MAYO CLINIC LABORATORIES

Test Definition: MESOF

Mesothelioma, CDKN2A FISH, Tissue

Overview

Useful For

Aiding in the diagnosis of mesothelioma by detecting a neoplastic clone associated with homozygous loss involving the *CDKN2A* gene region at 9p21.3 when used conjunction with an anatomic pathology assessment

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, <25	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 probe application, analysis, and professional interpretation of results for one probe set (2 individual fluorescence in situ hybridization probes). Analysis charges are based on the number of cells analyzed per probe. No analysis charges apply if there are insufficient representative cells for evaluation.

Appropriate ancillary probes may be performed at the consultant's 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 is only performed on specimens for the purpose of differentiating mesothelioma from histologic mimics.

This test is **not appropriate** for identifying *CDKN2A* deletions when mesothelioma is not included in the differential diagnosis. If this test is ordered and the laboratory is informed that the purpose of testing is not to differentiate

mesothelioma from histologic mimics, the laboratory will cancel the testing.

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 and Oncology Test Selection Guide.

Additional Testing Requirements

Confirmation testing using targeted next-generation sequencing for homozygous *CDKN2A* gene deletion is available, order MCSTP / MayoComplete Solid Tumor Panel, Next-Generation Sequencing, 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.

2. The following information must be included in the report provided:

-Patient name

-Block number - **must be on all blocks, slides, and paperwork**

-Collection date

-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 (fresh tissue is **not acceptable**)

Collection Instructions:

1. Submit a formalin-fixed, paraffin-embedded tumor tissue block.
2. Blocks prepared with alternative fixation methods (eg, Prefer, Bouin's) will be attempted but are less favorable for successful results. Provide fixation method used.

Additional Information:

1. Paraffin-embedded specimens can be from any anatomic location (skin, soft tissue, lymph node, etc).
2. Decalcified paraffin-embedded specimens will have testing attempted; however, the success rate is approximately 50%. **Testing may be canceled** if sufficient tumor tissue is not present.
3. **Submitted fresh tissue specimens will be canceled upon receipt**. If only fresh tissue is available, embed in paraffin prior to sending.

Acceptable:

Specimen Type: Tissue slides

Slides: 1 Hematoxylin and eosin-stained and 4 unstained
Collection Instructions: Submit 1 slide stained with hematoxylin and eosin and 4 consecutive unstained, positively charged, unbaked slides with 5-micron thick sections of the tumor tissue.
Additional Information: Broken or cracked unstained slides will be rejected. Stained slides that were broken and repaired (ie, double mounted) at the client site will not be rejected, as, in most cases, they can still be reviewed under the microscope. However, due to the double mounting, digital scanning cannot be performed.

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

Broken or cracked unstained slides	Reject
Broken or cracked stained slides that cannot be repaired	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information
The histologic distinction of malignant mesothelioma from benign mesothelial proliferations can be challenging. Loss of both copies of *CDKN2A* has been described as a recurrent abnormality in 59% to 80% of pleural malignant mesotheliomas depending on histologic features.(1-3) Homozygous deletion of *CDKN2A* is less common in peritoneal mesothelioma, reported to occur in 25% to 35% of cases.(2,4,5) The detection of homozygous deletion of *CDKN2A* by fluorescence in situ hybridization has been suggested as a useful adjunct to histologic examination in the differentiation of malignant mesothelioma from other processes.(6,7)

Reference Values
An interpretive report will be provided.

Interpretation

CDKN2A will be clinically interpreted as positive, negative, or equivocal.

A neoplastic clone is detected when the percent of cells with an abnormality exceeds the normal cutoff for the CDKN2A/D9Z1 probe set.

In the proper clinical and histologic context, a positive result may support a diagnosis of mesothelioma. However, homozygous loss of *CDKN2A* can be identified in many neoplasms. Clinical and pathologic correlation is required.

A negative result suggests no homozygous deletion of the *CDKN2A* gene region at 9p21.3 is present but does not exclude the diagnosis of mesothelioma. Homozygous *CDKN2A* deletion is not present in all mesotheliomas. Clinical and pathologic correlation is required.

A negative result does not exclude 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.

This test is intended to be used for diagnostic purposes in mesothelioma.

Due to limitations of the technology, fluorescence in situ hybridization (FISH) cannot detect all *CDKN2A* deletions.

This 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%, but FISH will be attempted if sufficient tumor is present for analysis.

Fluorescence in situ hybridization 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 signal or a lack of sufficient tumor tissue is observed post-hybridization, the case will be reported indicating a lack of FISH results.

Clinical Reference

1. Illel P, Ladanyl M, Rusch V, Zakowski MF. The use of CDKN2A deletion as a diagnostic marker for malignant mesothelioma in body cavity effusions. Cancer. 2003;99:51-56
2. Chiosea C, Krasinkas A, Cagle P, Mitchell KA, Zander DS, Dacic S. Diagnostic importance of 9p21 homozygous deletion in malignant mesotheliomas. Mod Pathol. 2008;21:742-747
3. Hwang H, Pyott S, Rodriguez S, et al. BAP1 immunohistochemistry and p16 FISH in the diagnosis of sarcomatous and desmoplastic mesotheliomas. Am J Surg Pathol. 2016;40:714-718
4. Krasinskas A, Bartlett D, Cieply K, Dacic S. CDKN2A and MTAP deletions in peritoneal mesotheliomas are correlated

with loss of p16 protein expression and poor survival. Mod Pathol. 2010;23:531-538
5. Singhi A, Krasinskas A, Choudry H, et al. The prognostic significance of BAP1, NF2, and CDKN2A in malignant peritoneal mesothelioma. Mod Pathol. 2016;29:14-24
6. Monaco S, Shuai Y, Bansal M, Krasinskas AM, Dacic S. The diagnostic utility of p16 FISH and GLUT-1 immunohistochemical analysis in mesothelial proliferations. Am J Clin Pathol. 2011;135:619-627
7. Wu D, Hiroshima K, Yusa T, et al. Usefulness of p16/CDKN2A Fluorescence in situ hybridization and BAP1 immunohistochemistry for the diagnosis of biphasic mesothelioma. Ann Diagn Pathol. 2017;26:31-37

Performance

Method Description

The test is performed using a commercially available enumeration strategy *CDKN2A* and chromosome 9 centromere (D9Z1) fluorescence in situ hybridization probe set. 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 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 and E used for analysis are retained by the laboratory in accordance with regulatory requirements. Client provided paraffin blocks and extra unstained slides 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)
88275 - Interphase in situ hybridization, 100 to 300 cells, each probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MESOF	Mesothelioma, FISH, Ts	21614-3

Result ID	Test Result Name	Result LOINC® Value
609715	Result Summary	50397-9
609716	Interpretation	69965-2
609717	Result	62356-1
GC086	Reason for Referral	42349-1
609718	Specimen	31208-2
609719	Source	31208-2
609720	Tissue ID	80398-1
609721	Method	85069-3
609722	Additional Information	48767-8
609723	Disclaimer	62364-5
609724	Released By	18771-6