

MDM2 Gene Amplification by FISH

DETECTION OF MDM2 GENE AMPLIFICATION BY FLUORESCENT IN SITU HYBRIDIZATION (FISH) TO AID IN THE DIAGNOSIS OF WELL-DIFFERENTIATED LIPOSARCOMA

Test Highlights

- *MDM2* FISH detects amplification of the *MDM2* gene in formalin-fixed, paraffin-embedded (FFPE) tissue.
- *MDM2* FISH aids in the differential diagnosis between well-differentiated liposarcoma and benign lipoma.

Disease Overview

- Liposarcoma is a soft-tissue tumor that typically arises from deep-seated stroma in the limbs and retroperitoneum.
- Well-differentiated liposarcoma (atypical lipomatous tumor) is the most common liposarcoma subtype and can be difficult to distinguish from benign lipoma due to morphological similarities.
- Diagnosis of well-differentiated liposarcoma is important due to the risk of recurrence and progression to dedifferentiated liposarcoma, which is more aggressive.

Epidemiology

- Liposarcoma occurs primarily in older adults (average age of onset is 50) and accounts for approximately 20 percent of all soft-tissue sarcomas.
- Approximately 5,000 new liposarcoma cases are reported each year in the United States.

Genetics

- Well-differentiated liposarcoma is typically associated with giant chromosomes that contain amplicons of the 12q13-15 chromosomal region. This results in amplification of the *MDM2* oncogene, which controls cell growth and death by negatively regulating the tumor suppressor p53.
- Benign lipoma is not characterized by *MDM2* amplification.

Indications for Ordering

Patients diagnosed with or suspected of having well-differentiated liposarcoma based on tissue morphology.

Additional Ordering Notes

- The biopsy site, fixative used, elapsed time prior to fixation, and fixation time must be included.
- Only formalin-fixed (10 percent neutral buffered formalin for 6–48 hours), paraffin-embedded tissue samples containing sufficient viable tumor should be submitted. Decalcified specimens are not acceptable.

Interpretation

- Tissue with an *MDM2*/SE12 ratio ≤ 2 is non-amplified, while tissue with an *MDM2*/SE12 ratio > 2 is amplified.
- *MDM2* gene amplification strongly supports a diagnosis of well-differentiated liposarcoma.

Limitations

Results may be compromised if the recommended fixation procedures have not been followed.

Methodology

MDM2 FISH utilizes commercially available fluorescently-labeled DNA probes.

References

1. Veridex Repeat-Free™ Poseidon™ *MDM2* (12q15) & SE12 Control Probe (package insert) Raritan, NJ: Veridex,LLC;2009.
2. Weaver J, et al. Fluorescence in situ hybridization for *MDM2* gene amplification as a diagnostic tool in lipomatous neoplasms. *Mod Pathol* 2008;21:943–9.

Test Information

2003016

MDM2 Gene Amplification by FISH

For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.

AUTHOR

Michelle Wallander, PhD