

**SAMPLE IMMUNOHISTOCHEMISTRY REPORT**

**DIAGNOSIS:**

**ABC Hospital A06-33333 (Block A1)**

Lateral wall, thoracic cavity: Pseudomesotheliomatous adenocarcinoma of lung origin (please see comments).

**COMMENTS:**

While histologically (and grossly) this tumor appeared to represent mesothelioma, the immunophenotype of this tumor argues strongly against that diagnosis, with the tumor negative for three mesothelial-restricted markers (calretinin, podoplanin, and WT-1). Indeed, the tumor is positive for the adenocarcinoma-restricted markers identified by MOC-31 and Bg8, and furthermore is positive for expression of TTF-1, a lung carcinoma-specific nuclear transcription factor. In summary, this appears to be an example of a pseudomesotheliomatous adenocarcinoma, a variant of peripheral lung cancer first described thirty years ago by Harwood et al (Harwood TR et al., Am J Clin Pathol 65:159-67, 1976). Subsequent studies have demonstrated that these tumors display a highly aggressive course, with a mean survival of between 4.7 and 7 months (Koss M et al., Semin Diagn Pathol 9:117-23, 1992).

**SPECIMEN INFORMATION:**

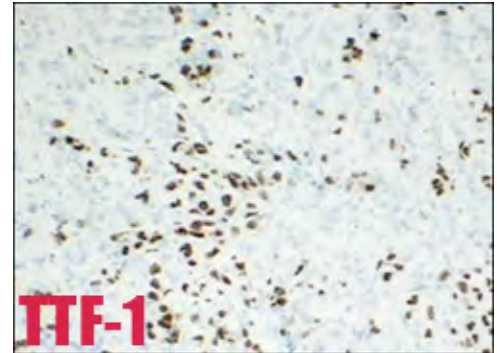
A1 = A06-33333, A1, 1 block/1 H&E

**RECEIVED FOR THE FOLLOWING:**

Assess for mesothelioma

**IMMUNOHISTOCHEMICAL FINDINGS:**

Tissue sections (along with appropriate positive control) are incubated with the following antibody. Localization is via a biotin-free, polymer-based immunoperoxidase technique according to an optimized protocol. The controls are reviewed for appropriate positive and negative reactivity and found to be satisfactory.



Block A1 (Surgery Date: 06/29/2006) - Thoracic cavity (PP2006XXXXX A1)

Target population: Tumor

Antibodies To	Clone	Result
TTF-1	SPT24	Variably positive
Surfactant ApoA1	PE10	Negative
WT-1 Wilms Tumor gene product	6F-H2	Negative
p63	4A4	Focally positive
Bg8 blood group Ag (Lewis Y)	F3	Uniformly positive
Epithelial antigen	MOC-31	Focally positive
Calretinin	5A5	Negative
Podoplanin	D2-40	Negative

**\*\*\*ELECTRONICALLY SIGNED\*\*\***

**Allen M. Gown, M.D.**

**Medical Director & Chief Pathologist**

In compliance with CMS regulations, the pathologist's signature on this report indicates that the case has been personally reviewed, and the diagnosis made or confirmed by the Pathologist.

NOTE: Some of the tests reported here may have been developed and performance characteristics determined by PhenoPath Laboratories. They have not been cleared or approved by the U.S. Food and Drug Administration (FDA). However, the FDA has determined that such clearance or approval is not necessary. Pursuant to the requirements of CLIA, this laboratory has established and verified the accuracy and precision of all tests, and additional information about these tests is available upon request. PhenoPath Laboratories is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical laboratory testing.

**EXPLANATORY NOTES ON ANTIBODIES AND PROBES**

**Thyroid transcription factor-1 (TTF-1)** - This is a nuclear transcription factor, expression of which is restricted to lung and thyroid epithelium and corresponding carcinomas. Studies have demonstrated that, within primary lung carcinomas, the sensitivity of TTF-1 is highest in neuroendocrine carcinomas (>90%), intermediate in nonsmall cell carcinomas (at least 80%), and lowest in squamous cell carcinomas (<5% or less). (Di Loreto, C, et al. J Clin Pathol 50:30-32, 1997; Folpe AL et al., Mod Pathol 12:5-8, 1999; Kaufmann O and Dietel M, Histopathol 36:8-16, 2000. TTF-1 shows very high specificity for lung and thyroid tumors in the context of non-neuroendocrine carcinomas; however, TTF-1 can also be expressed by high grade neuroendocrine carcinomas of other sites. Furthermore, it has been demonstrated that the SPT24 anti-TTF-1 clone employed here shows significantly higher sensitivity than anti-TTF-1 antibodies employed in earlier studies (Comperat E et al., Mod Pathol 18:1371-6, 2005).

**Surfactant ApoA1** - Surfactant A is a protein, expression of which is highly restricted to lung epithelium and a large subset (approximately 60-70%) of primary lung non-small cell carcinomas. Published studies, corroborated by work performed by my laboratory, confirm the specificity of Surfactant A for non-small cell lung adenocarcinoma. The highest level of expression is seen in bronchioloalveolar carcinomas, and the lowest in tumors showing squamous differentiation. (Nicholson, AG et al. Histopathology 27:57-60, 1995.)

**Wilms tumor suppressor gene product (WT-1)** - The Wilms' tumor suppressor gene product (WT-1) has been recently described as a novel positive marker of mesothelial cells and mesothelioma, distinguishing the latter from non-small cell carcinoma, e.g., of the lung, which does not express this protein (Amin KM et al., Am J Pathol 146:344-56, 1995). Furthermore, WT-1 protein expression has not been found in carcinomas of the lung, breast, or colon, but has been found in serous papillary carcinomas of the ovary (Hwang H et al., Appl Immunohistochem Mol Morphol 12:122-6, 2004). WT-1 expression has also been demonstrated to be the hallmark of desmoplastic small round cell tumor, where it is overexpressed as a consequence of the EWS-WT1 [t(11;22)(p13;q12)] translocation, helping to distinguish it from other small blue round cell tumors such as PNET/ES (Hill DA et al. Am J Clin Pathol 114:345-53, 2000).

**p63** - p63 is a nuclear protein, expression of which is restricted to a number of cell types, including the myoepithelium of breast and salivary gland, the outer cell layer in the prostate, and transitional and squamous epithelium (DiComo et al., Clin Cancer Res 8:494-501, 2002; Reis-Filho JS et al., Virchows Arch 443:122-332, 2003). Published studies performed in this laboratory have demonstrated the utility of p63 as myoepithelial marker in assessing the presence of absence of invasive carcinoma in breast specimens (Werling RW et al., Am J Surg Pathol 27:82-90 2003). The utility of antibodies to p63 in looking for the loss of the outer cell layer in the prostate as a marker of prostatic adenocarcinoma has also been documented (Weinstein MH et al., Modern Pathol 15:1302-8, 2002). p63 has also been found to be a highly sensitive and specific marker of squamous and transitional cell carcinomas (Kaufmann O et al. Am J Clin Pathol 116:823-30, 2001), as well as selected other tumors (e.g., of salivary gland origin) that show myoepithelial differentiation (Bilal H et al., J Histochem Cytochem 51:133-9, 2003). p63 has also recently been demonstrated to be a marker of the 'basal-like' variant of breast cancer.

**Bg8** - Bg8 (Lewis Y) is a blood group related antigen which has been demonstrated to be a sensitive marker of adenocarcinoma, not reacting with mesothelial cells or mesothelioma (Riera JR et al. Am J Surg Pathol 1997;21(12):1409-19; Ordonez NG. Am J Surg Pathol 2000;24(4):598-606).

**Epithelial antigen (MOC-31)** - MOC-31 is a monoclonal antibody that has recently been demonstrated to help in the distinction of adenocarcinoma (positive) from mesothelioma (negative). It has significant advantages over previous adenocarcinoma-related markers such as CEA and CD15 owing to its high sensitivity among adenocarcinomas of different primary sites. In our recent study, MOC-31 manifested the highest combined sensitivity and specificity of any adenocarcinoma marker in this clinicopathologic setting. (Ordonez NG, Human Pathol 29:166-9, 1998; Yaziji H et al., Mod Pathol 15:331a, 2002).

**Calretinin** - Antibodies to calretinin have been demonstrated to be a highly sensitive and specific marker of mesothelial cells and mesothelioma, helping to distinguish the latter from adenocarcinoma (Ordonez N. Modern Pathol 11:929-33, 1998; Doglioni C et al., Am J Surg Pathol 20:1037-46, 1996).

**Podoplanin** - Podoplanin (previously referred to as the D2-40 antigen) is a sensitive and specific marker of lymphatic endothelium, as well as neoplasms related to the latter, including Kaposi's sarcoma (Kahn HJ et al., Mod Pathol 15:434-40, 2002). In the context of epithelial tumors, however, podoplanin has also been demonstrated to be a highly sensitive and specific marker of mesothelium and mesothelioma, complementing other markers such as calretinin and the Wilms tumor gene product (Ordonez NG., Hum Pathol 36:372-40, 2005; Chu AY et al., Mod Pathol 18:105-10, 2005).