MAYO CLINIC LABORATORIES

Test Definition: ROS1F

Lung Cancer, ROS1 (6q22) Rearrangement, FISH, Tissue

Overview

Useful For

Fluorescence in situ hybridization (FISH) testing for *ROS1* allows for the detection of most *ROS1* rearrangements, therefore, is useful for identifying tumors that may be sensitive to directed therapy

ROS1 FISH testing may also support the diagnosis of inflammatory myofibroblastic tumor, certain cutaneous melanocytic tumors, or other neoplasms when used in conjunction with pathologic assessment

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
_I099	Interphases, 25-99	No, (Bill Only)	No
_I300	Interphases, >=100	No, (Bill Only)	No
_IL25	Interphases, <25	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
_PBCT	Probe, +2	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 probes). No analysis charges will be incurred if an insufficient number of representative cells are available for analysis.

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.

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Tissue

Ordering Guidance

This test does not include a pathology consultation. If a pathology consultation is requested, order PATHC / Pathology Consultation, and appropriate testing will be added at the discretion of the pathologist and performed at an additional charge.

Multiple oncology (cancer) gene panels are also available. For more information see Hematology, Oncology, and Hereditary Test Selection Guide

Additional Testing Requirements

Confirmation testing for the presence of a possible *ROS1* fusion transcript by next generation sequencing to resolve atypical or unbalanced fluorescence in situ hybridization results is available, order MCLNR / MayoComplete Lung Rearrangements, Rapid Test, Tumor.

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. A pathology report is required for testing to be performed. If not provided, appropriate testing and/or interpretation may be compromised or delayed. Acceptable pathology reports include working drafts, preliminary pathology, or surgical pathology reports.

The following information must be included in the report provided.?

1. Patient name
2. Block number - must be on all blocks, slides, and paperwork
3. Date of collection
4. Tissue Source

3. **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.

Specimen Required

Submit only 1 of the following specimens:

Preferred

Specimen Type: Tissue block

Collection Instructions: Submit a formalin-fixed, paraffin-embedded tumor tissue block. Blocks prepared with alternative fixation methods will be attempted but are less favorable for successful results by FISH testing; provide fixation method used.

Additional Information:

1. Paraffin-embedded specimens can be from any anatomic location (skin, soft tissue, lymph node, etc).
2. Bone specimens that have been decalcified will be attempted for testing, but the success rate is approximately 50%.

Acceptable

Specimen Type: Tissue slides

Slides: 1 Hematoxylin and eosin stained and 4 unstained

Collection Instructions: Submit 4 consecutive unstained, positively charged, unbaked slides with 5 micron-thick sections of the tumor tissue and 1 slide stained with hematoxylin and eosin.

Forms

If not ordering electronically, complete, print, and send an Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume
Slides: 1 Hematoxylin and eosin stained and 2 unstained

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

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Tissue	Ambient (preferred)		
	Refrigerated		

Clinical & Interpretive

Clinical Information
The *ROS1* gene at 6q22 encodes a tyrosine kinase receptor. Chromosomal rearrangements resulting in fusion of the 3' aspect of the *ROS1* gene with the 5' aspect of various partner genes was first identified in non-small cell carcinomas of the lung. *ROS1* fusions have since been identified in various other neoplasms including but not limited to inflammatory myofibroblastic tumors and cutaneous melanocytic tumors.

Clinical data has shown that tumors harboring *ROS1* fusions may be sensitive to directed tyrosine kinase inhibitor therapy.

Reference Values
An interpretive report will be provided.

Interpretation
A result is considered positive when the percent of cells separation of the *ROS1* FISH probes exceeds the normal cutoff for the *ROS1* FISH probe set.

A positive result is consistent with rearrangement of the *ROS1* gene and likely reflects *ROS1* fusion with a partner gene. The significance of this finding is dependent on the clinical and pathologic features.

A positive result suggests that the tumor may be responsive to directed therapy in the proper clinical and pathologic context. While results may indicate the potential response to directed tyrosine kinase inhibitors, selection of treatment remains a clinical decision.

A positive result may support a certain diagnosis in a particular clinical and pathologic context.

A negative result does not exclude the presence of a *ROS1* fusion or exclude the possible sensitivity to targeted therapy.

Cautions
This test is not approved by the U.S. Food and Drug Administration, and it is best used as an adjunct to existing clinical

and pathologic information.

This fluorescence in situ hybridization (FISH) assay does not rule out other chromosome abnormalities.

Fixatives other than formalin (eg, Prefer, Bouin's) may not be successful for FISH assays. Non-formalin fixed specimens will not be rejected.

Paraffin-embedded tissues that have been decalcified may not be successful for FISH analysis. The success rate of FISH studies on decalcified tissue is approximately 50%.

FISH studies will be attempted if sufficient tumor is present for analysis. The pathologist reviewing the hematoxylin and eosin-stained slide may find it necessary to cancel testing if insufficient tissue/tumor is available for testing.

If no FISH signals are observed post-hybridization, the case will be released indicating a lack of FISH results.

Clinical Reference

1. Cui M, Han Y, Li P, et al. Molecular and clinicopathological characteristics of ROS1-rearranged non-small-cell lung cancers identified by next-generation sequencing. Molecular Oncology. 2020;14(11):2787-95
2. Bergethon K, Shaw AT, Ou SH, et al. ROS1 rearrangements define a unique molecular class of lung cancers. J Clin Oncol. 2012;30(8):863-870. doi:10.1200/JCO.2011.35.6345
3. Antonescu CR, Suurmeijer AJ, Zhang L, et al. Molecular characterization of inflammatory myofibroblastic tumors with frequent ALK and ROS1 gene fusions and rare novel RET rearrangement. Am J Surg Pathol. 2015;39(7):957-967
4. Wiesner T, He J, Yelensky R, et al. Kinase fusions are frequent in Spitz tumours and spitzoid melanomas. Nature communications. 2014;5(1):3116
5. Shaw AT, Ou SH, Bang YJ, et al. Crizotinib in ROS1-rearranged non-small-cell lung cancer. N Engl J Med. 2014;371(21):1963-1971

Performance

Method Description

The test is performed using a laboratory-developed ROS1 (6q22) dual-color, break-apart strategy probe (BAP). Paraffin-embedded tissue samples are cut at 5 microns and mounted on positively charged glass slides. The selection of tissue and the identification of target areas on the hematoxylin and eosin (H and E)-stained slide are performed by a pathologist. Using the H and E-stained slide as a reference, target areas are etched with a diamond-tipped engraving tool on the back of the unstained slide to be assayed. The probe set is hybridized to the appropriate target areas, and 2 technologists each independently analyze 50 interphase nuclei (100 total) with the results expressed as the percent of abnormal nuclei.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available
7 to 10 days

Specimen Retention Time
Slides and H&E used for analysis are retained by the laboratory in accordance with regulatory requirements. Client provided paraffin blocks and extra unstained slides (if provided) will be returned after testing is complete.

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, 88291-DNA probe, each (first probe set), Interpretation and report
88271x2-DNA probe, each; each additional probe set (if appropriate)
88271x1-DNA probe, each; coverage for sets containing 3 probes (if appropriate)
88271x2-DNA probe, each; coverage for sets containing 4 probes (if appropriate)
88271x3-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)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ROS1F	ROS1 (6q22), FISH, Ts	81747-8

Result ID	Test Result Name	Result LOINC® Value
52235	Result Summary	50397-9
52237	Interpretation	69965-2
54595	Result	62356-1
CG755	Reason for Referral	42349-1
52238	Specimen	31208-2
52239	Source	31208-2

52240	Tissue ID	80398-1
52241	Method	85069-3
55035	Additional Information	48767-8
52242	Released By	18771-6
53821	Disclaimer	62364-5