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

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<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
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<td>1300</td>
<td>Interphases, &gt;=100</td>
<td>No, (Bill Only)</td>
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</table>

Testing Algorithm

This test includes a charge for application of the first probe set (2 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**

Indicate if the entire panel is to be performed. If the patient is being treated for known abnormalities, indicate which probes should be used.

Indicate the subtype, as well as, which abnormalities need to be investigated from the following profile:

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

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

11p15.4 rearrangement, NUP98
11q23 rearrangement, [M0-M7], MLL (KMT2A)
inv(16), [M4, Eos], MYH11/CBFB
+8, [M0-M7], D8Z2/MYC
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(3;5)(q25.32;q35.1), MLF1/NPM1
t(1;22), [M7], RBM15/MKL1*
-5/5q-, D5S630/EGR1
-7/7q-, D7S486/D7Z1
13q-, D13S319/LAMP1
17p-, TP53/D17Z1
20q-, D20S108/20qter
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 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).

-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 rearrangement probe 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 this test is ordered and the laboratory is informed that the patient is on a 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**

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<th>Time</th>
<th>Special Container</th>
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<td>Refrigerated</td>
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<tr>
<td>Bone Marrow</td>
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</tbody>
</table>

**Reject Due To**

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

**Specimen Stability Information**

**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 subtypes of AML have been recognized (termed AML-M0, M1, M2, M3, M4, M5, M6, and M7) based on the cell morphology and myeloid lineage involved.

In addition to morphology, several recurrent chromosomal abnormalities have been linked to specific subtypes of AML. The most common chromosome abnormalities associated with AML include t(8;21), t(15;17), inv(16), +8, t(6;9), t(8;16), t(1;22), t(9;22), t(3;5), and abnormalities of the MLL (KMT2A) gene at 11q23. The most common genes juxtaposed with MLL through translocation events in AML include AFF1- t(4;11), MLT4- t(6;11), MLLT3- t(9;11), MLLT10- t(10;11), CREBBP- t(11;16), ELL- t(11;19p13.1), and MLLT1- t(11;19p13.3).

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-, +8, 13q-, 17p-, 20q-, t(1;3), and t(3;21). In combination, the multiple 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: eg, inv(16), MLL and NUP98.
abnormalities.

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 this 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 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 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


Performance

Method Description
This test is performed using commercially available and laboratory-developed probes. Deletion or monosomy of chromosomes 5, 7, 13, trisomy of chromosome 8 and deletion or rearrangement of chromosome 17 and 20 are detected using enumeration strategy probes. Rearrangements involving MLL (KMT2A) and NUP98 are detected using a dual-color break-apart (BAP) strategy probe. Dual-color, dual-fusion (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(3:5), 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. CST.

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 Definition: AMLF
AML, FISH

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