A major study of the use of immunohistochemistry to distinguish adenocarcinoma from mesothelioma was published in the April 2006 issue of *Modern Pathology* by PhenoPath Laboratories pathologists Todd S. Barry, Harry Hwang, Steven Kussick, and Allen M. Gown, in conjunction with pathologists Hector Battifora, Carlos Bacchi, and Hadi Yaziji, and the statistician Martin W. McIntosh. While there have been numerous previous attempts to define the immunophenotype of mesothelioma, in this study the most up-to-date panel of mesothelial and adenocarcinoma markers was employed, combined with a unique statistical method called logic regression analysis. The latter was used to determine which combinations of the positive and negative markers of mesothelioma were most powerful in separating these tumors. The most powerful discriminatory markers were found to be calretinin, a positive marker of mesothelioma, and the antibodies Bg8 and MOC-31, which identify glycoproteins that are positive markers of adenocarcinoma. The conclusions of this paper have important diagnostic implications, as many laboratories continue to use antibodies in this clinical setting (e.g., B72.3 and antibodies to CEA) that do not have the high discriminatory properties of antibodies to calretinin, and the antibodies Bg8 and MOC-31.

#### Evaluation of 12 antibodies for distinguishing epithelial mesothelioma from adenocarcinoma: identification of a three-antibody immunohistochemical panel with maximal sensitivity and specificity

- **Hadi Yaziji**
- **Todd S. Barry**
- **Carlos Bacchi**
- **Hector Battifora**
- **Martin W. McIntosh**
- **Allen M. Gown**

We evaluated the sensitivity and specificity of 10 monoclonal and two polyclonal antibodies for distinguishing epithelioid mesothelioma from adenocarcinoma (AdCA). The antibodies were directed against the mesothelial-associated antigens mesothelin, calretinin, cytokeratin 5, thrombomodulin, Wilms’ tumor-1 (WT-1) gene product and HBME-1, and the nonmesothelial antigens Lewis-Y blood group antigen, Lewis-X blood group antigen, and MUC1. The conclusions of this paper have important diagnostic implications, as many laboratories continue to use antibodies in this clinical setting (e.g., B72.3 and antibodies to CEA) that do not have the high discriminatory properties of antibodies to calretinin, and the antibodies Bg8 and MOC-31.
PhenoPath Laboratories offers many services of particular interest to dermatopathologists, assisting them with ancillary services essential to arriving at an accurate diagnosis.

**Direct Immunofluorescence Studies** looking for the presence of deposits of immunoglobulin and/or complement in specific locations within a skin or mucosal biopsy can play an important role in the identification of selected skin disorders. For example, granular deposition of IgA at the dermal-epidermal junction is the *sine qua non* of dermatitis herpetiformis, whereas the presence of linear IgG deposits in a ‘chicken wire’ pattern within the epidermis is characteristic of the pemphigus family of disorders. PhenoPath Laboratories’ pathologists have more than two decades of experience reading skin immunofluorescence studies. (Note: these studies require fresh tissue that should be sent in ammonium sulfate-based transport media; please contact PhenoPath Laboratories and we will gladly ship media to you.)

**Hematolymphoid Processes in the Skin** can pose particularly difficult diagnostic problems given their protean histologic appearances, the considerable morphologic overlap between benign and malignant processes in the skin, and the rapidly evolving nomenclature and classification schemes for lymphomas presenting in the skin. PhenoPath Laboratories has on staff two board-certified hematopathologists, Dr. Todd Barry and Dr. Steven Kussick, with extensive expertise in the evaluation of these processes. This evaluation frequently requires the application of immunohistochemical studies employing antibodies to lymphoid subsets (e.g., B and T cell-associated markers) and/or myelomonocytic cells, mast cells, and Langerhans cells. Flow cytometric and/or gene rearrangement studies can also be of assistance in this clinicopathologic setting. All of these specialized testing services are provided at PhenoPath.

The differential diagnosis of **Spindle Cell Lesions of the Skin** generally includes spindle cell carcinoma, melanoma, dermatofibroma, dermatofibrosarcoma protuberans, leiomyoma, etc., and immunohistochemical studies can be quite useful in ruling in or out most of these diagnoses. As usual, the approach at PhenoPath Laboratories is not “one size fits all” and we recognize that the histology and clinical context will often restrict the differential diagnosis. We take a very selective approach to the application of antibody panels in this (and all other) settings.

The images demonstrate a very unusual case of **ALK-positive anaplastic large cell lymphoma (ALCL)** presenting in the skin. The ALK positivity raises a concern that this represents a cutaneous manifestation of a systemic ALCL.
Billing Lead par excellence, Sheryl joined PhenoPath Laboratories in 1998, one year after its inception. Many of us regard overseeing all aspects of coding, reimbursement and collection as one of the most challenging jobs at the company; dealing with patients who are not only ill but also facing potentially large financial burdens requires skill, patience, good judgment and compassion. With over 10 years of medical billing experience, Sheryl works tirelessly to help clients and patients understand the intricacies of medical billing and how to navigate today's complex insurance systems for the maximum benefit of the patient. In the past year, Sheryl has also been instrumental in the implementation of PhenoPath’s new medical billing system. Should you have any questions or concerns regarding PhenoPath’s medical billing policies or procedures, we encourage you to contact Sheryl directly at 206-374-1480 or toll free, at 866-927-4366.

**PhenoPath’s requisition form has been expanded**

PhenoPath’s requisition form has been expanded. The back of the form now includes a listing of antibodies for flow cytometry and immunohistochemistry, sorted by diagnostic setting. In addition, in response to your feedback, we have removed the requirement for the ordering physician’s signature. If you have any questions regarding the new form or would like to obtain forms with your institution’s name, address, phone number, and fax number preprinted, contact a member of our Client Services Staff at 888-92-PHENO (888-927-4366) or e-mail lab@phenopath.com.

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**See our pathologists at the following upcoming meetings:**

**2006 ASCO Annual Meeting, June 2-6, 2006**

Georgia World Congress Center, Atlanta, Georgia
Advocating Survivorship, Clinical Science, & Oncology Quality Care

Dr. Gown will present a poster entitled "Multivariate analysis of expression of the microtubule-associated protein, tau, predicts improved progression free and overall survival in patients with metastatic HER-2-negative breast cancers treated with docetaxel and vinorelbine plus filgrastim" on Saturday, June 3, 2006 from 8:00 AM to 12:00 PM in Building B, Level 4, Room B401. Check our website www.phenopath.com for further updates. For additional information about this meeting, please visit http://www.asco.org/.

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**Breast Pathology: Current Concepts and Controversies June 5-6, 2006**

The Fairmont Copley Plaza Hotel, Boston, MA
Beth Israel Deaconess Medical Center, Department of Pathology

Dr. Allen M. Gown is a featured speaker at the Breast Pathology: Current Concepts and Controversies course to be held June 5-6, 2006 at the Fairmont Copley Plaza Hotel in Boston, MA. Dr. Gown will give the following presentations:

**Monday, June 5**

11:30 AM – 12 PM Special Lecture: Current Status of ER/PR Testing
1:15 PM – 1:45 PM Special Lecture: Current Status of HER2 Testing

For additional information about this meeting, please visit http://cme.hms.harvard.edu/.
Dr. Torsten O. Nielsen of the University of British Columbia in Vancouver, Canada, will present “Translating Expression Profiles into Clinical Care” at the Quarterly Pathology/Immunohistochemistry Conference on Thursday, May 11, 2006 at PhenoPath Laboratories. The format of the conference is a social hour commencing at 6:30 p.m., followed by the lecture at 7:30 p.m. A catered light dinner will be provided during the social hour.

Dr. Nielsen’s research interests involve understanding how molecular changes in cancer cells impact diagnosis, prognosis, and treatment, and in developing new and clinically practical molecular diagnostics for targeted therapies for human cancer, particularly sarcomas and breast cancer. His active research areas are gene expression profiling, tissue microarrays and experimental therapeutics. As one of the directors of the Genetic Pathology Evaluation Centre in Vancouver, he leads several projects focusing on the validation and clinical correlation of results from gene expression profiling of sarcomas and breast cancer (including the basal-like phenotype). Dr. Nielsen will speak on how expression profile results can be applied in practice using techniques (immunohistochemistry, FISH, PCR) that are applicable on standard paraffin material and accessible/affordable for hospital laboratories.

Torsten Nielsen completed his MD/PhD at McGill University and is currently an Assistant Professor and clinician-scientist in the Departments of Pathology and Orthopaedics at the University of British Columbia. He is based at the Vancouver General Hospital and British Columbia Cancer Agency. The spring Quarterly Conference will be co-sponsored by Dako Corporation.