Test Definition: APLDF

Acute Promyelocytic Leukemia-PML::RARA Fusion, Expedited Diagnostic FISH, Varies

Overview

Useful For

Detecting, at diagnosis, acute promyelocytic leukemia (APL)

This test **should not** be used to screen for residual APL.

Reflex Tests

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

Testing Algorithm

This test includes a charge for the 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 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 should only be ordered at the time of diagnosis.

In the absence of *PML::RARA* fusion, when an extra RARA FISH signal is identified, reflex testing using the break-apart RARA probe set will be performed to resolve or confirm RARA rearrangement concerns. If additional RARA testing is required, results will be delayed until the next business day.

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.

Special Instructions

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

Highlights

This test is automatically expedited within the FISH laboratory. Test results are finalized and released 7 days a week.

All attempts will be made to provide final results the day of specimen receipt at Mayo Clinic Laboratories. Some results may not be reported until the following day due to established cutoff times or if additional *RARA* testing is required.

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available
Yes

Specimen

Specimen Type
Varies

Ordering Guidance
This test is intended for **diagnostic samples only** when *PML::RARA* fusion is presumed and targeted PML and RARA fluorescence in situ hybridization (FISH) probes are needed to diagnose acute promyelocytic leukemia (APL).

Complete acute myeloid leukemia (AML) diagnostic FISH panel tests for adults and pediatric patients are also available. AML panel tests will be automatically prioritized by the laboratory when *PML::RARA* fusion is present. Most often, AML panel tests found with *PML::RARA* fusion will be reported the next business day from receipt in the Genomics laboratory. Same day testing is not available for panel testing. If panel testing is warranted, order either AMLFA / Adult Acute Myeloid Leukemia Panel, FISH, Varies or AMLFP / Pediatric Acute Myeloid Leukemia Panel, FISH, Varies, as appropriate based on patient age.

This test **should not** be used to screen for residual AML or when the diagnosis of APL is not strongly suggested. Monitoring patients known to have *PML::RARA* fusion should be performed by quantitative reverse transcription-polymerase chain reaction (RT-PCR) testing and **not** FISH testing. If the specimen does not meet the criteria for RT-PCR, follow-up FISH testing for *PML::RARA* fusion should be ordered as AMLMF / Acute Myeloid Leukemia (AML), Specified FISH, Varies with a PML/RARA specific probe request.

If this test is received in the laboratory concurrently with an order for either AMLFA / Adult Acute Myeloid Leukemia Panel, FISH, Varies or AMLFP / Pediatric Acute Myeloid Leukemia Panel, FISH, Varies, panel testing will be held pending the results of this test. Ordering an AML panel test concurrently with this test will result in an approximate 1 business day delay of the panel test reporting. If *PML::RARA* fusion is detected, the AMLFA or AMLFP panel test will be cancelled by the laboratory. If no fusion is identified, the complete AML FISH panel test will be performed, except for the PML/RARA FISH probe set.

If the entire AML FISH panel is preferred for an **adult** patient (aged 31 years or older), order AMLFA / Adult Acute Myeloid Leukemia panel, FISH, Varies.

If the entire AML FISH panel is preferred for a **pediatric** patient (aged 30 years or younger), order AMLFP / Pediatric Acute Myeloid Leukemia panel, FISH, Varies.

If upfront break-apart *RARA* FISH testing is desired, order AMLMF / Acute Myeloid Leukemia (AML), Specified FISH, Varies. Results will be reported the next business day.

For more information see Acute Promyelocytic Leukemia: Guideline to Diagnosis and Follow-up

Additional Testing Requirements

At diagnosis, PMLR / *PML::RARA* Quantitative, PCR, Varies should be performed in parallel with this test.
At follow-up, only PMLR / *PML::RARA* Quantitative, PCR, Varies should be performed.

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. 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.
2. 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.
3. If a result callback by phone is needed after finalized results are released, **the ordering healthcare professional must supply the name and direct phone number of a licensed physician (MD or DO) at the time the order is received**.
-Result callbacks are only available during regular business hours.
-Preliminary results or exact times the finalized report will be available **will not** be provided under any circumstances.

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
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. Acute promyelocytic leukemia (APL) is a subtype of AML and is most often associated with t(15;17)(q24;q21) with subsequent fusion of the *PML* gene with the *RARA* gene.

Real-time quantitative polymerase chain reaction is currently the standard method for molecular monitoring in APL(1), fluorescence in situ hybridization is not recommended for APL monitoring.

Reference Values
An interpretive report will be provided

Interpretation
Detection of *PML::RARA* (promyelocytic leukemia/retinoic acid receptor alpha) fusion confirms the clinical diagnosis of acute promyelocytic leukemia (APL). In rare cases, APL is caused by fusion between *RARA* and one of several other partner genes. When APL is highly suspected and fluorescence in situ hybridization (FISH) shows no *PML::RARA* fusion, FISH for *RARA* rearrangement is recommended. A *PML-RARA* fusion positive APL may also have other clonal chromosome abnormalities that can be detected by chromosome analysis. A *PML::RARA* fusion may be accompanied by gene mutations that can be detected by polymerase chain reaction (PCR) or sequencing. Disease monitoring for APL is preferably done by quantitative PCR for the *PML::RARA* fusion gene transcripts.

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.

If additional RARA testing is required, results will be delayed until the next business day. The laboratory is unable to provide preliminary results.

This test will only utilize the fluorescence in situ hybridization (FISH) algorithm described in the testing algorithm. The break-apart RARA FISH probe set cannot be preemptively added to this test.

This assay may not detect rare, unusual *PML::RARA* fusion.

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. Pollyea DA, Altman JK, Assi R, et al. Acute Myeloid Leukemia, Version 3.2023, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2023;21(5):503-513. doi:10.6004/jnccn.2023.0025
2. WHO Classification of Tumours Editorial Board, eds. Haematolymphoid tumours. 5th ed. IARC Press; 2024. WHO Classification of Tumours, Volume 11
3. De Braekeleer E, Douet-Guilbert N, De Braekeleer M. RARA fusion genes in acute promyelocytic leukemia: a review. Expert Rev Hematol. 2014;7(3):347-357
4. Sanz MA, Fenaux P, Tallman MS, et al. Management of acute promyelocytic leukemia: updated recommendations from an expert panel of the European LeukemiaNet. Blood. 2019;133(15):1630-1643
5. Mannan A, Muhsen I, Barragan E, et al. Genotypic and phenotypic characteristics of acute promyelocytic leukemia translocation variants. Hematol Oncol Stem Cell Ther. 2020:13(4):189-201
6. Gagnon MF, Berg HE, Meyer RG, et al. Typical, atypical and cryptic t(15;17)(q24;q21) (PML::RARA) observed in acute promyelocytic leukemia: A retrospective review of 831 patients with concurrent chromosome and PML::RARA dual-color dual-fusion FISH studies. Genes Chromosomes Cancer. 2022;61(10):629-634. doi:10.1002/gcc.23070
7. Dohner H, Wei AH, Appelbaum FR, et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. Blood. 2022;140(12):1345-1377. doi:10.1182/blood.2022016867

Performance

Method Description

This test is performed using a commercially available probe set. A dual-color, dual-fusion fluorescence in situ hybridization (D-FISH) strategy probe set is used to detect *PML::RARA* fusion. Following probe hybridization, 200 interphase nuclei are scored, and the results are expressed as the percent abnormal nuclei. When needed to resolve a potential RARA disruption, 100 interphase nuclei are scored using the dual-color break-apart RARA FISH probe.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

1 to 3 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
APLDF	APL - PML::RARA fusion, FISH, BL/BM	77031-3

Result ID	Test Result Name	Result LOINC® Value
622914	Result Summary	50397-9
622915	Interpretation	77031-3
622916	Result Table	93356-4
622917	Result	62356-1
GC168	Reason for Referral	42349-1
GC169	Specimen	31208-2
622918	Source	31208-2
622919	Method	85069-3
622920	Additional Information	48767-8
622921	Disclaimer	62364-5
622922	Released By	18771-6