MAYO CLINIC LABORATORIES

Test Definition: NGAML

MayoComplete Acute Myeloid Leukemia, 11-Gene Panel, Varies

Overview

Useful For

Evaluation of acute myeloid leukemia using a focused 11-gene panel at the time of diagnosis, or possibly at the time of relapsed/refractory disease, to help guide classification and possible therapeutic approaches

Genetics Test Information

This test includes next-generation sequencing to evaluate for the following 11 genes: *CEBPA, DNMT3A, FLT3, IDH1, IDH2, KIT, KRAS, NPM1, NRAS, RUNX1,* and *TP53.*

Testing Algorithm

For a list of genes and exons targeted by this test see Targeted Genes Interrogated by Acute Myeloid Leukemia, 11-Gene Panel.

Special Instructions

- Hematopathology Patient Information
- Targeted Genes Interrogated by Acute Myeloid Leukemia, 11-Gene Panel

Highlights

Next-generation sequencing detection of somatic gene mutations, including type, pattern, and distribution, has diagnostic, prognostic, and potential therapeutic implications for patients with hematologic cancers, such as acute myeloid leukemia (AML).

This test enables more accurate classification and prognostic assessment of AML.

Method Name

Next-Generation Sequencing (NGS)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This gene panel is a subset of the NGSHM / MayoComplete Myeloid Neoplasms, Comprehensive OncoHeme Next-Generation Sequencing, Varies test and focuses more specifically on the gene mutations that are most prevalent and clinically significant in acute myeloid leukemias (AML). If a wider gene mutation analysis is desired or the indication

for testing is for a myeloid malignancy other than AML, consider NGSHM.

Shipping Instructions

Bone marrow and whole blood specimens must arrive within 14 days of collection.

Necessary Information

The following information is required:

1. Clinical diagnosis
2. Pertinent clinical history, including disease phase (diagnostic, remission, relapse/refractory) and therapy status (especially if patient has received a hematopoietic stem cell transplant).
3. Clinical or morphologic suspicion
4. Date of collection
5. Specimen source

Specimen Required

Submit only 1 of the following specimens:

Preferred:

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

Specimen Stability Information: Ambient (preferred) 14 days/Refrigerate 14 days
Additional Information: To ensure minimum volume and concentration of DNA is met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.

Acceptable:

Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA) or yellow top (ACD)
Acceptable: Green top (sodium heparin)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**
3. Label specimen as blood.

Specimen Stability Information: Ambient (preferred) 14 days/Refrigerate 14 days
Additional Information: To ensure minimum volume and concentration of DNA is met, the requested volume must be

submitted. Testing may be canceled if DNA requirements are inadequate.

Specimen Type: Extracted DNA from blood or bone marrow
Container/Tube: 1.5 to 2 mL tube
Specimen Volume: Entire specimen
Collection Instructions:
1. DNA must be extracted within 14 days after collection.
2. Label specimen as extracted DNA and source of specimen.
3. Provide volume and concentration of the DNA.
Specimen Stability Information: Frozen (preferred)/Refrigerated/Ambient
Additional Information: DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). We cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied.

Forms

1. Hematopathology Patient Information (T676)
2. If not ordering electronically, complete, print, and send a Hematopathology/Cytogenetics Test Request (T726) with the specimen.

Specimen Minimum Volume

Whole blood, one marrow: 1 mL; Extracted DNA: 100 mcL at 20 ng/mcL concentration

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Bone marrow biopsies Slides Paraffin shavings or frozen tissues Paraffin-embedded tissues Paraffin-embedded bone marrow aspirates Moderately to severely clotted	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies	14 days	

Clinical & Interpretive

Clinical Information

Next-generation sequencing is a comprehensive molecular diagnostic methodology that can interrogate multiple regions of genomic tumor DNA in a single assay. Many hematologic neoplasms, including acute myeloid leukemia (AML), are characterized by morphologic or phenotypic similarities but can have characteristic somatic mutations in several genes that enable more specific categorization. In addition, many cases of AML lack a clonal cytogenetic finding at diagnosis (normal karyotype) and can be better classified according to gene mutation profile. The presence and pattern of gene mutations in AML can provide critical prognostic information and may help in guiding therapeutic management decisions by physicians, particularly if targeted therapies are available.

Reference Values

An interpretive report will be provided

Interpretation

Detailed variant assessment and interpretive comments will be provided for all reportable genetic alterations.

Cautions

This test is a targeted next-generation sequencing (NGS) assay that encompasses 11 genes with variable full exon, partial region (including select intronic or noncoding regions), or hot spot coverage (depending on specific locus). Therefore, this test will not detect other genetic abnormalities in genes or regions outside the specified target areas. The test detects single base substitutions (ie, point mutations), as well as small insertion or deletion type events, but it does not detect gene rearrangements (ie, translocations), gene fusions, copy number alterations, or large scale (segmental chromosome region) deletions and complex changes.

This assay does not distinguish between somatic and germline alterations in analyzed gene regions, particularly with variant allele frequencies near 50% or 100%. If nucleotide alterations in genes associated with germline variant syndromes are present and there is a strong clinical suspicion or family history of malignant disease predisposition, additional genetic testing and appropriate counseling may be indicated. A low incidence of gene mutations associated with myeloid neoplasms can be detected in nonmalignant hematopoietic cells in individuals with advancing age (clonal hematopoiesis of indeterminate potential), and these may not be clearly distinguishable from tumor-associated mutations. Some apparent mutations classified as variants of uncertain significance may represent rare or low-frequency polymorphisms.

Prior treatment for hematologic malignancy could affect the results obtained in this assay. In particular, a prior allogeneic hematopoietic stem cell transplant may cause difficulties in resolving somatic or polymorphic alterations or assigning variant calls correctly to donor and recipient fractions, if pertinent clinical or laboratory information (eg, chimerism engraftment status) is not provided.

The finding of a genetic alteration does not necessarily indicate the presence of a myeloid neoplasm. Correlation with clinical, histopathologic, and additional laboratory findings is required for final interpretation of NGS results and is the responsibility of the managing physician.

Clinical Reference

1. Pollyea DA, Altman JK, Assi R, et al. Acute Myeloid Leukemia, Version 3.2023, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2023;21(5):503-513. doi:10.6004/jnccn.2023.0025
2. DiNardo CD, Stein EM, de Botton S, et al. Durable remissions with ivosidenib in IDH1-mutated relapsed or refractory AML. N Engl J Med. 2018;378(25):2386-2398. doi:10.1056/NEJMoa1716984
3. Stein EM, DiNardo CD, Fathi AT, et al. Molecular remission and response patterns in patients with mutant-IDH2 acute myeloid leukemia treated with enasidenib. Blood. 2019;133(7):676-687. doi:10.1182/blood-2018-08-869008
4. Dohner H, Estey E, Grimwade D, et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. Blood. 2017;129(4):424-447. doi:10.1182/blood-2016-08-733196
5. Smith CC. The growing landscape of FLT3 inhibition in AML. Hematology Am Soc Hematol Educ Program. 2019;2019(1):539-547. doi:10.1182/hematology.2019000058
6. Daver N, Schlenk RF, Russell NH, Levis MJ. Targeting FLT3 mutations in AML: review of current knowledge and evidence. Leukemia. 2019;33(2):299-312. doi:10.1038/s41375-018-0357-9

Performance

Method Description

Next-generation sequencing (NGS) is performed to test for the presence of a mutation in targeted regions in 11 genes. For more information see Targeted Genes Interrogated by Acute Myeloid Leukemia, 11-Gene Panel. This is a laboratory-developed target enriched NGS panel. DNA is extracted from validated specimen sources including whole blood and bone marrow. Library preparation for NGS is performed followed by probe hybridization and capture. Sequencing of the final sample library is performed on a NGS instrument. Following bioinformatic processing of the sequencing data, the sequencing results are interpreted to provide a final clinical report. Genomic alterations are called according to human genome reference build GRCh37 (hg19).(Unpublished Mayo method)

Genes analyzed: *CEBPA, DNMT3A, FLT3, IDH1, IDH2, KIT, KRAS, NPM1, NRAS*, *RUNX1*, and *TP53*

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

16 to 21 days

Specimen Retention Time

Whole blood, bone marrow: 2 weeks; Extracted DNA 3 months

Test Definition: NGAML

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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

81450

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
NGAML	AML, 11 Gene, NGS, V	105343-8

Result ID	Test Result Name	Result LOINC® Value
43554	NGAML Result	No LOINC Needed
43488	Pathogenic Mutations Detected	82939-0
43487	Interpretation	69047-9
43489	Clinical Trials	82786-5
43490	Variants of Unknown Significance	93367-1
43491	Additional Notes	48767-8
43492	Method Summary	85069-3
43493	Disclaimer	62364-5
43494	AML Panel Gene List	36908-2
43495	Reviewed By	18771-6
MP038	Specimen Type	31208-2