Overview

Useful For

Detecting a neoplastic clone associated with the common chromosome abnormalities seen in patients with acute myeloid leukemia or other myeloid malignancies

Evaluating specimens in which standard cytogenetic analysis is unsuccessful

Identifying and tracking known chromosome abnormalities in patients with myeloid malignancies and tracking response to therapy

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
_PBCT	Probe, +2	No, (Bill Only)	No
_PADD	Probe, +1	No, (Bill Only)	No
_PB02	Probe, +2	No, (Bill Only)	No
_PB03	Probe, +3	No, (Bill Only)	No
_IL25	Interphases,	No, (Bill Only)	No
_I099	Interphases, 25-99	No, (Bill Only)	No
_I300	Interphases, >=100	No, (Bill Only)	No

Testing Algorithm

This test includes a charge for application of the first probe set (2 fluorescence in situ hybridization: FISH probes) and professional interpretation of results. Additional charges will be incurred for all reflex probes 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.

The following algorithms are available in Special Instructions:

-Acute Leukemias of Ambiguous Lineage Testing Algorithm

-Acute Myeloid Leukemia: Testing Algorithm

-Acute Promyelocytic Leukemia: Guideline to Diagnosis and Follow-up

For diagnostic samples, all probes in the initial panel will be performed. The initial panel includes testing for the following abnormalities using the probes listed:

t(8;21), [M2], *RUNX1T1*/*RUNX1*

t(15;17), [M3], *PML*/*RARA*

11q23 rearrangement, [M0-M7], *MLL* (*KMT2A*)

inv(16), [M4, Eos], *MYH11*/*CBFB*

Based on the results from the initial panel, reflex testing may be performed to identify the following abnormalities:

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], *MYST3*/*CREBBP*

t(1;22), [M7], *RBM15*/*MKL1**

-5/5q-, *D5S630*/*EGR1*

-7/7q-, *D7S486*/D7Z1

17p-, *TP53*/D17Z1

t(9;22), *BCR*/*ABL1*

*The *RBM15/MKL1* probe set will only be used to test patients with a suspected or confirmed diagnosis of M7 or to confirm a t(1;22) identified by chromosome analysis.

-When a *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/MLL*, t(9;11)(p22;q23) *MLLT3/MLL*, t(10;11)(p13;q23) *MLLT10/MLL*, t(11;16)(q23;p13.3) *MLL/CREBBP,* t(11;19)(q23;p13.1) *MLL/ELL*, or t(11;19)(q23;p13.3) *MLL*/*MLLT1*.

-When 3 copies of *MECOM* are observed with no fusion with *RPN1,* reflex testing using the *MECOM/RUNX1* probe set will be performed to identify a potential t(3;21)(q26.2;q22) rearrangement.

-When 3 copies of *RPN1* are observed with no fusion with *MECOM*, reflex testing using the *PRDM16*/*RPN1* probe set will be performed to identify a potential t(1;3)(p36;q21).

-When 3 copies of *RARA* are observed with no fusion with *PML*, reflex testing using the 5'*RARA/3'RARA* rearrangementprobe set will be performed to identify a potential variant translocation involving *RARA*; example: t(17;var)(q21;?).

-In the absence of *BCR/ABL1* fusion, when an extra signal for *ABL1* is identified, reflex testing will be performed using the *ABL1* break-apart probe set to evaluate for the presence or absence of an *ABL1* rearrangement.

If the patient is being treated for known abnormalities, indicate which probes should be used.

If this test is ordered and the laboratory is informed that the patient is on a Children's Oncology Group (COG) 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.

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

Advisory Information

This assay detects chromosome abnormalities observed in the blood and bone marrow of patients with acute myeloid leukemia.For testing paraffin-embedded tissue samples from patients with myeloid sarcoma, see MSTF / Myeloid Sarcoma, FISH, Tissue.

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. Provide a reason for referral 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.

2. A pathology and/or flow cytometry report may be requested by the Genomics Laboratory to optimize testing and aid in interpretation of results.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Whole blood

Container/Tube: Green top (sodium heparin)

Specimen Volume: 7-10 mL

Collection Instructions:

1. Invert several times to mix blood.

2. Other anticoagulants are not recommended and are harmful to the viability of the cells.

Specimen Type: Bone marrow

Container/Tube: Green top (sodium heparin)

Specimen Volume: 1-2 mL

Collection Instructions:

1. Invert several times to mix bone marrow.

2. Other anticoagulants are not recommended and are harmful to the viability of the cells.

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 and 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*- 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 diagnostic and prognostic chromosome abnormalities observed in patients with AML. When recurrent translocations or inversions are identified, FISH testing can also be used to track response to therapy.

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.

Detection of an abnormal clone likely indicates a diagnosis of an acute myeloid leukemia of various subtypes.

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.

Bone marrow is the preferred specimen type for this fluorescence in situ hybridization 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 hematopathology).

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. For each probe set a series of chromosomally abnormal specimens were evaluated to confirm each 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 Jul;116(3):354-365

2. Swerdlow SH, Campo E, Harris NK, et al: eds. International Agency for Research on Cancer (IARC): World Health Organization Classification of Tumour of Haematopoietic and Lymphoid Tissues. 4th ed. IARC Press, Oxford University Press; 2008

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 probes. Deletion or monosomy of chromosomes 5 and 7, and deletion or rearrangement of chromosome 17 are detected using enumeration strategy probes. Rearrangements involving *MLL* (*KMT2A*) 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(11;22), t(9;22), t(1;22), and in reflex testing when rearrangements of the *MLL* gene are detected. For enumeration and BAP strategy probe sets, 200 interphase nuclei are scored; 500 interphase nuclei are scored when D-FISH probes are used. Two technologists analyze each probe set and all results are expressed as the percent abnormal nuclei.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Samples processed Monday through Sunday.Results reported Monday through Friday, 8 a.m.-5 p.m.

Analytic Time

7 days

Maximum Laboratory Time

10 days

Specimen Retention Time

4 weeks

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed using an analyte specific reagent. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

88271 x 2, 88291-DNA probe, each (first probe set), Interpretation and report

88271 x 2-DNA probe, each; each additional probe set (if appropriate)

88271-DNA probe, each; coverage for sets containing 3 probes (if appropriate)

88271 x 2-DNA probe, each; coverage for sets containing 4 probes (if appropriate)

88271 x 3-DNA probe, each; coverage for sets containing 5 probes (if appropriate)

88274 w/modifier 52-Interphase in situ hybridization, <25 cells, each probe set (if appropriate)

88274-Interphase in situ hybridization, 25 to 99 cells, each probe set (if appropriate)

88275-Interphase in situ hybridization, 100 to 300 cells, each probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
AMLF	AML, FISH	In Process

Result ID	Test Result Name	Result LOINC Value
51894	Result Summary	50397-9
51896	Interpretation	69965-2
51895	Result Table	93356-4

Test Definition: AMLF

AML, FISH

Result ID	Test Result Name	Result LOINC Value
54545	Result	62356-1
CG682	Reason for Referral	42349-1
CG683	Specimen	31208-2
51897	Source	31208-2
51898	Method	49549-9
54454	Additional Information	48767-8
53868	Disclaimer	62364-5
51899	Released By	18771-6