Test Definition: JMDMF

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

Overview

Useful For
Supporting a diagnosis of well-differentiated liposarcoma/atypical lipomatous tumor

Testing Algorithm
The test includes a charge for technical application and professional interpretation of results.

Method Name
Fluorescence In Situ Hybridization (FISH)

NY State Available
No

Specimen

Specimen Type
Tissue

Shipping Instructions
Advise Express Mail or equivalent if not on courier service.

If sending a paraffin block, ship with an icepack during warm seasons.

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
-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 are not accepted; provide fixation method used.

Acceptable:
Specimen Type: Tissue slides
Slides: 1 Hematoxylin and eosin-stained and 2 unstained
Collection Instructions: Submit 1 slide stained with hematoxylin and eosin and 2 consecutive, unstained, positively charged, unbaked slides with 4 to 5-micron-thick sections of the tumor tissue.

Forms
If not ordering electronically, complete, print, and send a Molecular Pathology Test Request (T726) with the specimen.

Specimen Minimum Volume
Slides: 1 hematoxylin and eosin-stained and 1 unstained

Reject Due To

Decalcified specimens	Reject

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. However, standard cytogenetic identification of ring and giant rod chromosomes strongly support the diagnosis of WDL/ALT. These abnormal chromosomes are mainly composed of amplified sequences derived from chromosome bands 12q13-15 and contain several amplified genes including *MDM2, CPM, CDK4,* and *TSPAN31*. *MDM2* is amplified in greater than 99% of WDL and up to 30% of other types of sarcomas.

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 chromosome 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

Differential diagnosis of well-differentiated liposarcoma/atypical lipomatous tumor:
A neoplastic clone is detected when the percentage of cells with an abnormality exceeds the normal reference range for the *MDM2* fluorescence in situ hybridization (FISH) probe (positive result). A positive result is consistent with amplification of the *MDM2* gene locus (12q15) and supports the diagnosis of well-differentiated liposarcoma/atypical lipomatous tumor (WDL/ALT). A negative result is consistent with absence of amplification of the *MDM2* gene locus (12q15). However, negative results do not exclude the diagnosis of WDL/ALT. Amplification varies in individual tumors and among different cells in the same tumor.

Differential diagnosis of osteosarcoma:
A positive result is consistent with amplification of the *MDM2* gene locus (12q15) and supports the diagnosis of parosteal osteosarcoma or low-grade central osteosarcoma. A negative result indicates an absence of amplification of the *MDM2* gene locus (12q15). However, negative results do not exclude the diagnosis of low-grade central osteosarcoma or parosteal osteosarcoma.

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.

Fixatives other than formalin (eg, Prefer, Bouin) may not be successful for fluorescence in situ hybridization (FISH) assays; Optimum fixation should be performed in 10% neutral buffered formalin. Non-formalin-fixed samples will be rejected.

Paraffin-embedded tissues that have been decalcified may not be successful for FISH analysis. Decalcified samples will be rejected.

Clinical Reference

1. Erickson-Johnson MR, Seys AR, Roth CW, et al. Carboxypeptidase M: a biomarker for the discrimination of well-differentiated liposarcoma from lipoma. 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 tissues 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 LA, 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 MB, Bouvier 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. Fletcher DM, Bridge JA, Hogendoorn PCW, Mertens F eds. WHO Classification of Tumours of Soft Tissue and Bone. International Agency for Research on Cancer; 2013

Performance

Method Description

This test is performed using commercially available *MDM2* (12q15) and chromosome 12 centromere (D12Z3) probes. Formalin-fixed, paraffin-embedded tissues are cut at 4 to 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 30 interphase nuclei (60 total) per probe set with the results expressed as a ratio *MDM2:*D12Z3 signals.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

2 to 8 days

Specimen Retention Time

Images are saved indefinitely. Extra unstained slides (if provided) and hematoxylin and eosin slide will be sent to histology after testing is complete.

Performing Laboratory Location

Mayo Clinic Jacksonville Clinical Lab

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.

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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

88377

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
JMDMF	MDM2 (12q15) Amp, FISH, Tissue	93808-4

Result ID	Test Result Name	Result LOINC® Value
616054	Result Summary	50397-9
616055	Interpretation	69965-2
616057	Result	62356-1
616058	Reason for Referral	42349-1
616059	Specimen	31208-2
616060	Source	31208-2
616061	Tissue ID	80398-1
616062	Method	85069-3
616063	Additional Information	48767-8
616064	Disclaimer	62364-5
616065	Released By	18771-6