MAYO CLINIC LABORATORIES

Test Definition: COGMF

Acute Myeloid Leukemia (AML), Children's Oncology Group Enrollment Testing, FISH, Varies

Overview

Useful For

Detecting, at diagnosis, recurrent common chromosome abnormalities associated with acute myeloid leukemia (AML) in patients being considered for enrollment in Children's Oncology Group (COG) clinical trials and research protocols

As an adjunct to conventional chromosome studies in pediatric patients with AML being considered for enrollment in COG protocols

Evaluating specimens in which chromosome studies are unsuccessful

This test **should not be used** to screen for residual AML

Reflex Tests

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

Testing Algorithm

This test is only performed on specimens from pediatric patients being considered for enrollment in a Children's Oncology Group (COG) protocol. Additional charges will be incurred for all reflex or additional probe sets performed. Analysis charges will be incurred based on the number of cells analyzed per probe set. If no cells are available for analysis, no analysis charges will be incurred.

This test is performed as panel testing only using the following analysis algorithm.

The **diagnostic** pediatric/young adult fluorescence in situ hybridization (FISH) panel includes testing for the following abnormalities using the FISH probes listed:
inv(3) or t(3;3) or *GATA2::MECOM* fusion, GATA2/MECOM probe set
-5/5q-, D5S630/EGR1 probe set
t(6;9)(p22.3;q34) or *DEK::NUP214* fusion, DEK/NUP214 probe set
-7/7q-, D7Z1/D7S486 probe set
t(7;12)(q36;p13) or *MNX1::ETV6* fusion, MNX1/ETV6 probe set
t(8;16)(p11;p13) or *KAT6A::CREBBP* fusion, KAT6A/CREBBP probe set
t(8;21)(q21.3;q22) or *RUNX1::RUNX1T1* fusion, RUNX1T1/RUNX1 probe set
t(11p15;var) or *NUP98* rearrangement, NUP98 break-apart probe set
t(11q23;var) or *KMT2A* rearrangement, KMT2A break-apart probe set
t(15;17)(q24;q21) or *PML::RARA* fusion, PML/RARA probe set
inv(16) or t(16;16) or *CBFB::MYH11* fusion, MYH11/CBFB probe set

inv(16)(p13q24) or *CBFA2T3::GLIS2* fusion, CBFA2T3/GLIS2 probe set

Appropriate ancillary probes may be performed at consultant discretion to render comprehensive assessment. Any additional probes used will have the results included within the final report and will be performed at an additional charge. In the following situations, additional (reflex) testing may be performed at the laboratory's discretion and may be influenced by available karyotype results or other FISH testing.

In the absence of *GATA2::MECOM* fusion, when an extra GATA2 signal is identified, testing using the PRDM16/GATA2 probe set to identify a potential t(1;3)(p36;q21) may be performed.

In the absence of *GATA2::MECOM* fusion, when an extra MECOM signal is identified, testing using the break-apart MECOM probe to identify a potential variant translocation involving *MECOM*, t(3;var)(q26.2;?) may be performed.

When a *KMT2A* rearrangement is identified, testing with 1 or more dual-fusion FISH probe sets may be performed in an attempt to identify the translocation partner for the following abnormalities:
t(4;11)(q21;q23) or *KMT2A::AFF1* fusion, AFF1/KMT2A probe set
t(6;11)(q27;q23) or *KMT2A::AFDN* ;fusion, AFDN/KMT2A probe set
t(9;11)(p22;q23) or *KMT2A::MLLT3* fusion, MLLT3/KMT2A probe set
t(10;11)(p12;q23) or *KMT2A::MLLT10* fusion, MLLT10/KMT2A probe set
t(11;16)(q23;p13.3) or *KMT2A::CREBBP* fusion, KMT2A/CREBBP probe set
t(11;19)(q23;p13.1) or *KMT2A::MLLT1* fusion, KMT2A/ELL probe set
t(11;19)(q23;p13.3) or *KMT2A::ELL* fusion, KMT2A/MLLT1 probe set

In the absence of *PML::RARA* fusion, when an extra or atypical RARA signal is identified, testing using the RARA break-apart probe set to identify a potential variant translocation involving *RARA,* t(17;var)(q21;?) may be performed.

In the absence of *CBFB::MYH11* fusion, when an extra CBFB signal is identified, using the CBFB break-apart probe set to evaluate for the presence or absence of a potential variant translocation involving *CBFB*, t(16;var)(q22;?) may be performed.

In the absence of *RUNX1::RUNX1T1* fusion, when an extra RUNX1 signal is identified, testing using the RUNX1 break-apart probe set to evaluate for the presence or absence of a potential variant translocation involving *RUNX1,* t(21;var)(q22;?) may be performed.

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 only performed on specimens from pediatric patients being considered for enrollment in a Children's Oncology Group (COG) protocol. If this test is ordered and the laboratory is informed that the patient is not on a Children's Oncology Group (COG) protocol, this test will be canceled and automatically reordered by the laboratory as AMLFP / Pediatric Acute Myeloid Leukemia panel, FISH, Varies.

At follow-up, conventional cytogenetic studies (CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow) and targeted AML fluorescence in situ hybridization (FISH) probes can be evaluated based on the abnormalities identified in the diagnostic study. Order AMLMF / Acute Myeloid Leukemia (AML), Specified FISH, Varies and request specific probes or abnormalities.

For children in whom disease relapse or a secondary myeloid neoplasm is a concern and enrollment in a new COG protocol is being considered; order COGBM / Chromosome Analysis, Hematologic Disorders, Children's Oncology Group Enrollment Testing, Bone Marrow.

Additional Testing Requirements
At diagnosis, conventional cytogenetic studies (COGBM / Chromosome Analysis, Hematologic Disorders, Children's Oncology Group Enrollment Testing, Bone Marrow) and this panel should be performed. If there is limited specimen available, only this test will be performed.

Shipping Instructions
Advise Express Mail or equivalent if not on courier service.

Necessary Information
1. Children's Oncology Group (COG) registration number and protocol number should be submitted with each specimen. The laboratory will not reject testing if this information is not provided; however, appropriate testing may be compromised or delayed.
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.
4. If the patient has received an opposite sex bone marrow transplant, note this information on the request.
5. If the patient has Down syndrome, note this information on the request.

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 specimen 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 specimen in original tube. **Do not aliquot.**

Forms

If not ordering electronically, complete, print, and send a Children's Oncology Group Test Request (T829) 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-, -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 (FISH) analysis of nonproliferating (interphase) cells can be used to detect the common diagnostic and prognostic chromosome abnormalities observed in patients with AML.

Metaphase FISH confirmation of classic translocations that are cryptic and not visually detectable by chromosome analysis [ie, t(6;11) associated with *KMT2A::AFDN* fusion] is performed as required by Children's Oncology Group (COG) and is included as part of the electronic case submission by the Mayo Clinic Genomics Laboratory to COG for central review.

Additional cytogenetic techniques such as chromosomal microarray (CMAH / Chromosomal Microarray, Hematologic Disorders, Varies) may be helpful to resolve questions related to ploidy (hyperdiploid clone vs doubled hypodiploid clone).

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 be missed in a targeted acute myeloid leukemia FISH panel 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 malignant cells 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 cytogenetics classification in acute myeloid leukemia: determination of prognostic significance or rare recurring chromosomal abnormalities among 5876 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 Tumours of Haematopoietic and Lymphoid Tissues. 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

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 and 7 are detected using enumeration strategy probes. Rearrangements involving *MECOM*, *NUP98, KMT2A*, *CBFB, RARA*, and *RUNX1* are detected using a dual-color break-apart (BAP) strategy probe set. Dual-color, dual-fusion (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(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

Test Definition: COGMF

Acute Myeloid Leukemia (AML), Children's Oncology Group Enrollment Testing, FISH, Varies

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
88271 x 2, 88275, 88291-FISH Probe, Analysis, Interpretation; 1 probe set
88271 x 2, 88275-FISH Probe, Analysis; each additional probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
COGMF	COG, AML, FISH	102101-3

Result ID	Test Result Name	Result LOINC® Value
602276	Result Summary	50397-9
602277	Interpretation	69965-2
602278	Result Table	93356-4
602279	Result	62356-1
GC013	Reason for Referral	42349-1
GC014	Specimen	31208-2
602281	Source	31208-2
602282	Method	85069-3
602283	Additional Information	48767-8
602284	Disclaimer	62364-5
602285	Released By	18771-6