Test Definition: AMLMF

Acute Myeloid Leukemia (AML), Specified FISH, Varies

Overview

Useful For

Detecting recurrent common chromosome abnormalities associated with acute myeloid leukemia (AML) using client-specified probe sets

As an adjunct to conventional chromosome studies in patients with AML

Evaluating specimens in which chromosome studies are unsuccessful

Identifying and tracking known chromosome abnormalities in patients with AML and monitoring response to therapy

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 probe application, analysis, and professional interpretation of results for 1 probe set (2 individual fluorescence in situ hybridization [FISH] probes). Additional charges will be incurred for all reflex testing, if requested, or additional probe sets performed. Analysis charges are based on the number of cells analyzed per probe. No analysis charges apply if there are insufficient representative cells for evaluation.

This test is performed using client-specified FISH probes and is not intended as a panel test. Specific probes must be listed in the probe request field. Reflex probes can be performed when appropriate if specified in the order request field.

When specified, any of the following probes will be performed:
inv(3) or t(3;3) or *GATA2::MECOM* fusion, request probe GATA2/MECOM
t(1;3)(p36;q21) or *GATA2::PRDM16* fusion, request probe PRDM16/GATA2
t(3q26.2;var) or *MECOM* rearrangement, request probe MECOM break-apart
-5/5q-, request probe D5S630/EGR1
t(6;9)(p22.3;q34) or *DEK::NUP214* fusion, request probe DEK/NUP214
-7/7q-, request probe D7Z1/D7S486
t(7;12)(q36;p13) or *MNX1::ETV6* fusion, request probe MNX1/ETV6
t(8;16)(p11;p13) or *KAT6A::CREBBP* fusion, request probe KAT6A/CREBBP
t(8;21)(q21.3;q22) or *RUNX1::RUNX1T1* fusion, request probe RUNX1T1/RUNX1
t(21q22;var) or *RUNX1* rearrangement, request probe RUNX1 break-apart
t(9;22)(q34;q11) or *BCR::ABL1* fusion, request probe ABL1/BCR
t(9q34;var) or *ABL1* rearrangement, request probe ABL1 break-apart
t(11p15;var) or *NUP98* rearrangement, request probe NUP98 break-apart

t(11q23;var) or *KMT2A* rearrangement, request probe KMT2A break-apart
t(4;11)(q21;q23) or *KMT2A:: AFF1* fusion, request probe AFF1/KMT2A
t(6;11)(q27;q23) or *KMT2A::AFDN* fusion, request probe AFDN/ KMT2A
t(9;11)(p21.3;q23) or *KMT2A::MLLT3* fusion, request probe MLLT3/KMT2A
t(10;11)(p12;q23) or *KMT2A::MLLT10* fusion, request probe MLLT10/KMT2A
t(11;16)(q23;p13.3) or *KMT2A::CREBBP* fusion, request probe KMT2A/CREBBP
t(11;19)(q23;p13.3) or *KMT2A::MLLT1* fusion, request probe KMT2A/MLLT1
t(11;19)(q23;p13.1) or *KMT2A::ELL* fusion, request probe KMT2A/ELL
t(15;17)(q24;q21) or *PML::RARA* fusion, request probe PML/RARA
t(17q21;var) or *RARA* rearrangement, request probe RARA break-apart
inv(16) or t(16;16) or *CBFB::MYH11* fusion, request probe MYH11/CBFB
t(16q22;var) or *CBFB* rearrangement, request probe CBFB break-apart
inv(16)(p13q24) or *CBFA2T3::GLIS2* fusion, request probe CBFA2T3/GLIS2
-17/17p-, request probe TP53/D17Z1

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. The FISH probes

to be analyzed must be specified on the ordering request. 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 AMLFA / Adult Acute Myeloid Leukemia Panel, FISH, Varies or AMLFP / Pediatric Acute Myeloid Leukemia Panel, FISH, Varies depending on the age of the patient.

Specimens requiring expedited *PML* and *RARA* results should be ordered as APLDF / Acute Promyelocytic Leukemia-*PML::RARA* fusion, Expedited Diagnostic FISH, Varies.

This test includes evaluation of the *PML* and *RARA* gene regions (if requested); however, testing is not initially performed on an expedited basis. If *PML*::*RARA* fusion is identified during analysis, testing will be automatically expedited by the laboratory. Results will not be provided until testing is finalized. The laboratory is unable to provide preliminary results.

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

If a complete AML FISH panel is preferred for an adult patient, order AMLFA / Adult Acute Myeloid Leukemia Panel, FISH, Varies.

If a complete AML FISH panel is preferred for a pediatric patient, order AMLFP / Pediatric Acute Myeloid Leukemia Panel, FISH, Varies.

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

It is recommended that MRD monitoring in patients with AML 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 age 30 years 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. If a paraffin-embedded tissue sample is submitted for this test, this test will be canceled and MSTF will be added and performed as the appropriate test.

Additional Testing Requirements

At diagnosis, conventional cytogenetic studies (CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow) and a complete AMLFA / Adult Acute Myeloid Leukemia Panel, FISH, Varies or AMLFP / Pediatric Acute Myeloid Leukemia Panel, FISH, Varies should be performed, depending on patient's age. If there is limited specimen available, only fluorescence in situ hybridization testing will be performed.

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. A list of targeted probes requested for analysis is required. Probes available for this test are listed in the Testing Algorithm section.
2. A reason for testing must be provided. If this information is not provided, an appropriate indication for testing may be entered by Mayo Clinic Laboratories.
3. A flow cytometry and/or a bone marrow pathology report should be submitted with each specimen. The laboratory will not reject testing if this information is not provided, but appropriate testing and interpretation may be compromised or delayed.

Specimen Required

Submit only 1 of the following specimens:

Preferred
Specimen Type: Bone marrow
Container/Tube:
Preferred: Yellow top (ACD)
Acceptable: Green top (sodium 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: Whole blood
Container/Tube:
Preferred: Yellow top (ACD)
Acceptable: Green top (sodium 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

Bone marrow: 1 mL; Whole blood: 2 mL

Reject Due To

Fresh tissue	Reject

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 *KMT2A* gene at 11q23. The most common genes juxtaposed with *KMT2A* through translocation events in AML include *AFDN*- t(6;11), *MLLT3*- t(9;11), *MLLT10*- t(10;11), and *ELL*-t(11;19p13.1).

Acute myeloid leukemia 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-, and -7/7q-. 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 *KMT2A* 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 a neoplastic disorder.

Cautions

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

pathologic information.

Fluorescence in situ hybridization (FISH) is not a substitute for conventional chromosome studies because the latter detects chromosome abnormalities associated with other hematological disorders that would go undetected in a targeted acute myeloid leukemia FISH test.

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).

If no FISH signals are observed post-hybridization, the case will be released indicating a lack of FISH results.

Clinical Reference

1. Grimwade D, Hills RK, Moorman AV, et al. Refinement of cytogenetic classification in acute myeloid leukemia: determination of prognostic significance of rare recurring chromosomal abnormalities among 5876 younger adult patients treated in the United Kingdom Medical 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. NCCN Guidelines Insights: Acute Myeloid Leukemia, Version 2.2021. J Natl Compr Canc Netw. 2021;19(1):16-27. Published 2021 Jan 6. doi:10.6004/jnccn.2021.0002

Performance

Method Description

This test is performed using commercially available and laboratory-developed fluorescence in situ hybridization (FISH) probes. Deletion or monosomy of chromosomes 5, 7, and 17 are detected using enumeration strategy probes. Rearrangements involving *MECOM*, *ABL1*, *NUP98*, *KMT2A*, *CBFB*, *RARA*, and *RUNX1* are detected using dual-color break-apart (BAP) strategy probes. Dual-color FISH (D-FISH) strategy probe sets are used to detect t(1;3), inv(3) or t(3;3), t(6;9), t(7;12), t(8;16), t(8;21), t(9;22), t(15;17), inv(16) or t(16;16), and in reflex testing when rearrangements of the *KMT2A* 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
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
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