MAYO CLINIC LABORATORIES

Test Definition: MDM2F

MDM2 (12q15) Amplification, Well-Differentiated Liposarcoma/Atypical Lipomatous Tumor, FISH, Tissue

Overview

Useful For

Identifying *MDM2* amplification

Supporting the diagnosis of many neoplasms, including, but not limited to, well-differentiated liposarcoma, atypical lipomatous tumor, dedifferentiated liposarcoma, parosteal osteosarcoma and central low-grade osteosarcoma

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 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 the appropriate fluorescence in situ hybridization test will be added 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

To resolve atypical fluorescence in situ hybridization results, confirmation testing by microarray is available; order CMAPT / Chromosomal Microarray, Tumor, Formalin-Fixed Paraffin-Embedded.

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 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

-Date of collection

-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 fluorescence in situ hybridization 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 1 slide stained with hematoxylin and eosin and 4 consecutive unstained, positively charged, unbaked slides with 5 micron-thick sections of the tumor tissue.

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
Differential Diagnosis of Well-Differentiated Liposarcoma/Atypical Lipomatous Tumor:
The histological discrimination of well-differentiated liposarcoma/atypical lipomatous tumor (WDL/ALT) from lipoma can be diagnostically challenging. Amplification of genomic material derived from the chromosome band 12q13-15, which contains several genes, including *MDM2*, has been shown to be a recurrent finding in most WDL/ALT. Therefore, the detection of *MDM2* gene amplification by fluorescence in situ hybridization may be a useful adjunct to support a diagnosis of WDL/ALT in the proper histopathologic context.

Differential Diagnosis of Osteosarcoma:
The histological discrimination of parosteal or low-grade central osteosarcoma from other morphologically similar, but clinically distinct, entities can be difficult. Amplification of genomic material derived from the chromosome band 12q13-15, which contains several genes, including *MDM2*, has been shown to be a recurrent finding in a large proportion (67%-100%) of parosteal and central low-grade osteosarcomas. Therefore, the detection of *MDM2* gene amplification by fluorescence in situ hybridization may be a useful adjunct to support a diagnosis of low-grade central or parosteal osteosarcoma in the proper histopathologic context. Amplifications of 12q13-15 (including *MDM2*) are less common in conventional high-grade osteosarcoma, estimated to occur in approximately 5% to 10% of tumors.

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 the *MDM2* fluorescence in situ hybridization probe set.

Differential Diagnosis of Well-Differentiated Liposarcoma/Atypical Lipomatous Tumor:

A positive result is consistent with amplification of the *MDM2* gene locus (12q15) and, in the proper clinical and pathologic context, may support the diagnosis of well-differentiated liposarcoma/atypical lipomatous tumor (WDL/ALT). *MDM2* amplification may be seen in other neoplasms and is not diagnostic in isolation. Clinical and pathologic correlation is required.

A negative result is consistent with absence of amplification of the *MDM2* gene locus (12q15) but does not exclude the diagnosis of WDL/ALT. Clinical and pathologic correlation is required.

Differential Diagnosis of Osteosarcoma:
A positive result is consistent with amplification of the *MDM2* gene locus (12q15) and, in the proper clinical and pathologic context, may support the diagnosis of parosteal osteosarcoma or low-grade central osteosarcoma. *MDM2* amplification may be seen in other neoplasms and is not diagnostic in isolation. Clinical and pathologic correlation is required.

A negative result is consistent with absence of amplification of the *MDM2* gene locus (12q15) but does not exclude the diagnosis of low-grade central osteosarcoma or parosteal osteosarcoma. Clinical and pathologic correlation is required.

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

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.

Supportive Data

Fluorescence in situ hybridization (FISH) analysis was performed on 10 formalin-fixed, paraffin-embedded, well-differentiated liposarcoma/atypical lipomatous tumors (WDL/ALT) tumor samples and 25 normal controls. Amplification of *MDM2* was identified in the WDL/ALT samples and correlated with the CPM results. Amplification of *MDM2* was not observed in any of the control samples tumors.

Clinical Reference

1. Erickson-Johnson MR, Seys AR, Roth CW, et al. Carboxypeptidase M: a biomarker for the discrimination of lipoma from liposarcoma. Mod Pathol. 2009;22(12):1541-1547

2. Jacob E, Erickson-Johnson MR, Wang X, et al. Assessment of *MDM2* amplification using fluorescence in situ hybridization on paraffin-embedded tissue discriminates atypical lipomatous tumors from lipomas. Mod Pathol. 2006;19:13A
3. He X, Pang Z, Zhang X, et al. Consistent amplification of FRS2 and MDM2 in low-grade osteosarcoma: A genetic study of 22 cases with clinicopathologic analysis. Am J Surg Pathol. 2018;42(9):1143-1155
4. Duhamel LAE, Ye H, Halai, D, et al. Frequency of Mouse Double Minute 2 (MDM2) and Mouse Double Minute 4 (MDM4) amplification in parosteal and conventional osteosarcoma subtypes. Histopathology. 2012;60(2):357-359
5. Dujardin F, Binh MBN, Bourvier C, et al. MDM2 and CDK4 immunohistochemistry is a valuable tool in the differential diagnosis of low-grade osteosarcomas and other primary fibro-osseous lesions of the bone. Mod Pathol. 2011;24(5):624-637
6. WHO Classification of Tumours Editorial Board. Soft Tissue and Bone. 5th ed. IARC; 2020. World Health Organization Classification of Tumours. Vol 3

Performance

Method Description
This test is performed using a commercially available MDM2 probe set with a MDM2 probe and a chromosome 12 centromere probe (D12Z3). Formalin-fixed, paraffin-embedded tissues 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 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 30 interphase nuclei (60 total) with the results expressed as a ratio MDM2:D12Z3 signals.(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 (if provided) will be returned after testing is complete.

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

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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)
88271-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
MDM2F	MDM2 (12q15) Amp, FISH, Ts	93808-4

Result ID	Test Result Name	Result LOINC® Value
54681	Result Summary	50397-9
54684	Interpretation	69965-2
54683	Result	62356-1
54917	Specimen	31208-2
54686	Source	31208-2
54687	Tissue ID	80398-1
54688	Released By	19139-5
CG929	Reason For Referral	42349-1
55132	Method	85069-3
55133	Additional Information	48767-8
53396	Disclaimer	62364-5