The differential diagnosis of mesothelioma versus adenocarcinoma is one that usually has both medical and legal implications. In the past, the application of special techniques, such as mucicarmine and electron microscopic analysis, were required to distinguish between these tumors. At present, the vast majority of cases can be diagnosed by IHC studies utilizing a limited number of antibodies.

There is a set of robust immunohistochemically defined markers of mesothelioma, such as calretinin, cytokeratin 5, the Wilms tumor gene product (WT-1), and podoplanin (D2-40). While in earlier IHC studies the diagnosis of mesothelioma was associated with the absence of expression of adenocarcinoma-restricted proteins, such as CEA and CD15, more sensitive and specific markers of adenocarcinoma, such as Lewis Y (Bg8), MOC-31 and Ber-Ep4-defined antigens, are currently the preferred 'first line' reagents.

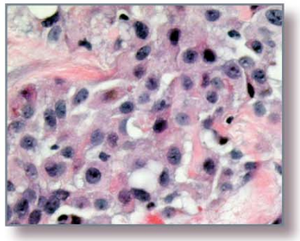
Positive markers of mesothelioma play a critical role in the analysis of these tumors.The sensitivities of the mesothelial markers also vary, with markers such as cytokeratin 5 showing diminished sensitivity in sarcomatoid variants. A small subset of adenocarcinomas can express each one of these mesothelial markers (e.g., WT-1 in papillary serous carcinomas of the ovary, and cytokeratin 5 in a subset of pancreatic, breast and other carcinomas); therefore, it is critical that results of IHC studies be integrated with the histologic findings and clinical setting.

	Mesothelioma	Adenocarcinoma
Calretinin		
Podoplanin (D2-40)		
Heatmap content available in the printed Pathology Reference Guide		
Tumor Glycoprotein (MOC-31)		
Tumor Glycoprotein (Ber-Ep4)		
WT-1		

Almost always positive	Usually positive	Not helpful	Usually negative	Almost always negative

See introduction to heat maps page 15

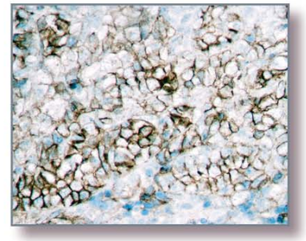
Mesothelioma



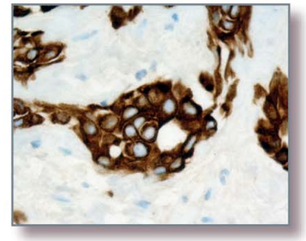
H&E

This pleural-based tumor occurred in a patient without a well-documented history of asbestos exposure. Nonetheless, the clinical differential diagnosis included mesothelioma.

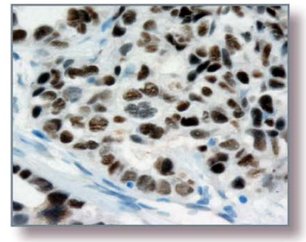
The tumor does not express the MOC-31-defined glycoprotein, the Lewis Y antigen, or the cell surface glycoprotein identified by the antibody Ber-Ep4.The tumor is strongly positive with antibodies to calretinin (a nuclear and cytoplasmic marker), cytokeratin 5 (a cytoplasmic marker), and WT-1 (a nuclear marker), as well as the D2-40-defined cell surface marker, confirming the diagnosis of mesothelioma.



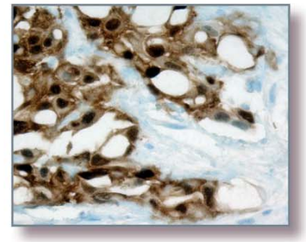
Podoplanin (D2-40)



CK5

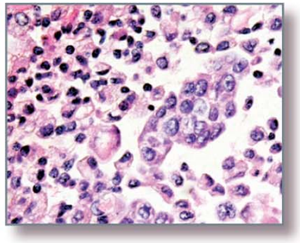


WT-1



Calretinin

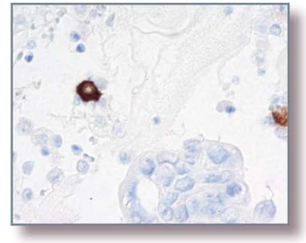
Adenocarcinoma



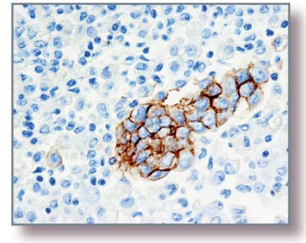
H&E

Malignant pleural effusion in a 68-year-old male with a history of smoking and workplace-related asbestos exposure. H&E-stained sections show clusters of malignant epithelial cells with the differential diagnosis of mesothelioma vs. adenocarcinoma.

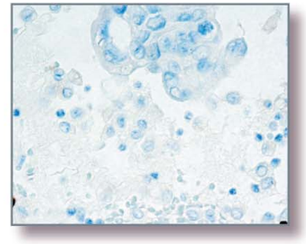
The immunophenotype of these malignant cells is unequivocally that of adenocarcinoma, as the tumor cells are negative for expression of the mesothelial-related markers, calretinin and cytokeratin 5, with scattered background reactive mesothelial cells serving as positive 'internal controls'. The tumor cells demonstrate expression of Bg8 and the MOC-31-defined antigen, pointing to the diagnosis of adenocarcinoma. Additional studies demonstrate expression of TTF-1, further identifying this as an adenocarcinoma of lung origin.



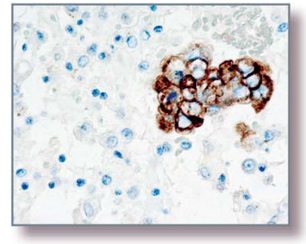
Calretinin



MOC-31



CK5



Bg8