred: Green top (sodium heparin)
Acceptable: Lavender top (EDTA)
Specimen Volume: 7-10 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.

Forms

If not ordering electronically, complete, print, and send a Hematopathology/Cytogenetics Test Request (T726) with the specimen.

Specimen Minimum Volume

Blood: 2 mL
Bone marrow: 1 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
Varies	Ambient (preferred)		
	Refrigerated		

Clinical & Interpretive

Clinical Information

The importance of identifying chromosome abnormalities in hematologic disorders is well established and often provides important diagnostic, prognostic, and therapeutic information critical to proper patient management. Although many chromosomal abnormalities are large enough to be detected with conventional chromosome analysis, many others are below its limits of resolution, and conventional chromosome analysis does not detect copy-neutral loss of heterozygosity.

Chromosomal microarray (CMA) improves the diagnostic yield to identify genetic changes that are not detected by conventional chromosome analysis or fluorescence in situ hybridization (FISH) studies. CMA utilizes greater than 1.9 million copy number probes and approximately 750,000 single nucleotide polymorphism probes to detect copy number changes and regions of copy-neutral loss of heterozygosity.

CMA analysis is appropriate to identify gain or loss of chromosome material throughout the genome at a resolution of 30 to 60 kilobases. CMA can do the following:
-Define the size, precise breakpoints, and gene content of copy number changes to demonstrate the complexity of abnormalities
-Characterize unidentified chromosome material, marker chromosomes, and DNA amplification detected by conventional chromosome and FISH studies
-Determine if apparently balanced chromosome rearrangements identified by conventional chromosome studies have cryptic imbalances
-Assess regions of copy-neutral loss of heterozygosity, which is common in neoplasia and often masks homozygous mutations involving tumor suppressor genes

The limit of detection is dependent on size of the abnormality, type of abnormality (deletion or duplication) and DNA quality. When a deletion or duplication exceeds the reporting limits, mosaicism can confidently be detected as low as 25% and may be lower if the abnormality is large and DNA quality is good.

Reference Values

An interpretive report will be provided.

Interpretation

The interpretive report describes copy number changes and any loss of heterozygosity that may be associated with the neoplastic process. Abnormal clones with subclonal cytogenetic evolution will be discussed if identified.

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.

Although the presence of a clonal abnormality usually indicates a neoplasia, in some situations it may reflect a benign or constitutional genetic change. If a genetic change is identified that is likely constitutional and clearly pathogenic (eg, XYY), consultation with a Clinical Geneticist may be suggested.

The absence of an abnormal clone may be the result of specimen collection from a site that is not involved in the neoplasm or may indicate that the disorder is caused by a point mutation that is not detectable by chromosomal microarray (CMA).

CMA, fluorescence in situ hybridization (FISH), and conventional cytogenetics are to some extent complementary methods. In some instances, additional FISH or conventional cytogenetic studies will be recommended to clarify interpretive uncertainties.

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.

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

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

Low level abnormal clones may not be detected by this test; as such it is not recommended for minimal residual disease.

This test does not identify tetraploidy, although in concert with other studies tetraploidy can be inferred.

The results of this test may reveal incidental findings not related to the original reason for testing.

Supportive Data

The chromosomal microarray was validated on the Affymetrix CytoScan HD platform in a blinded study of 30 specimens from a variety of hematologic disorders. Results were correlated to previous conventional karyotype and fluorescence in situ hybridization analysis.

Clinical Reference

1. Cooley L, Lebo M, Li M, et al: American College of Medical Genetics and Genomics technical standards and guidelines: microarray analysis for chromosome abnormalities in neoplastic disorders. Genet Med. 2013 Jun;15(6):484-494
2. Dougherty M, Wilmoth D, Tooke L, et al: Implementation of high resolution single nucleotide polymorphism array analysis as a clinical test for patients with hematologic malignancies. Cancer Genetics. 2011 Jan;204(1):26-38
3. Schwartz, S: Clinical Utility of Single Nucleotide Polymorphism Arrays. Clin Lab Med. 2011 Dec;31(4):581-594
4. Braggio E, Kay N, VanWier S, et al: Longitudinal genome-wide analysis of patients with chronic lymphocytic leukemia reveals complex evolution of clonal architecture at disease progression and at the time of relapse. Leukemia. 2012 Jul;26(7):1698-1701

Performance

Method Description

DNA extracted from the patient's bone marrow or 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 with loss of heterozygosity. Chromosomal microarray data alone do not provide information about the structural nature of an imbalance. Thus, it may be of

benefit to utilize fluorescence in situ hybridization or additional techniques to further characterize a patient sample.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
8 to 21 days

Specimen Retention Time
4 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
81277

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CMAH	Chromosomal Microarray, Hematologic	94087-4

Result ID	Test Result Name	Result LOINC® Value
54721	Result Summary	50397-9
54722	Result	62356-1
54723	Nomenclature	62378-5
54724	Interpretation	69965-2

CG902	Reason for Referral	42349-1
CG903	Specimen	31208-2
54725	Source	31208-2
54726	Method	85069-3
53423	Additional Information	48767-8
54727	Released By	18771-6