MAYO CLINIC LABORATORIES

Test Definition: EOSMF

Chronic Eosinophilia, Specified FISH, Varies

Overview

Useful For

Detecting recurrent common chromosome abnormalities associated with myeloid/lymphoid neoplasms with eosinophilia and gene rearrangements (including *PDGFRA*, *PDGFRB*, *FGFR1*, *JAK2,* and *ABL1*) using **client-specified** probe set(s)

Evaluating specimens in which chromosome studies are unsuccessful

An adjunct to conventional chromosome studies in patients with eosinophilia

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
EOSMB	Probe, Each Additional (EOSMF)	No, (Bill Only)	No
EOS3B	Probe, Tri-color (EOSMF)	No, (Bill Only)	No

Testing Algorithm

This test includes a charge for the probe application, analysis, and professional interpretation of results for one probe set (2 individual fluorescence in situ hybridization [FISH] probes or 3 individual FISH probes). Additional charges will be incurred for 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 using client-specified FISH probes and is not intended as a panel test. Specific probes must be listed in the probe request field. Reflex probes can be performed when appropriate if specified in the order request field.

When specified, any of the following probes will be performed:
4q12 deletion or rearrangement, request probe FIP1L1, CHIC2, PDGFRA
t(4q12;var) or *PDGFRA* rearrangement, request probe PDGFRA break-apart
t(5q32;var) or *PDGFRB* rearrangement, request probe PDGFRB break-apart
t(8p11.2;var) or *FGFR1* rearrangement, request probe FGFR1 break-apart
t(9p24.1;var) or *JAK2* rearrangement, request probe JAK2 break-apart
t(9q34;var) or *ABL1* rearrangement, request probe ABL1 break-apart
t(9;22)(q34;q11) or *BCR::ABL1* fusion, request probe ABL1/BCR
t(13q12.2;var) or *FLT3* rearrangement, request probe FLT3 break-apart

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.

For more information see Eosinophilia: Bone Marrow Diagnostic Algorithm.

Special Instructions

- Eosinophilia: Bone Marrow Diagnostic Algorithm

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test is intended for instances when **limited** chronic eosinophilia fluorescence in situ hybridization (FISH) probes are needed based on specific abnormalities or abnormalities identified in the diagnostic sample. **The FISH probes to be analyzed must be specified on the ordering request.** If targeted FISH probes are not included with this test order, test processing will be delayed and the test may be canceled and automatically reordered by the laboratory as EOSFD / Chronic Eosinophilia panel, Diagnostic FISH, Varies.

At diagnosis, conventional cytogenetic studies (CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow) and a complete EOSFD / Chronic Eosinophilia panel, Diagnostic FISH, Varies. panel should be performed.

If a complete chronic eosinophilia FISH panel is preferred, order EOSFD / Chronic Eosinophilia panel, Diagnostic FISH, Varies.

Paraffin embedded tissue testing is **not available** for chronic eosinophilia.

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. A list of probes requested for analysis is required. Probes available for this test are listed in the Testing Algorithm section.
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.

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: 2-3 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 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
The myeloid/lymphoid neoplasms with eosinophilia and rearrangements of *PDGFRA*, *PDGFRB*, *FGFR1*, and *JAK2* represent a significantly diverse group of hematologic malignancies. Despite the disparate clinical presentations, which include chronic myeloid neoplasms (chronic myelomonocytic leukemia, chronic myeloproliferative neoplasms, chronic eosinophilic leukemia) versus more acute myeloid and lymphoid neoplasms (acute myeloid leukemia, B- and

T-lymphoblastic leukemia/lymphoma and mixed phenotypic acute leukemias), this diagnostic subgroup shares rearrangements involving 4 specific gene regions: *PDGFRA*, *PDGFRB*, *FGFR1*, and *JAK2*.

While conventional chromosome studies may detect many of the rearrangements associated with these gene rearrangements, several are cytogenetically "cryptic", including the most common abnormality involving *PDGFRA* activation. This one megabase submicroscopic, intrachromosomal deletion results in loss of the *CHIC2* gene region with subsequent fusion of neighboring genes *FIP1L1* and *PDGFRA*. In addition to this more common, cryptic deletion, the *PDGFRA* gene has many translocation partners described (at least 15) that similarly result in *PDGFRA* upregulation.

The *PDGFRB*, *FGFR1*, and *JAK2* gene regions similarly have numerous translocation/inversion partners described, at least 50 for *PDGFRB*, 10 for *FGFR1*, and 40 for *JAK2*. Despite the significant heterogeneity in gene partners, the identification of *PDGFRA*, *PDGFRB*, *FGFR1*, and *JAK2* rearrangements is critical for disease categorization and potential therapeutic intervention. Both *PDGFRA* and *PDGFRB* have the potential for response to targeted tyrosine kinase inhibitor therapies such as imatinib mesylate. Similarly, *JAK2* rearrangements have the potential for response to targeted inhibitor therapy. Rearrangements of *FGFR1* are typically more aggressive and less responsive to targeted inhibitors.

While not formally included in the World Health Organization categorization of myeloid/lymphoid neoplasms with *PDGFRA*, *PDGFRB*, *FGFR1*, or *JAK2* rearrangements, rearrangements of the *ABL1* gene, other than with the *BCR* locus, can result in similar clinical phenotypes. Thus, the *ABL1* gene region has been included in this fluorescence in situ hybridization panel evaluation to appropriately interrogate this gene region, particularly since these patients may not be identified by conventional karyotype analysis and may significantly benefit from targeted tyrosine kinase therapies.

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 go undetected in a targeted FISH test.

Bone marrow is the preferred sample type for this FISH test. If bone marrow is not available, a blood specimen may be used if there are neoplastic 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

Myeloid/lymphoid neoplasms with eosinophilia and gene rearrangement. In: Swerdlow SH, Campo E, Harris NL, et al,

eds. WHO Classification of Tumours. Vol 2. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. IARC Press; 2017:71-80

Performance

Method Description

This test is performed using commercially available and laboratory-developed probes. Rearrangements or deletions involving *CHIC2, PDGFRA, PDGFRB, FGFR1*, *JAK2*, and *ABL1* are detected using a tri or dual-color break-apart (BAP) strategy probe sets. Dual-color, dual-fusion fluorescence in situ hybridization (D-FISH) strategy probe sets are used in reflex testing when rearrangements of the *PDGFRB* and *ABL1* 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

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 x2, 88275 x1, 88291 x1-FISH Probe, Analysis, Interpretation; 1 probe sets
88271 x2, 88275 x1-FISH Probe, Analysis; each additional probe set (if appropriate)

88271 x1-FISH Probe; coverage for sets containing 3 probes (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
EOSMF	Chronic Eosinophilia, Spec FISH	107544-9

Result ID	Test Result Name	Result LOINC® Value
614256	Result Summary	50397-9
614257	Interpretation	69965-2
614258	Result Table	93356-4
614259	Result	62356-1
GC113	Reason for Referral	42349-1
GC114	Probes Requested	78040-3
GC115	Specimen	31208-2
614260	Source	31208-2
614261	Method	85069-3
614262	Additional Information	48767-8
614263	Disclaimer	62364-5
614264	Released By	18771-6