Background
Neoplasms composed of well-differentiated adipose tissue are among the most common soft tissue tumors encountered by the pathologist. These neoplasms can be classified as lipoma or atypical lipomatous tumor (ALT)/well-differentiated liposarcoma (WDLPS). Classification of this group of tumors can be challenging, since many ALT/WDLPS do not have cytologic atypia or lipoblasts and therefore mimic benign lipomas when histopathologic analysis alone is used.

Clinical Significance
The distinction between a lipoma and ALT/WDLPS is very important, as lipomas do not exhibit locally aggressive behavior and do not require clinical follow up. Conversely, ALT/WDLPS do exhibit locally aggressive behavior and require long-term follow up. Lipoma and ALT/WDLPS both are treated surgically, but the extent of surgery that is indicated differs radically between the two types of tumors.

Interpretation
Methodology used for the assay is fluorescence in situ hybridization (FISH) using a DNA probe with specificity for the chromosomal locus that includes the MDM2 gene and a control centromeric probe to chromosome 12 (CEP12). Signals for MDM2 and CEP12 are enumerated for individual tumor cell nuclei, and the MDM2/CEP12 ratio is calculated.

Limitations of the Assay
It is very important that the tissue used for the FISH assay be fixed in formalin. Alternative fixative solutions frequently and unpredictably compromise hybridization between the probe and the target MDM2 gene and centromeric control loci. Also, necrosis within the neoplasm or very extended fixation will interfere with successful hybridization and compromise assay performance.

Methodology
1. The target tissue is the patient's tumor, obtained from formalin-fixed, paraffin-embedded tissue samples.
2. The tumor should be viable, and blocks should be selected in which the tumor tissue is relatively dense and as free as possible of adjacent normal tissue, necrosis, blood or dense inflammation.
3. As long as tumor tissue is present in the biopsy specimen, the specimen can be analyzed, including needle biopsy specimens.
4. Fixation should be 10% neutral buffered formalin, or other formalin-based fixative solution. Alternative fixatives often compromise hybridization between probe and target, and blocks prepared from tissue fixed in non-formalin-based solutions should not be submitted for evaluation.
5. Result provided is a ratio between the MDM2 signals and the centromeric chromosome 12 control signals. An MDM2/CEP12 ratio exceeding 2.0 is indicative of gene amplification.

References
Test Name: FISH for MDM2 gene amplification

Special Information: Formalin-fixed tissue embedded in paraffin or 5 unstained slides. Need 2 days to complete test. Tissue fixed in B5 not acceptable.

Specimen Requirements:
- Type: Paraffin block of formalin-fixed tissue. Note: Block must contain representative tumor tissue.
- Tube/Container: Clean container. Transport Temperature: Ambient. Note: Unstained sections of formalin-fixed paraffin-embedded tissue can also be evaluated, as long as tumor tissue is present and the specimen has been fixed in formalin-based fixative for between 6-72 hours.

Billing Code: 84397

CPT Code: 88368(x2)

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