MAYO CLINIC LABORATORIES

Test Definition: COGMF

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

Overview

Useful For

Evaluation of pediatric bone marrow and peripheral blood specimens by fluorescence in situ hybridization (FISH) probe analysis for classic rearrangements and chromosomal copy number changes associated with acute myeloid leukemia (AML) in patients being considered for enrolment in Children's Oncology Group (COG) clinical trials and research protocols

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

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.

The fluorescence in situ hybridization (FISH) panel includes testing for the following abnormalities using the FISH probes listed:
inv(16), [M4, Eos], MYH11/CBFB
t(8;21), [M2], RUNX1T1/RUNX1
t(15;17), [M3], PML/RARA
11q23 rearrangement, [M0-M7], MLL (KMT2A)
t(6;9), [M2,M4], DEK/NUP214
inv(3) or t(3;3), [M1,2,4,6,7], RPN1/MECOM
t(8;16), [M4,M5], KAT6A/CREBBP
t(1;22), [M7], RBM15/MKL1
-5/5q-, D5S630/EGR1
-7/7q-, D7Z1/ D7S486
12p13 rearrangement, ETV6
inv(16), GLIS2/CBFA2T3
11p15.4 rearrangement, NUP98

When an MLL (KMT2A) rearrangement is identified, reflex testing will be performed to identify the translocation partner. Probes include identification of:
t(4;11)(q21;q23) AFF1/MLL

t(6;11)(q27;q23) MLLT4(AFDN)/MLL
t(9;11)(p22;q23) MLLT3/MLL
t(10;11)(p12;q23) MLLT10/MLL
t(11;16)(q23;p13.3) MLL/CREBBP
t(11;19)(q23;p13.1)
MLL/ELL
t(11;19)(q23;p13.3) MLL/MLLT1

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.

In the absence of *RPN1::MECOM* fusion, when an extra MECOM signal is identified, the MECOM/RUNX1 probe set will be considered to identify a potential t(3;21)(q26.2;q22) rearrangement.

In the absence of *RPN1::MECOM* fusion, when an extra RPN1 signal is identified, reflex testing using the PRDM16/RPN1 probe set will be considered to identify a potential t(1;3)(p36;q21).

In the absence of *MYH11::CBFB* fusion, when an extra CBFB signal is identified, reflex testing will be performed using the CBFB break-apart probe set to evaluate for the presence or absence of an *CBFB* rearrangement.

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

When an *ETV6* rearrangement is identified, reflex testing using the MNX1/ETV6 probe set will be performed to identify a potential t(7;12)(q36;p13) rearrangement.

When a *NUP98* rearrangement is identified, reflex testing using the HOXA9/NUP98 probe set will be performed to identify a potential t(7;11)(p15;p15.4) rearrangement.

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

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 AMLPF / Acute Myeloid Leukemia (AML), FISH, Pediatric, Varies.

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.

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

Necessary Information
1. A reason for testing, a flow cytometry and/or a bone marrow pathology report, and a 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, but appropriate testing and interpretation may be compromised or delayed. If this information is not provided, an appropriate indication for testing may be entered by Mayo Clinic Laboratories.
2. If a patient has received an opposite sex bone marrow transplant prior to specimen collection for this protocol, 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 (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.

Acceptable:
Specimen Type: Blood
Container/Tube:
Preferred: Yellow top (ACD)
Acceptable: Green top (heparin) or lavender top (EDTA)
Specimen Volume: 6 mL
Collection Instructions: Invert several times to mix blood.

Forms
If not ordering electronically, complete, print, and send a Children's Oncology Group Test Request (T829) 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. The most common chromosome abnormalities associated with AML include t(8;21), t(15;17), inv(16), and abnormalities of the *MLL* (*KMT2A*) gene at 11q23. The most common genes juxtaposed with *MLL* through translocation events in AML include *MLTT4(AFDN)*- t(6;11), *MLLT3*- t(9;11), *MLLT10*- t(10;11), and *ELL*- t(11;19p13.1).

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-, 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) and *MLL* rearrangements.

Fluorescence in situ hybridization (FISH) analysis of nonproliferating (interphase) cells can be used to detect the common chromosome abnormalities observed in patients with AML. The abnormalities have diagnostic and prognostic relevance, and FISH testing can also be used to track response to therapy.

Metaphase FISH confirmation of classic translocations that are cryptic and not visually detectable by chromosome analysis [ie, t(6;11) associated with *KMT2A/MLLT4(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.

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 existing clinical and pathologic information.

Fluorescence in situ hybridization (FISH) is not a substitute for conventional chromosome studies because the latter detects many chromosome abnormalities associated with other hematological disorders that would be missed by this 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 malignant cells 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 25 normal specimens. Each probe set was evaluated 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 5876 younger adult

patients treated in the United Kingdom Research Council trials. Blood. 2010 Jul 22;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 Jan 26;129(4):424-447. doi: 10.1182/blood-2016-08-733196

Performance

Method Description

This test is performed using commercially available and laboratory-developed probes. Deletion or monosomy of chromosomes 5 and 7 are detected using enumeration strategy probes. Rearrangements involving *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), inv(16), t(8;21), t(15;17), t(6;9), t(8;16), t(3;21), t(1;3), t(1;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

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

Test Definition: COGMF

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

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