IMP3 and GLUT-1 Immunohistochemistry for Distinguishing Benign From Malignant Mesothelial Proliferations

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Abstract: Distinguishing malignant mesotheliomas from benign mesothelial proliferations on hematoxylin and eosin-stained sections can be extremely challenging. Various immunohistochemical stains have been suggested to help in making this distinction, but all are controversial. Recently, IMP3 (insulin-like growth factor II mRNA binding protein 3) and GLUT-1 (glucose transporter protein 1) have been proposed as immunohistochemical markers that are positive in mesotheliomas but not in benign proliferations. We evaluated the performance of these markers on a tissue microarray containing 30 malignant mesotheliomas and 48 benign thoracic or abdominal mesothelial proliferations. IMP3 was positive in 53% of malignant and 27% of benign cases ($P = 0.03$), whereas GLUT-1 was positive in 60% of malignant and 13% of benign cases ($P = 0.0003$). Forty-three percent of malignant cases, but only 4% of benign cases, were positive for both IMP3 and GLUT-1 ($P = 0.00003$). We conclude that, statistically, both IMP3 and GLUT-1 are more frequently positive in malignant compared with benign mesothelial processes; however, the frequency of positive staining in benign cases is too high to allow their diagnostic use as single stains. The combination of both markers may be of greater diagnostic value, but this hypothesis should be confirmed in further studies.

Key Words: mesothelioma, immunohistochemistry, benign mesothelial proliferations, IMP3, GLUT-1

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Distinguishing benign from malignant mesothelial proliferations is crucial in determining patient care and prognosis. Although this distinction is clear in most instances, in some cases, particularly in small or poorly oriented biopsies, determining whether a mesothelial process is benign or malignant can be extremely difficult (reviewed in Churg and colleagues[1–3]). Cytologic atypia, mitoses, and architectural complexity may be seen in both benign and malignant mesothelial processes, and these features are not reliable for making an unequivocal diagnosis of malignancy. Invasion and destructive growth by mesothelial cells into underlying normal structures such as fat or muscle, formation of solid tumor nodules, lack of zonation, and severe nuclear pleomorphism/atypical mitoses are better criteria on which to base a pathologic diagnosis of malignant mesothelioma,[1] but these features may not be assessable in limited biopsy material.

In addition to routine stains, a variety of immunohistochemical stains have been proposed as useful in making this distinction. Desmin positivity has been claimed to be a sign of a benign process.[4] In contrast, positivity for p53[5–7] or epithelial membrane antigen[4,8] has been viewed as indicative of malignancy. More recently, X-linked inhibitor of apoptosis,[9,10] CD147,[11] glucose transporter protein 1 (GLUT-1),[12] and insulin-like growth factor II mRNA binding protein 3 (IMP3)[13] have been promoted as markers of malignant mesotheliomas. The question of whether any or all of these markers are actually reliable is controversial, and for some markers, only 1 or a handful of series have been published[3,14] (see the Discussion section). In this paper, we examine the utility of GLUT-1 and IMP3 staining.

MATERIALS AND METHODS

Case Selection and Tissue Microarray Construction

This study was conducted under the auspices of the University of British Columbia/British Columbia Cancer Agency Research Ethics Board (certificate #H02-61375). The 78 cases in the tissue microarray (TMA), accessioned between 1997 and 2011, were obtained from the archives of the Vancouver General Hospital and from the consultation files of 1 of the authors (A.C.). To make the distinction between benign and malignant accurate, only mesotheliomas with typical histologic patterns and characteristic traditional immunohistochemical staining were selected. For benign mesothelial reactions, only cases in which the clinical features were unequivocally those of a

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benign process and in which microscopic examination showed nothing to suggest a malignant process were used. The cases were reviewed by 2 of the authors (A.C. and A.F.L.) and were designated as having epithelial, spindled, or mixed epithelial and spindled morphology. In all, 48 benign mesothelial proliferations (27 pleural, 21 peritoneal) and 30 malignant mesotheliomas (26 pleural, 3 peritoneal, 1 pericardial) were selected for inclusion in the TMA. At least 2 representative 0.6 mm tissue cores were obtained per case.

Immunohistochemistry

Immunohistochemical staining was performed at PhenoPath Laboratories under the supervision of A.M.G. For IMP3 immunohistochemistry, mouse monoclonal anti-human IMP3 clone 69 (Dako, Carpinteria, CA) was used at 1:100 dilution. Pretreatment for antigen retrieval was carried out for 25 minutes in Lab Vision Pretreatment Module, retrieval solution pH 9.0. The Ultravision Quanto polymer detection system was used. For GLUT-1 immunohistochemistry, mouse monoclonal anti-human GLUT-1 clone SPM498 (Thermo Fisher Scientific, Kalamazoo, MI) was used at 1:200 dilution after a 20-minute antigen retrieval in a vegetable steamer in a microwave oven with Tris-EDTA pH 9.0. Staining for both markers was run in a Lab Vision Autostainer 360.

Scoring of IMP3 and GLUT-1 Staining

For IMP3 staining, diffuse, easily visible, cytoplasmic staining of target cells was scored as positive. For GLUT-1 staining, dark brown membranous staining of target cells was scored as positive. A case was considered to be positive for staining if at least 1 of the replicate cores was positive. For both IMP3 and GLUT-1, a negative or faint staining result in all replicate cores of a single case was considered to be negative for staining. Cores lacking target mesothelial cells were not included in the analysis. GLUT-1 is also normally strongly expressed in red blood cells and served as positive internal control; all cases in which lesional cells were negative for GLUT-1 had expression of GLUT-1 in red blood cells.

Statistical Analysis

The 2-tailed Fisher exact test (significance level set at 0.05) was used to evaluate the difference in staining between benign and malignant mesothelial proliferations.

RESULTS

Overall Performance of IMP3 and GLUT-1

Both the malignant and the benign mesothelial processes showed positivity for IMP3 and GLUT-1 in a subset of cases (Fig. 1), and there was no obvious or consistent difference in staining intensity between benign and malignant proliferations.

In the whole series, consisting of 30 malignant and 48 benign mesothelial proliferations, IMP3 was positive in 16/30 (53%) of malignant and 13/48 (27%) of benign cases (significantly different; $P = 0.030$); sensitivity was 0.53, specificity 0.73, positive predictive value (PPV) 0.55, and negative predictive value (NPV) 0.71. GLUT-1 was positive in 18/30 (60%) of malignant and 6/48 (13%) of benign cases (significantly different; $P = 0.0003$); sensitivity was 0.60, specificity 0.88, PPV 0.75, and NPV 0.78. The specificity was improved with the use of both markers combined: 13/30 (43%) of malignant cases but only 2/48 (4%) of benign cases were positive for both IMP3 and GLUT-1 (significantly different; $P = 0.00003$); sensitivity was 0.43, specificity 0.96, PPV 0.87, and NPV 0.73 (Table 1).

Performance of IMP3 and GLUT-1 in Malignant and Benign Mesothelial Processes With Epithelial, Spindled, or Mixed Patterns

We further evaluated the expression of IMP3 and GLUT-1 in malignant/benign cases with epithelial morphology (Table 2), and in malignant/benign cases with spindled morphology (Table 3). Our TMA series contained a small number of cases (1 malignant and 6 benign) showing mixed epithelial and spindled elements. However, the number of these cases was too small to evaluate them as a separate group, so the 7 mixed cases were added to both the epithelial morphology and the spindled morphology groups. Therefore in Tables 2 and 3, the epithelial morphology group contained 56 cases (49 pure epithelial + 7 mixed), and the spindled morphology group contained 29 cases (22 pure spindled + 7 mixed).

In the epithelial morphology category, IMP3 was positive in 9/17 (53%) malignant cases and 12/39 (31%) benign cases (not significantly different; $P = 0.14$); sensitivity was 0.53, specificity 0.69, PPV 0.43, and NPV 0.77. GLUT-1 was positive in 9/17 (53%) malignant cases and 4/39 (10%) benign cases (significantly different; $P = 0.001$); sensitivity was 0.53, specificity 0.90, PPV 0.69, and NPV 0.81. The specificity was improved with the use of both markers: 7/17 (41%) malignant cases and 1/39 (3%) benign cases were positive for both IMP3 and GLUT-1 (significantly different; $P = 0.0005$); sensitivity 0.41, specificity 0.97, PPV 0.88, and NPV 0.79 (Table 2).

In the spindled morphology category, IMP3 was positive in 7/14 (50%) malignant cases and 2/15 (13%) benign cases (not significantly difference; $P = 0.050$); sensitivity was 0.50, specificity 0.87, PPV 0.78, and NPV 0.65. GLUT-1 was positive in 9/14 (64%) malignant cases and 2/15 (13%) of benign cases (significantly different; $P = 0.008$); sensitivity was 0.64, specificity 0.87, PPV 0.82, and NPV 0.72. The specificity was improved with the use of both markers: 6/14 (43%) malignant cases and 0/15 (0%) benign cases were positive for both IMP3 and GLUT-1 (significantly different; $P = 0.006$); sensitivity was 0.43, specificity 1.00, PPV 1.00, and NPV 0.65 (Table 3).

DISCUSSION

The question of mesothelial versus nonmesothelial malignancy can usually be answered by a combination of routine stain morphology and a panel of antibodies, some of which are generally positive in mesotheliomas and

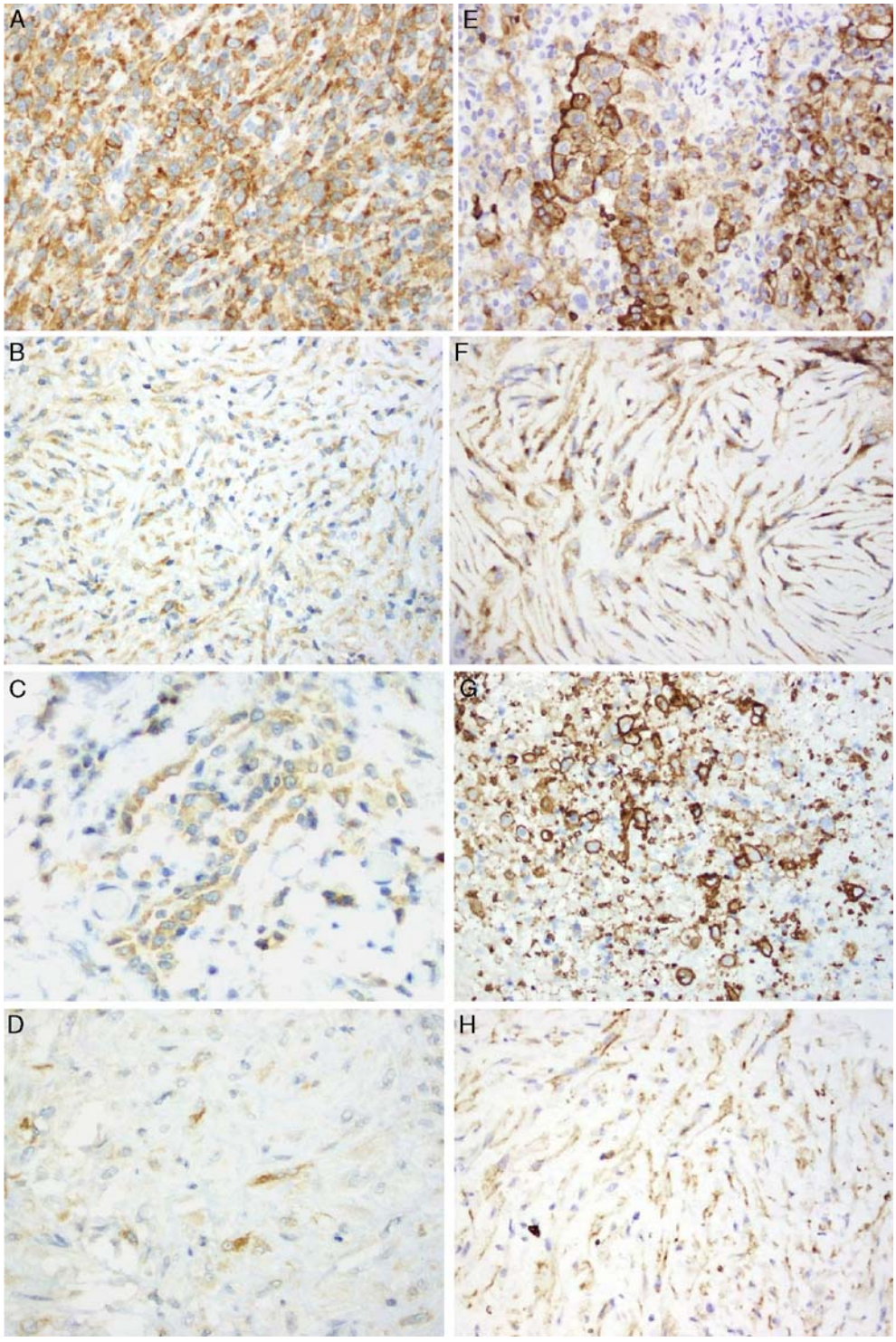

FIGURE 1. IMP3 staining of (A) malignant epithelial, (B) malignant spindle cell, (C) benign epithelial, and (D) benign spindle cell mesothelial proliferations. GLUT-1 staining of (E) malignant epithelial, (F) malignant spindle cell, (G) benign epithelial, and (H) benign spindle cell mesothelial proliferations.

some in nonmesothelial malignancies.[15] However, mesothelial markers such as calretinin, CK5, WT-1, mesothelin, and D2-40, which are used to distinguish mesotheliomas from nonmesothelial malignancies, are positive not only in mesotheliomas but also in benign mesothelial reactions.[16–18]

Although it is widely accepted that immunohistochemical stains are valuable in distinguishing mesotheliomas

TABLE 1. Summary of IMP3 and GLUT-1 Staining in the Series of 78 Malignant and Benign Mesothelial Proliferations

	IMP3	GLUT-1	IMP3 + GLUT-1
Malignant [n (%)]	16/30 (53)	18/30 (60)	13/30 (43)
Benign [n (%)]	13/48 (27)	6/48 (13)	2/48 (4)
Sensitivity	0.53	0.60	0.43
Specificity	0.73	0.88	0.96
PPV	0.55	0.75	0.87
NPV	0.71	0.78	0.73

from other types of malignancies, the idea that there exist immunohistochemical markers that stain only malignant or only benign mesothelial cells is much more controversial. As noted in the introduction, epithelial membrane antigen and p53 have previously been proposed as candidate malignant mesothelioma–specific markers, whereas desmin has been suggested as a marker of benign processes. However, none of these markers has been shown by multiple independent groups to be consistently reliable to help distinguish malignant from benign mesothelial processes.[2,3,14] Indeed, in a review of this issue in 2006, King et al[14] concluded that routine morphology on hematoxylin and eosin stain was the best predictor of a benign or malignant course.

Recently, IMP3 and GLUT-1 were reported to be expressed in malignant but not benign mesothelial processes, suggesting that these markers could be used to solve difficult cases in which the differential diagnosis is between a malignant mesothelioma and a benign reactive mesothelial proliferation. IMP3 was first identified in a screen for pancreatic carcinoma–specific markers.[19] It is normally expressed in humans during embryogenesis but becomes upregulated in a wide variety of malignancies.[20] Notably, it is highly expressed in both mesotheliomas and lung carcinomas.[21–23] Although it is not useful for distinguishing mesothelial from nonmesothelial malignancies, IMP3 has been suggested as a useful immunohistochemical marker of malignancy when the process in question is clearly mesothelial. Hanley et al[24] found that, in effusion cytology specimens, IMP3 marked 10/11 (91%) cases of malignant mesothelial cells but only 1/14 (7%) benign cells. Ikeda et al[25] noted a lower sensitivity and found that IMP3 marked 4/11 (36%) malignant mesothelial cells and 2/39 (5%) cases of benign cells

TABLE 2. Summary of IMP3 and GLUT-1 Staining in Malignant and Benign Mesothelial Proliferations With Epithelial Morphology

	IMP3	GLUT-1	IMP3 + GLUT-1
Malignant* [n (%)]	9/17 (53)	9/17 (53)	7/17 (41)
Benign† [n (%)]	12/39 (31)	4/39 (10)	1/39 (3)
Sensitivity	0.53	0.53	0.41
Specificity	0.69	0.90	0.97
PPV	0.43	0.69	0.88
NPV	0.77	0.81	0.79

*Includes 1 case with mixed epithelial and spindle cell morphology.
†Includes 6 cases with mixed epithelial and spindle cell morphology.

TABLE 3. Summary of IMP3 and GLUT-1 Staining In Malignant and Benign Mesothelial Proliferations With Spindle Cell Morphology

	IMP3	GLUT-1	IMP3 + GLUT-1
Malignant* [n (%)]	7/14 (50)	9/14 (64)	6/14 (43)
Benign† [n (%)]	2/15 (13)	2/15 (13)	0/15 (0)
Sensitivity	0.50	0.64	0.43
Specificity	0.87	0.87	1.00
PPV	0.78	0.82	1.00
NPV	0.65	0.72	0.65

*Includes 1 case with mixed epithelial and spindle cell morphology.
†Includes 6 cases with mixed epithelial and spindle cell morphology.

in effusion cytology specimens. With respect to histologic sections of malignant and benign mesothelial processes, IMP3 is similarly claimed to be differentially expressed. A study by Shi et al[13] found that 33/45 (73%) of malignant pleural/peritoneal mesotheliomas expressed IMP3, whereas none (n = 64) of the benign mesothelial proliferations expressed IMP3.

GLUT-1 is a high-affinity glucose transporter that is expressed in normal human tissues including red blood cells, endothelium of the blood-brain barrier, and placenta.[26,27] It also appears to be upregulated in certain types of malignancies, including those of lung,[28] breast,[29] head and neck (squamous),[30] and ovary.[31] Kato et al[12] reported that GLUT-1 was expressed in 48/48 (100%) tissue sections of pleural epithelial and spindle cell mesotheliomas as well as most lung adenocarcinomas, but was not detectable in any reactive mesothelial proliferations (0/40 cases).

Although some studies of IMP3 and GLUT-1 found no staining at all in benign mesothelial reactions, other did not. As noted above, Ikeda et al[25] found that 6% of benign mesothelial cells were positive for IMP3 in effusion cytology specimens; they also reported that, in the same cases, 100% of malignant mesotheliomas were positive compared with 20% of benign mesothelial cells. Lagana et al[32] studied GLUT-1 expression in whole-tissue sections of malignant mesotheliomas and benign mesothelial proliferations of thoracic and abdominal origin. In the thorax, they found that 13/30 (43%) malignant and 2/38 (5%) benign mesothelial lesions were positive for GLUT-1. In the abdomen, they found that 73/135 (54%) malignant and 0/21 (0%) benign mesothelial lesions were positive for GLUT-1. This corresponded to a lower overall sensitivity (53%) and specificity (98%) for GLUT-1 than that reported by Kato et al.[12]

In the present study we examined the performance of IMP3 and GLUT-1 immunohistochemistry on a TMA containing malignant mesotheliomas and benign mesothelial proliferations of pleural, pericardial, and peritoneal origin. We hypothesized that evaluating both markers together could improve specificity.

The results presented here suggest that IMP3 or GLUT-1 immunohistochemistry, if performed in isolation, is not helpful in benign mesothelial proliferations, in part because of very modest sensitivity but, more

importantly, because of much less specificity than originally claimed. The reasons for the higher staining frequencies of both IMP3 and GLUT-1 in benign processes in this study compared with others are not clear but might relate in part to greater sensitivity because of the technical staining approach used and also to differences in the particular antibodies selected.

Although both IMP3 expression and GLUT-1 expression were statistically more frequent in malignant compared with benign mesothelial processes, the relatively high rate of staining of benign reactions (27% for IMP3 and 13% for GLUT-1), in our opinion, renders these stains unsuitable as individual markers. One could argue that 13% positivity is a reasonable error rate, and had the question been one of distinguishing 2 clearly malignant processes, that would probably be true; however, given the vastly different therapeutic approaches and prognoses for benign compared with malignant mesothelial proliferations, we believe that 13% is too high.

Much better specificity was obtained when evaluating IMP3 and GLUT-1 coexpression. For the entire series, coexpression of IMP3 and GLUT-1 identified 43% of the malignant mesotheliomas but only 4% of the benign mesothelial proliferations. The difference in coexpression was largest in the spindled morphology subgroup, in which coexpression of IMP3 and GLUT-1 was seen in 43% of the malignant mesotheliomas but in none of the benign mesothelial proliferations. Even in the epithelial proliferations, only 3% of benign cases were positive for both. Although use of both markers improves specificity, it is at the expense of overall sensitivity (0.41).

Thus, the presence of IMP3 and GLUT-1 coexpression can potentially help identify malignant mesotheliomas, but the lack of expression of both markers is not diagnostic of a benign process. However, we emphasize the word "potentially" in the previous sentence. The idea that a combined panel of immunohistochemical stains might be a useful approach is, at this point, only a hypothesis. This hypothesis needs testing by multiple investigators on independent data sets before one could recommend the combination of IMP3 and GLUT-1, or any other combination of stains, for distinguishing benign from malignant mesothelial proliferations. At present we believe that there is no individual immunohistochemical stain that can be used for this purpose (reviewed briefly in Churg and Galateau-Salle[3]), and even if a multistain panel were devised, hematoxylin and eosin-stained sections will still remain as the most important diagnostic test.

REFERENCES

1. Churg A, Cagle PT, Roggli VL. *Tumors of the Serosal Membranes*. Washington, DC: American Registry of Pathology; 2006.
2. Churg A, Colby TV, Cagle P, et al. The separation of benign and malignant mesothelial proliferations. *Am J Surg Pathol*. 2000; 24:1183–1200.
3. Churg A, Galateau-Salle F. The separation of benign and malignant mesothelial proliferations. *Arch Pathol Lab Med*. 2012. [In press].
4. Attanoos RL, Griffin A, Gibbs AR. The use of immunohistochemistry in distinguishing reactive from neoplastic mesothelium. A novel use for desmin and comparative evaluation with epithelial membrane antigen, p53, platelet-derived growth factor-receptor, P-glycoprotein and Bcl-2. *Histopathology*. 2003;43:231–238.
5. Cagle PT, Brown RW, Lebovitz RM. p53 immunostaining in the differentiation of reactive processes from malignancy in pleural biopsy specimens. *Hum Pathol*. 1994;25:443–448.
6. Mayall FG, Goddard H, Gibbs AR. p53 immunostaining in the distinction between benign and malignant mesothelial proliferations using formalin-fixed paraffin sections. *J Pathol*. 1992;168: 377–381.
7. Ramael M, Lemmens G, Eerdekens C, et al. Immunoreactivity for p53 protein in malignant mesothelioma and non-neoplastic mesothelium. *J Pathol*. 1992;168:371–375.
8. Wolanski KD, Whitaker D, Shilkin KB, et al. The use of epithelial membrane antigen and silver-stained nucleolar organizer regions testing in the differential diagnosis of mesothelioma from benign reactive mesothelioses. *Cancer*. 1998;82:583–590.
9. Wu M, Sun Y, Li G, et al. Immunohistochemical detection of XIAP in mesothelium and mesothelial lesions. *Am J Clin Pathol*. 2007;128:783–787.
10. Wu M, Yuan S, Szporn AH, et al. Immunocytochemical detection of XIAP in body cavity effusions and washes. *Mod Pathol*. 2005;18:1618–1622.
11. Pinheiro C, Longatto-Filho A, Soares TR, et al. CD147 immunohistochemistry discriminates between reactive mesothelial cells and malignant mesothelioma. *Diagn Cytopathol*. 2012;40:478–483.
12. Kato Y, Tsuta K, Seki K, et al. Immunohistochemical detection of GLUT-1 can discriminate between reactive mesothelium and malignant mesothelioma. *Mod Pathol*. 2007;20:215–220.
13. Shi M, Fraire AE, Chu P, et al. Oncofetal protein IMP3, a new diagnostic biomarker to distinguish malignant mesothelioma from reactive mesothelial proliferation. *Am J Surg Pathol*. 2011;35: 878–882.
14. King J, Thatcher N, Pickering C, et al. Sensitivity and specificity of immunohistochemical antibodies used to distinguish between benign and malignant pleural disease: a systematic review of published reports. *Histopathology*. 2006;49:561–568.
15. Carella R, Deleonardi G, D'Errico A, et al. Immunohistochemical panels for differentiating epithelial malignant mesothelioma from lung adenocarcinoma: a study with logistic regression analysis. *Am J Surg Pathol*. 2001;25:43–50.
16. Cury PM, Butcher DN, Fisher C, et al. Value of the mesothelium-associated antibodies thrombomodulin, cytokeratin 5/6, calretinin, and CD44H in distinguishing epithelioid pleural mesothelioma from adenocarcinoma metastatic to the pleura. *Mod Pathol*. 2000; 13:107–112.
17. Hanna A, Pang Y, Bedrossian CW, et al. Podoplanin is a useful marker for identifying mesothelioma in malignant effusions. *Diagn Cytopathol*. 2010;38:264–269.
18. Nagel H, Hemmerlein B, Ruschenburg I, et al. The value of anti-calretinin antibody in the differential diagnosis of normal and reactive mesothelia versus metastatic tumors in effusion cytology. *Pathol Res Pract*. 1998;194:759–764.
19. Mueller-Pillasch F, Lacher U, Wallrapp C, et al. Cloning of a gene highly overexpressed in cancer coding for a novel KH-domain containing protein. *Oncogene*. 1997;14:2729–2733.
20. Yaniv K, Yisraeli JK. The involvement of a conserved family of RNA binding proteins in embryonic development and carcinogenesis. *Gene*. 2002;287:49–54.
21. Findeis-Hosey JJ, Xu H. Insulin-like growth factor II-messenger RNA-binding protein-3 and lung cancer. *Biotech Histochem*. 2012;87:24–29.
22. Findeis-Hosey JJ, Xu H. The use of insulin like-growth factor II messenger RNA binding protein-3 in diagnostic pathology. *Hum Pathol*. 2011;42:303–314.
23. Ikeda K, Tate G, Suzuki T, et al. IMP3/L523S, a novel immunocytochemical marker that distinguishes benign and malignant cells: the expression profiles of IMP3/L523S in effusion cytology. *Hum Pathol*. 2010;41:745–750.

24. Hanley KZ, Facik MS, Bourne PA, et al. Utility of anti-L523S antibody in the diagnosis of benign and malignant serous effusions. *Cancer*. 2008;114:49–56.
25. Ikeda K, Tate G, Suzuki T, et al. Diagnostic usefulness of EMA, IMP3, and GLUT-1 for the immunocytochemical distinction of malignant cells from reactive mesothelial cells in effusion cytology using cytospin preparations. *Diagn Cytopathol*. 2011;39:395–401.
26. Farrell CL, Yang J, Pardridge WM. GLUT-1 glucose transporter is present within apical and basolateral membranes of brain epithelial interfaces and in microvascular endothelia with and without tight junctions. *J Histochem Cytochem*. 1992;40:193–199.
27. Thorens B. Glucose transporters in the regulation of intestinal, renal, and liver glucose fluxes. *Am J Physiol*. 1996;270:G541–G553.
28. Ito T, Noguchi Y, Satoh S, et al. Expression of facilitative glucose transporter isoforms in lung carcinomas: its relation to histologic type, differentiation grade, and tumor stage. *Mod Pathol*. 1998;11:437–443.
29. Brown RS, Wahl RL. Overexpression of Glut-1 glucose transporter in human breast cancer. An immunohistochemical study. *Cancer*. 1993;72:2979–2985.
30. Reisser C, Eichhorn K, Herold-Mende C, et al. Expression of facilitative glucose transport proteins during development of squamous cell carcinomas of the head and neck. *Int J Cancer*. 1999; 80:194–198.
31. Cantuaria G, Fagotti A, Ferrandina G, et al. GLUT-1 expression in ovarian carcinoma: association with survival and response to chemotherapy. *Cancer*. 2001;92:1144–1150.
32. Lagana SR, Taub RN, Borczuk AC. Utility of glucose transporter 1 in the distinction of benign and malignant thoracic and abdominal mesothelial lesions. *Arch Pathol Lab Med*. 2012;136:804–809.