Test Definition: MPAML

MatePair, AML Panel

Overview

Useful For

Detecting a neoplastic clone associated with the common chromosome abnormalities seen in patients with acute myeloid leukemia or myelodysplasia or other myeloid malignancies

Evaluating specimens when standard cytogenetic or FISH analysis is unsuccessful

Determining the size, precise breakpoints, gene content, and any unappreciated complexity of abnormalities detected by other methods such as conventional chromosome and FISH studies

Providing important diagnostic, prognostic, and therapeutic information critical to proper patient management

Genetics Test Information

This assay detects targeted chromosome abnormalities observed in the blood and bone marrow of patients with acute myeloid leukemia.

Special Instructions

- Informed Consent for Genetic Testing
- Informed Consent for Genetic Testing (Spanish)

Method Name

Mate-Pair Whole Genome Sequencing

NY State Available

No

Specimen

Specimen Type

Varies

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. **A reason for referral 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: Green top (sodium heparin)

Specimen Volume: 1-2 mL

Collection Instructions:

1. Invert several times to mix bone marrow.

2. If sodium heparin is not available, EDTA is acceptable.

Specimen Type: Whole blood

Container/Tube: Green top (sodium heparin)

Specimen Volume: 7-10 mL

Collection Instructions:

1. Invert several times to mix blood.

2. If sodium heparin is not available, EDTA is acceptable.

Forms

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 in Special Instructions:

-Informed Consent for Genetic Testing (T576)

-Informed Consent for Genetic Testing-Spanish (T826)

Specimen Minimum Volume

Bone Marrow: 1 mL
Blood: 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 and Interpretive

Clinical Information

Acute myeloid leukemia (AML) is one of the most common adult leukemias, with almost 10,000 new cases diagnosed per year. AML also comprises 15% of pediatric acute leukemia and accounts for the majority of infant (<1 year old) leukemia. Several subtypes of AML have been recognized based on the cell morphology and myeloid

lineage involved.

In addition to morphology, several recurrent chromosomal abnormalities have been linked to specific subtypes of AML. The most common chromosome abnormalities associated with AML include t(8;21), t(15;17), inv(16), +8, t(6;9), t(8;16), t(1;22), t(9;22), t(3;5), and abnormalities of the *KMT2A* (MLL) gene at 11q23. The most common genes juxtaposed with *KMT2A* (MLL) through translocation events in AML include *AFF1* t(4;11), *MLLT4* t(6;11), *MLLT3* t (9;11), *MLLT10* t(10;11), *CREBBP* t(11;16), *ELL* t(11;19p13.1), and *MLLT1* t(11;19p13.3).

AML can also evolve from myelodysplasia (MDS). Thus, the common chromosome abnormalities associated with MDS can also be identified in AML, which include: inv(3), -5/5q-, -7/7q-, +8, 13q-, 17p-, 20q-, t(1;3), and t(3;21). In combination, the multiple recurrent chromosome abnormalities identified in patients with AML are observed in approximately 60% of diagnostic AML cases.

Conventional chromosome analysis is the gold standard for identification of the common, recurrent chromosome abnormalities in AML; however, some of the subtle rearrangements can be missed (eg, inv[16] and *KMT2A* [MLL] abnormalities). FISH analysis of nonproliferating (interphase) cells can be used to detect the common chromosome abnormalities observed in patients with AML, however, only a few *KMT2A* (MLL) gene partners are detected. The abnormalities have diagnostic and prognostic relevance and this testing can also be used to track response to therapy.

Mate-pair sequencing (MPS) is a next-generation sequencing technology that can aid in the further characterization of chromosome abnormalities by sequencing the entire genome and bioinformatically mapping short fragments of the genome to create a structural map of the genome. This technique enables the mapping of chromosome rearrangements to a resolution of approximately 2 kilobases or less, which allows for determination of genes at or near the breakpoints. MPS, similar to FISH analysis, can also be used on nonproliferating cells to detect common chromosome abnormalities observed in patients with AML. In addition, MPS is able to detect all gene partners for all the genes included on the panel, for example *KMT2A* (MLL) gene partners.

Reference Values

An interpretive report will be provided.

Interpretation

The interpretation describes the common chromosome abnormalities observed in patients with acute myeloid leukemia (AML) and the abnormalities have diagnostic and prognostic relevance. Mate-pair sequencing (MPS) is also able to further characterize previously identified acquired abnormalities. When possible the interpretation will state how the finding might be associated with the hematologic process and any potential information on diagnosis, prognosis, and treatment options given the finding.

The continual discovery of novel structural rearrangements and published clinical reports means that the interpretation of any finding 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, follow-up with a medical genetics consultation 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 genetic abnormality is not detectable by this assay.

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 is not appropriate when the reason for referral indicates acute promyelocytic leukemia (APL). FISH testing for t(15;17) is more appropriate.

This test does not detect point mutations, small deletions or insertions below the resolution of the assay, or other types of mutations 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 monitoring.

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

Clinical Reference

1. Grimwade D, Hills RK, Moorman AV, et al: Refinement of cytogenetics classification in acute myeloid leukemia: determination of prognostic significance or rare recurring chromosomal abnormalities among 5879 younger adult patients treated in the United Kingdom Research Council trials. Blood 2010 Jul;116(3):354-365

2. International Agency for Research on Cancer (IARC): World Health Organization (WHO) classification of tumour of haematopoietic and lymphoid tissues. Edited by SH Swerdlow, E Campo, NL Harris, et al. IARC Press, Oxford: Oxford University Press (distributor), 2008

Performance

Method Description

DNA is extracted from the patientâ€™s peripheral blood or bone marrow and a genomic DNA library is prepared for mate-pair sequencing. Reads are aligned to the human genome and evaluated for the rearrangement of interest.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Specimens are processed Monday through Friday.

Results reported Monday through Friday, 8 a.m.-5 p.m.

Analytic Time

14 days

Maximum Laboratory Time

28 days

Specimen Retention Time

4 weeks

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

0056U

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
MPAML	MatePair, AML Panel	94588-1

Result ID	Test Result Name	Result LOINC Value
113478	Result Summary	50397-9
113479	Interpretation	69965-2
113480	Result Table	93356-4
113481	Result	94592-3
113482	Nomenclature	62356-1
GC010	Reason for Referral	42349-1
GC011	Specimen	31208-2
113483	Source	22633-2
113484	Method	49549-9
113485	Additional Information	48767-8
113486	Released By	18771-6