**NEW TESTS**

Now Available at PhenoPath

**PAX8, MDM2, BRAF**

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The PAX proteins are a family of nine proteins, critical during organogenesis, with expression of individual PAX genes helping guide development of specific tissue types. In recent years, however, several members of this nuclear transcription factor family have also emerged as useful lineage-restricted immunohistochemical markers for the analysis of tumors.

**PAX2** and **PAX5** have been utilized for several years as markers of renal cell and B cell malignancies, respectively. PAX8 is expressed in thyroid and non-ciliated mucosal cells of the fallopian tubes and simple ovarian inclusion cysts, but not the ovarian surface epithelial cells. PAX8 is also emerging as an extremely sensitive, and in the appropriate context, specific, marker of ovarian carcinomas. Unlike WT-1, which is only positive in ovarian serous carcinomas, PAX8 is expressed by ovarian serous, endometrioid, and clear cell carcinomas, but only rarely in primary ovarian mucinous adenocarcinomas. A subset of endometrial adenocarcinomas are also PAX8-positive, but studies have demonstrated absence of expression of PAX8 in breast and other non-GYN carcinomas other than those primary to the thyroid. PAX8 is an important new marker of ovarian cancer.


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<table>
<thead>
<tr>
<th>Examples of Embryonic Expression</th>
<th>Examples of Tumors Identified</th>
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<tbody>
<tr>
<td>PAX2</td>
<td>Kidney</td>
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<tr>
<td></td>
<td>Renal cell carcinoma</td>
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<tr>
<td>PAX5</td>
<td>B lymphocytes</td>
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<td></td>
<td>B cell lymphoma</td>
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<tr>
<td>PAX8</td>
<td>Mullerian duct</td>
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<td>Ovarian carcinomas (non-mucinous)</td>
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H&E stained section of clear cell tumor metastatic to liver in 56-year-old female with remote history of ovarian tumor.

Uniform expression of PAX8 confirms diagnosis of metastatic clear cell ovarian carcinoma.

(continued on page 2)
Well-differentiated liposarcoma/atypical lipomatous tumors are unique in harboring ring and giant marker chromosomes consisting of amplicons of the q13-15 region of chromosome 12, which includes the MDM2 gene. MDM2 is a nuclear phosphoprotein that binds and inhibits transactivation by the tumor suppressor gene product, p53. Recently, Weaver and colleagues have demonstrated that the technique of fluorescence in situ hybridization (FISH) can be employed to detect the presence of MDM2 gene amplification and hence assist in the diagnosis of these tumors. FISH testing for MDM2 has been validated and is now available at Phenopath Laboratories. The assay employs a dual-color MDM2 FISH probe, which is composed of labeled probes to MDM2 as well as the centromere of chromosome 12 (SE12). The accompanying image demonstrates the finding in well-differentiated liposarcoma, with multiple orange MDM2 signals and eusomic green SE12 signals. As demonstrated by Weaver and colleagues, this FISH assay can be helpful in distinguishing well-differentiated liposarcoma from other soft tissue neoplasms. Most importantly, MDM2 amplification is not present in benign lipoma and angiolipoma. The histologic spectrum of lipomatous neoplasms that show MDM2 amplification includes not only well-differentiated liposarcoma/atypical lipomatous tumor, but also dedifferentiated liposarcoma and a minority of myxoid liposarcomas. Spindle cell/pleomorphic lipoma shows polysomy at this locus. This MDM2 FISH assay can prove especially helpful, given the dearth of immunostains which can be employed to identify liposarcoma and distinguish it from histologic mimics.


**MDM2 FISH studies require a paraffin block of formalin-fixed tissue or unstained 4 micron sections.** Please contact Dr. Harry Hwang, Director of Molecular Pathology at Phenopath Laboratories, if you have any specific questions about this, or any other molecular assay.

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**New Molecular Testing Requisition Form**

We have introduced a new requisition form specifically for ordering molecular tests (e.g., FISH, PCR). You can download this requisition form directly from our website, www.phenopath.com, or call us at 206-374-9000, and we will send you pre-printed forms with your information.
VISIT US AT THE FOLLOWING MEETINGS:
For up-to-date information, visit our website: www.phenopath.com

South Bay Pathology Society Presents:
Immunohistochemistry in Surgical Pathology: Challenges and Diagnostic Pitfalls
**May 9, 2009**, Monterey Conference Center, Monterey, CA
Allen M. Gown, MD presented as follows:
- **9:00 – 10:30 AM:**
  - General Issues – Allen Gown, MD
  - Thyroid – Saul Suster, MD
  - Breast – Allen Gown, MD
- **11:00 AM to Noon:**
  - Lung & Pleura – Saul Suster, MD
  - Gastrointestinal Tract – Allen Gown, MD
- **1:30 – 3:00 PM:**
  - Soft Tissue – Saul Suster, MD
  - Liver – Allen Gown, MD
  - Skin Neoplasms – Saul Suster, MD
- **3:30 – 4:30 PM:**
  - Male Genitourinary – Allen Gown, MD
  - Miscellaneous Lesions – Saul Suster, MD

Pritzker Memorial Lecture
**June 15, 2009**, 5:00-6:00 pm, Mount Sinai Hospital, Toronto
Allen M. Gown, MD is a featured speaker and will present a talk entitled
“Immunohistochemistry: The Past as Prologue to the Future”

Oregon Pathologists Association
**September 11-12, 2009**.
Allen M. Gown, MD presents as follows:
- **September 11, 2009, 7:30 PM**, Oregon Medical Association Building
  “Seeing the World on a Bicycle”
- **September 12, 2009, 9:00 AM to Noon**, St. Vincent Hospital, Portland, OR
  “Applications of Immunohistochemistry to Problems in Surgical Pathology”

CAP Virtual Management Conference
**October 13, 2009**.
Allen M. Gown, MD is a featured speaker and will present a talk entitled
“Antibody & Test Validation in IHC”

24th Annual Clinical Cytometry Society Meeting & Course
**October 16-21, 2009**, Hyatt Regency Jacksonville Riverfront, Jacksonville, FL

California Society of Pathologists 62nd Annual Convention:
Seminars in Pathology
**December 2-5, 2009**, Hyatt Regency San Francisco, Embarcadero Center

San Antonio Breast Cancer Symposium
**December 9-13, 2009**, Henry B. Gonzalez Convention Center, San Antonio, TX
Philip LeBoit, M.D., of the University of California, San Francisco, CA, will present “Difficult Diagnoses in Dermatopathology made Easier with Molecular and Immunopathologic Techniques" at The PhenoPath Spring Conference on Thursday, June 4, 2009. The format of the conference is a social hour commencing at 6:30 PM, followed by Dr. LeBoit’s lecture at 7:30 PM. A light catered dinner will be served during the social hour.

Dr. LeBoit is a Professor of Pathology and Dermatology, and Co-Director of the UCSF Dermatopathology Service. He received an MD degree from Albany Medical College, and completed his residency at UCSF and at Mt. Sinai School of Medicine, followed by a Dermatopathology Fellowship at Cornell University Medical Center. Dr. LeBoit founded the UCSF Dermatopathology Service in 1987, which is the largest university-based outreach dermatopathology laboratory in the western United States. The service sees over 90,000 cases/year, including over 20,000 cases in which pathologists, dermatologists or dermopathologists seek a second opinion.

Dr. LeBoit’s main research interest in dermatopathology is how does one make a more accurate diagnosis based on a skin biopsy. To this end, he studies both inflammatory and neoplastic diseases, applying both high- and low-tech methods as the situation warrants. Of particular interest are entities whose essential natures are unclear, such as Spitz nevus, a tumor of melanocytes in which large cells occur, sometimes simulating melanoma.

Dr. LeBoit is one of the leading figures in contemporary dermatopathology, as a consultant, author and clinical investigator. He has written over 150 articles, edited or co-authored 8 books, including the two-volume text “Cutaneous Medicine and Surgery” (1996), “Histopathology of Nevi and Melanoma” (2004), and “Skin Tumors” in the WHO Tumors and Genetics Series (2006). He served as editor-in-chief of the American Journal of Dermatopathology from 1997-2007 and as co-editor of Seminars in Cutaneous Medicine and Surgery. He is currently President of the International Society of Dermatopathology. His contributions to the medical literature include the first comprehensive descriptions of bacillary angiomatosis, primitive polypoid granular cell tumor and nephrogenic fibrosing dermopathy, and many studies of Spitz nevus. A renowned speaker, Dr. LeBoit has given over 250 invited lectures, on every continent except Antarctica.