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 deletion involving the *CDKN2A* gene region at 9p21.

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 application of the first probe set (2 fluorescence in situ hybridization probes) and professional interpretation of results. Additional charges will be incurred for application of 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.

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Tissue

Ordering Guidance

This test does not include a pathology consult. If a pathology consultation is requested, PATHC / Pathology Consultation should be ordered and the appropriate fluorescence in situ hybridization (FISH) test will be ordered and performed at an additional charge.

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. A pathology report is required in order for testing to be performed. Acceptable pathology reports include working drafts, preliminary pathology or surgical pathology reports.
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.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Tissue
Preferred: Tissue block
Collection Instructions: Submit a formalin-fixed, paraffin-embedded (FFPE) tumor tissue block. Blocks prepared with alternative fixation methods may be acceptable; provide fixation method used.

Acceptable: Slides
Collection Instructions: Four consecutive, unstained, 5 micron-thick sections placed on positively charged slides, and 1 hematoxylin and eosin-stained slide.

Forms

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

Specimen Minimum Volume

Two consecutive, unstained, 5 micron-thick sections placed on positively charged slides and 1 hematoxylin and eosin-stained slide.

Reject Due To

No specimen should be rejected.

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 (FISH) 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

A neoplastic clone is detected when the percent of cells with an abnormality exceeds the normal cutoff. 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. Therefore, clinical and pathologic correlation are required.

A negative result suggests no deletion of the *CDKN2A* gene region at 9p21. However, as homozygous deletion is not present in all mesotheliomas, this result does not exclude the diagnosis of malignant mesothelioma. In addition, due to limitations of the technology, fluorescence in situ hybridization cannot detect all *CDKN2A* deletions.

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.

Fixatives other than formalin (eg, Prefer, Bouin's) may not be successful for fluorescence in situ hybridization (FISH) assays, however nonformalin-fixed samples will not be rejected.

Paraffin-embedded tissues that have been decalcified are generally unsuccessful for FISH analysis. The pathologist reviewing the hematoxylin and eosin-stained slide may find it necessary to cancel testing.

Supportive Data

Fluorescence in situ hybridization analysis was performed on 44 formalin-fixed, paraffin-embedded tissue samples including 35 with atypical mesothelioma and 9 with typical mesothelioma. The normal controls were used to generate a normal cutoff for this assay. A deletion of *CDKN2A* was identified in 7 of the 9 typical mesothelioma (77%) and 2 of 35 atypical mesothelioma (5.7%) specimens.

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 despoplastic 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 *CDKN2A* enumeration probe set. Formalin-fixed, 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 is performed by a pathologist. Using the H and E-stained slide as a reference, target areas are etched with a diamond-tipped etcher 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 lab indefinitely. Client provided paraffin blocks and extra unstained slides (if provided) will be returned after testing is complete.

Performing Laboratory Location

Rochester

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 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 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