MAYO CLINIC LABORATORIES

Test Definition: AMLMF

Acute Myeloid Leukemia (AML), Specified
FISH, Varies

Overview

Useful For

Detecting recurrent common chromosome abnormalities seen in patients with acute myeloid leukemia (AML) using a client-specified probe set

An adjunct to chromosome studies in patients with AML

Evaluating specimens in which chromosome studies are unsuccessful

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
AMLMB	Probe, Each Additional (AMLMF)	No, (Bill Only)	No

Testing Algorithm

This test includes a charge for the probe application, analysis, and professional interpretation of results for one probe set (2 individual fluorescence in situ hybridization probes). Additional charges will be incurred for all additional probe sets performed.

This is not intended as a panel test and the desired probes must be specified upon order. If the patient is being evaluated for known abnormalities, targeted probes must be listed in the probe request field. Reflex probes can be performed when appropriate **only** if specified in the order request field.

When specified, any of the following probes will be performed:
t(8;21), RUNX1T1::RUNX1
Reflex: t(3;21)(q26.2;q22) MECOM::RUNX1
t(15;17), PML::RARA
Reflex: 17q21 rearrangement, RARA break-apart
11q23 rearrangement, MLL (KMT2A)
Reflex: t(4;11)(q21;q23), AFF1::MLL
Reflex: t(6;11)(q27;q23), MLLT4(AFDN)::MLL
Reflex: t(9;11)(p22;q23), MLLT3::MLL
Reflex: t(10;11)(p13;q23), MLLT10::MLL
Reflex: t(11;16)(q23;p13.3), MLL::CREBBP
Reflex: t(11;19)(q23;p13.1), MLL::ELL
Reflex: t(11;19)(q23;p13.3), MLL::MLLT1
inv(16) or t(16;16), MYH11::CBFB
Reflex: 16q22 rearrangement, CBFB break-apart
inv(16), GLIS2::CBFA2T3
11p15.4 rearrangement, NUP98 break-apart

Reflex: t(7;11)(p15;p15.4), HOXA9::NUP98
12p13 rearrangement, ETV6 break-apart
Reflex: t(7;12)(q36;p13), MNX1::ETV6
t(6;9), DEK::NUP214
inv(3) or t(3;3), RPN1::MECOM
Reflex: t(1;3)(p36;q21), PRDM16::RPN1
Reflex: t(3;21)(q26.2;q22), MECOM::RUNX1
t(8;16), KAT6A::CREBBP
t(1;22), RBM15::MKL1
-5/5q-, D5S630/EGR1
-7/7q-, D7Z1/ D7S486
17p-, TP53/D17Z1
t(9;22), BCR::ABL1
Reflex: 9q34 rearrangement, ABL1 break-apart

Appropriate ancillary probes may be performed at consultant discretion to render comprehensive assessment. Any additional probes will have the results included within the final report and will be performed at an additional charge.

For more information see:
Acute Promyelocytic Leukemia: Guideline to Diagnosis and Follow-up
Acute Leukemias of Ambiguous Lineage Testing Algorithm
Acute Myeloid Leukemia: Testing Algorithm

Special Instructions

- Acute Promyelocytic Leukemia: Guideline to Diagnosis and Follow-up
- Acute Leukemias of Ambiguous Lineage Testing Algorithm
- Acute Myeloid Leukemia: Testing Algorithm

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test is intended for instances when limited acute myeloid leukemia (AML) fluorescence in situ hybridization (FISH) probes are needed based on specific abnormalities or abnormalities identified in the diagnostic sample. If targeted FISH

probes are not included with this test order, test processing will be delayed and the test may be canceled and automatically reordered by the laboratory as either AMLAF / Acute Myeloid Leukemia (AML), FISH, Adult, Varies or AMLPF / Acute Myeloid Leukemia (AML), FISH, Pediatric, Varies depending on the age of the patient.

If the entire AML FISH panel is preferred for an **adult** patient, order AMLAF / Acute Myeloid Leukemia (AML), FISH, Adult, Varies.

If the entire AML FISH panel is preferred for a **pediatric** patient, order AMLPF / Acute Myeloid Leukemia (AML), FISH, Pediatric, Varies.

At diagnosis, conventional cytogenetic studies (CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow) and a complete AML FISH panel (either AMLAF or AMLPF) should be performed.

Minimal residual disease (MRD) monitoring in patients with acute myeloid leukemia (AML) known to have either t(15;17) with PML::RARA fusion, inv(16) or t(16;16) with MYH11::CBFB fusion, t(8;21) with RUNX1T1::RUNX1 fusion, or t(9;22) with BCR::ABL1 fusion should be performed by quantitative reverse transcriptase polymerase chain reaction (RT-PCR) and **NOT** by FISH testing.

It is recommended that MRD monitoring in AML patients be performed by AML-MRD Flow cytometry rather than FISH testing using individual FISH probe sets. This is particularly true for the deletion/monosomy probe sets (5, 7, 17) which have cutoffs that exceed 10% of nuclei.

If this test is ordered and the laboratory is informed that the patient is 30 years of age or younger AND is on a Children's Oncology Group protocol, this test will be canceled and automatically reordered by the laboratory as COGMF / Acute Myeloid Leukemia (AML), Children's Oncology Group Enrollment Testing, FISH, Varies.

For testing paraffin-embedded tissue samples from patients with AML/myeloid sarcoma, order MSTF / Myeloid Sarcoma, FISH, Tissue.

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

A list of targeted probes requested for analysis is required. Probes available for this test are listed in the Testing Algorithm section.

A reason for testing and a flow cytometry and/or a bone marrow pathology report are requested with each specimen. The laboratory will not reject testing if this information is not provided; however, appropriate testing and/or interpretation may be compromised or delayed in some instances. If not provided, an appropriate indication for testing may be entered by Mayo Clinic Laboratories.

Specimen Required

Submit only 1 of the following specimens:

Preferred:

Specimen Type: Bone marrow
Container/Tube:
Preferred: Yellow top (ACD)
Acceptable: Green top (heparin) or lavender top (EDTA)
Specimen Volume: 2 to 3 mL
Collection Instructions:
1. It is preferable to send the first aspirate from the bone marrow collection.
2. Invert several times to mix bone marrow.
3. Send bone marrow in original tube. **Do not aliquot.**

Acceptable:
Specimen Type: Blood
Container/Tube:
Preferred: Yellow top (ACD)
Acceptable: Green top (heparin) or lavender top (EDTA)
Specimen Volume: 6 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood 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
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 recurrent chromosomal abnormalities have been identified in AML with associated clinical significance. The most common chromosome abnormalities associated with AML include t(8;21), t(15;17), inv(16) or t(16;16), and abnormalities of the *MLL* (*KMT2A*) gene at 11q23. The most common genes juxtaposed with *MLL* through translocation events in AML include *MLLT3*- t(9;11), *MLLT4*- t(6;11), *MLLT10*- t(10;11), and *ELL*- t(11;19p13.1).

Other recurrent chromosome abnormalities associated with AML include inv(3) or t(3;3), t(6;9) and t(9;22). In addition, 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) or t(3;3), -5/5q-, -7/7q-, and 17p. Overall, the 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 by karyotype, including inv(16) or t(16;16) and *MLL* rearrangements.

Fluorescence in situ hybridization analysis of nonproliferating (interphase) cells can be used to detect the common diagnostic and prognostic chromosome abnormalities observed in patients with AML.

Reference Values

An interpretive report will be provided.

Interpretation

A neoplastic clone is detected when the percent of cells with an abnormality exceeds the normal reference range for any given probe set.

The absence of an abnormal clone does not rule out the presence of an acute myeloid leukemia clone or another neoplastic disorder.

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.

Bone marrow is the preferred specimen type for this FISH test. If bone marrow is not available, a blood specimen may be used if there are circulating myeloblasts in the blood specimen (as verified by a hematopathologist).

Supportive Data

Each probe was independently tested and verified on unstimulated peripheral blood and bone marrow specimens. Normal cutoffs were calculated based on the results of at least 25 normal specimens. In addition, each probe set was evaluated in a blinded fashion to confirm the probe set detected the abnormality it was designed to detect.

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;116(3):354-365
2. Swerdlow SH, Campo E, Harris NL, et al, eds. WHO Classification of Tumour of Haematopoietic and Lymphoid Tissues. 4th ed. IARC Press; 2017

3. 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
4. Pollyea DA, Bixby D, Perl A, et al. Acute Myeloid Leukemia, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2021;19(1):17-27. doi: 10.6004/jnccn.2021.0002

Performance

Method Description
This test is performed using commercially available and laboratory-developed probes. Deletion or monosomy of chromosomes 5, 7, and 17 are detected using enumeration strategy probes. Rearrangements involving *ABL1, MLL* (*KMT2A*), *NUP98, ETV6, CBFB,* and *RARA* are detected using a dual-color break-apart (BAP) strategy probe. Dual-color, dual-fusion fluorescence in situ hybridization (D-FISH) strategy probe sets are used to detect inv(3) or t(3;3), inv(16) or t(16;16), t(8;21), t(15;17), t(6;9), t(8;16), t(3;21), t(1;3), t(1;22), t(9;22), t(7;11), t(7;12) and in reflex testing when rearrangements of the *MLL* gene are detected. For enumeration and BAP strategy probe sets, 100 interphase nuclei are scored; 200 interphase nuclei are scored when D-FISH probes are used. All results are expressed as the percent abnormal nuclei.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
7 to 10 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

88271x2, 88275x1, 88291x1- FISH Probe, Analysis, Interpretation; 1 probe set
88271x2, 88275x1-FISH Probe, Analysis; each additional probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
AMLMF	AML, Specified FISH	102103-9

Result ID	Test Result Name	Result LOINC® Value
614204	Result Summary	50397-9
614205	Interpretation	69965-2
614206	Result Table	93356-4
614207	Result	62356-1
GC097	Reason for Referral	42349-1
GC098	Probes Requested	78040-3
GC099	Specimen	31208-2
614208	Source	31208-2
614209	Method	85069-3
614210	Additional Information	48767-8
614211	Disclaimer	62364-5
614212	Released By	18771-6