Phenomena

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PhenoPath at USCAP 2006 Annual Meeting

PhenoPath Laboratories is actively participating in the 2006 Annual Meeting of the United States and Canadian Academy of Pathology in Atlanta, Georgia from February 11 – 17, 2006. Our pathologists will be presenting several abstracts highlighting our ongoing clinical research studies (see page 2). PhenoPath will also be exhibiting at the meeting from Feb. 13-15, showcasing new immunohistochemistry and molecular tests, along with our new 9-color flow cytometry service.

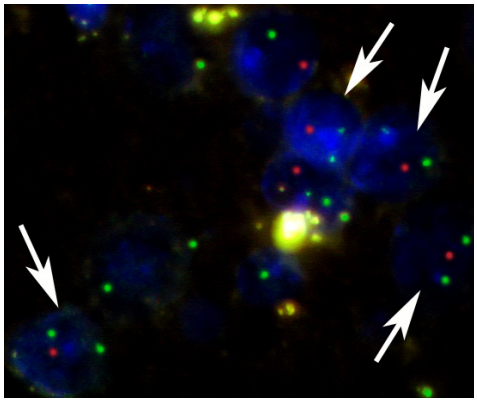
Short Course Presentation

Dr. Todd S. Barry of PhenoPath Laboratories, along with Dr. Neal Goldstein of William Beaumont Hospital, Michigan, have teamed up to present a brand new short course entitled, ***Update and Troubleshooting Immunohistochemistry for Pathologists*** on Thursday, February 16 from 1:00 to 4:30 PM in the Regency VII room at the Hyatt Regency Hotel, Atlanta. This course includes short lectures on creating antibody panels for, and interpreting immunostains performed on, small needle core biopsies. Topics also include: the advantages and disadvantages of specific commercial antibodies; troubleshooting guidelines for pathologists; the most common causes and solutions to suboptimal automated instrument immunostains. This course is designed for the practicing and in-training anatomic pathologist.

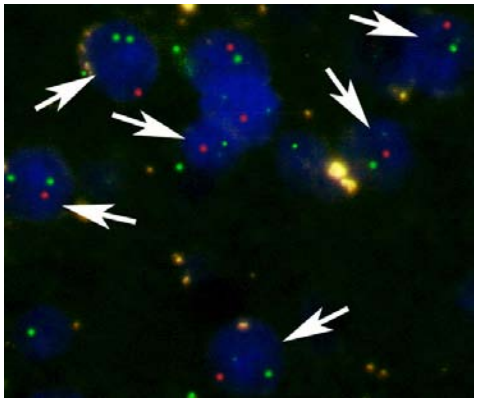
Special Evening Presentation

Dr. Allen M. Gown of PhenoPath Laboratories will be presenting a talk entitled, ***"Are we erring in the ER testing of breast cancer by IHC?"*** during a special evening presentation cosponsored by Lab Vision - NeoMarkers and PhenoPath. Dr. Gown will be joined by Dr. Paolo Dei Tos, from Treviso, Italy to share details from his recently published paper entitled, "A comparative study between a novel category of immunoreagents and the corresponding mouse monoclonal antibodies."

The presentation will be on Monday, February 13, 2006 from 5:30 to 7:30 pm in the Kennesaw Room at the Hyatt Regency Hotel, Atlanta. Please look for more details on our web site **(www.phenopath.com)** and on the Lab Vision web site **(www.labvision.com)**. Attendees of the annual USCAP meeting who are preregistered will receive an invitation by mail. Additional information will also be available at the PhenoPath and Lab Vision exhibit booths during the USCAP meeting. *(see additional USCAP presentations on page 2.)*



Oligodendroglioma showing loss of 1p36 (highlighted by arrows). Single 1p36 red signal is accompanied by two 1q25 green reference signals indicating 1p36 loss.



Oligodendroglioma showing loss of 19q13 (highlighted by arrows). Single19q13 red signal is accompanied by two 19p13 green reference signals indicating 19q13 loss.

New FISH Studies Available For Oligodendrogliomas

Gliomas are the most common primary neoplasm of the central nervous system and can have strikingly different clinical behaviors and responses to therapy. Distinguishing between different subtypes is often less than perfect with significant inter-observer variability. Although attempts have been made to define clinical and histologic features that correlate with a favorable prognosis, none have been sufficiently reliable at predicting response to adjuvant chemotherapy. However, recent studies have shown that loss of 1p36 and 19q13 are associated with an oligodendroglial phenotype, favorable response to chemotherapy and overall prolonged survival [1-3]. Fluorescence in situ hybridization (FISH) studies provide a direct method for identifying loss of 1p36 and 19q13 in formalin-fixed, paraffin-embedded tissue sections. Loss of 1p36 and 19q13 is performed by assessing the ratio of 1p36 and 19q13 to their corresponding reference genes, 1q25 and 19p13, respectively; and by assessing the number of nuclei showing clear 1p36 and 19q13 deletion, according to guidelines defined by the International Society of Pediatric Oncology (E-SIOP Europe Neuroblastoma Study Group) [1-4].

REFERENCES:

1.Burger PC et al. Losses of chromosomal arms 1p and 19q in the diagnosis of oligodendroglioma. A study of paraffin-embedded sections. Mod Pathol. 2001 Sep;14(9):842-53.

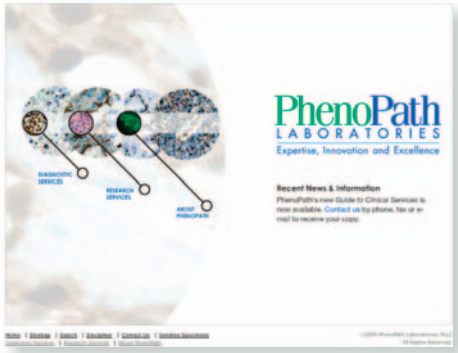
2.Smith JS et al. Alterations of chromosome arms 1p and 19q as predictors of survival in oligodendrogliomas, astrocytomas, and mixed oligoastrocytomas; J Clin Oncol. 2000 Feb;18(3):636-45.

3.Gelpi E et al. Fluorescent in situ hybridization on isolated tumor cell nuclei: a sensitive method for 1p and 19q deletion analysis in paraffin-embedded oligodendroglial tumor specimens. Mod Pathol. 2003 Jul;16(7):708-15.

4.Ambros PF et al. SIOP Europe Neuroblastoma Pathology, Biology, and Bone Marrow Group.Pathology and biology guidelines for resectable and unresectable neuroblastic tumors and bone marrow examination guidelines. Med Pediatr Oncol. 2001 Dec;37(6):492-504.

Website Update

With the release of the new Guide to Clinical Services in November 2005, we are currently updating and expanding our website (www.phenopath.com) to reflect the contents of the guide. We hope that the changes being made will provide you with enhanced information you need to successfully use PhenoPath for all of your clinical and research needs. If you have questions about the website, please feel free to call a member of our Client Services Staff at 888-92-PHENO (888-927-4366) or 206-374-9000 for assistance.



USCAP Presentations by PhenoPath Pathologists

Sunday, February 12, 2006:

A.M. Gown *presents, "FISH Testing for HER2 Detection." This 20-minute talk is to be held during an evening program entitled, "HER2 Assessment: Better Testing for Better Outcomes," sponsored by Albert Einstein College of Medicine and Montefiore Medical Center and M2 Communications. This program is supported by an unrestricted educational grant from Genentech, Inc. The 2-hour program starts at 5:30 pm in the Manila Room at the Hyatt Regency Hotel. Additional information is available at http://www.m2usa.com/uscap.*

Monday, February 13, 2006:

Poster #200, Morning Session
D.N. Ionescu, ***D. Treaba***, C.B. Gilks, J. Laskin, R. Wood-Baker, ***A.M. Gown***: *Tissue Microarray and Immunohistochemical Analysis of Neuroendocrine Differentiation in Non-Small Cell Lung Carcinoma (NSCC).*

Platform Presentation, Section C, 11 AM
R. Vang, ***A.M. Gown***, ***T.S. Barry***, D.T. Wheeler, K. Judson, B.M. Ronnett: *P16 Expression in Primary Ovarian Mucinous and Endometrioid Tumors and Metastatic Adenocarcinomas in the Ovary: Utility for Identification of Metastatic HPV-Related Endocervical Adenocarcinomas.*

Platform Presentation, Section C, 11:15 AM
D.N. Ionescu, H. Masoudi, S. Leung, ***A.M. Gown***, C.B. Gilks: *Expression of Mesothelial Markers in Ovarian Cancers: A Tissue Microarray Based Study of 471 Cases.*

Platform Presentation, Section H, 2:45 PM
R.R. Tubbs, J.D. Pettay, M.B. Hartke, ***T. Barry***, G. Payne, P.C. Roche, M. Loftus, E. Swain, T.M. Grogan: *Specificity of Interphase FISH Probes for Detection of Sarcoma and Lymphoma Associated Translocations in Paraffin Sections is Readily Assessed Using Tissue Microarrays Constructed from Murine Xenografts.*

Tuesday, February 14, 2006:

Poster #104, Morning Session
P.L. Kandalaft, ***T.S. Barry***, ***S.J. Kussick***, ***L.C. Goldstein***, C. Bacchi, P. Bitterman, ***A.M. Gown***: *Immunohistochemical Detection of Aquaporin 1 as an Aid in Identifying Renal Cell Carcinoma in the Setting of Metastatic Carcinomas of Unknown Primary.*

Poster #143, Morning Session
D. Cimbaluk, J. Scudiere, J. Rotmensch, ***A.M. Gown***, P. Bitterman: *Uterine Carcinosarcoma: Immunohistochemical Studies on Tissue Microarrays with Focus on Potential Therapeutic Targets.*

Poster #124, Afternoon Session
R. Vang, ***A.M. Gown***, C. Zhao, ***T.S. Barry***, B.M. Ronnett: *Expression of CK7 and CK20 in Ovarian Mucinous Tumors Arising in Association with Teratomas: A CK7-/CK20+ Subset can Cause Confusion with Metastatic Lower Gastrointestinal (GI) Tract Mucinous Tumors.*

Poster #129, Afternoon Session
M.A. Farinola, ***A.M. Gown***, ***T.S. Barry***, S. Movahedi-Lankarani, R. Vang: *Comparative Immunohistochemical Analysis of ER/PR Expression in Ovarian Sertoli Cell Tumors (SCT) and Adult Granulosa Cell Tumors (AGCT).*

Wednesday, February 15, 2006:

Poster #44, Afternoon Session
C.H. Tse, ***T.S. Barry***, ***H. Hwang***, ***D.O. Treaba***, ***A.M. Gown***: *Improved Detection of Breast Carcinoma Using Mammaglobin and Gross Cystic Disease Fluid Protein-15 (GCDFP-15) by Immunohistochemistry.*

Poster #210, Afternoon Session
S.J. Kussick, ***D. Ceniza***, ***B.K. Oppenlander***, ***T.S. Barry***, ***A.M. Gown***: *Nine-Color/Eleven-Parameter Flow Cytometry can be Utilized in the Clinical Laboratory to Diagnose a Broad Range of Hematolymphoid Neoplasms.*

Fellow IHC

SANDRA TIRRELL, M.D.
PHENOPATH 2005-2006
IHC FELLOW

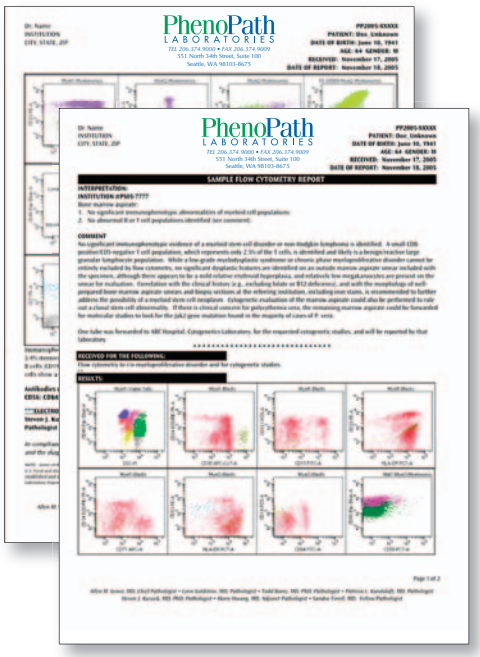
Sandra Tirrell, MD, is the 2005-2006 Fellow at PhenoPath Laboratories. Sandra received her MD degree from the University of Texas Health Science Center in San Antonio, TX. Following an internship in General Surgery at Vanderbilt Medical Center in Nashville, TN, she spent 2 years in residency training at Harvard Medical School-Beth Israel Deaconess Medical Center in Boston, MA. She went on to fulfill her residency requirements in AP/CP at the University of Washington in Seattle in 2004, where she subsequently completed a Surgical Pathology Fellowship in 2005. Sandra successfully received her AP/CP board certification in August 2005.

Sandra has received a number of honors and awards during her academic years, and has strong interests in hematopathology and flow cytometry. In July 2006 she will begin the Breast Pathology Fellowship at Harvard Medical School-Beth Israel Deaconess Medical Center in Boston, MA with Drs. Stuart Schnitt, Jim Connolly and Laura Collins.

Sandra's hobbies include running, drawing and travel.

The PhenoPath flow cytometry service was officially launched on November 1, 2005.

The specimens we have received since the inception of the service have enabled us to utilize the full range of flow cytometric assays that we offer, including evaluations for mature B and T cell lymphoproliferative disorders, plasma cell dyscrasias, chronic myeloid stem cell neoplasms, and acute myeloid and lymphoid leukemias. All the flow cytometry panels that we designed and validated have proven robust in clinical practice. Our flow cytometry staff, including Lead Technologist Donna Ceniza and Senior Technologist Barbara Oppenlander, have efficiently handled the workflow, generating high quality nine-color flow cytometry data. Case turnaround time has typically been within 24 hours of receipt of the specimen, and all flow cytometry reports have included multicolored "scattergrams" of the relevant flow cytometric data supporting the final interpretation.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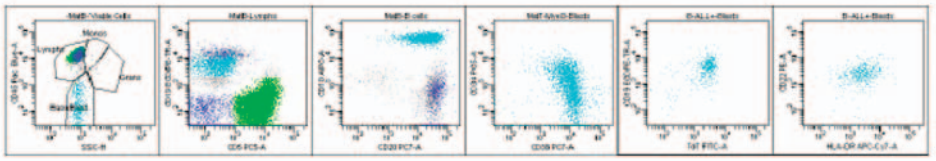
SAMPLE FLOW CYTOMETRY REPORT

A major new clinical flow cytometric assay, which we will begin offering in February 2006, is evaluation of T cell antigen receptor (ß gene) expression as a way to confirm clonality in immunophenotypically-abnormal T cell populations. This flow cytometric assay offers a very fast and convenient alternative to PCR testing for T cell clonality, and enables determination of clonality to be assigned definitively to a particular T cell subpopulation of interest.

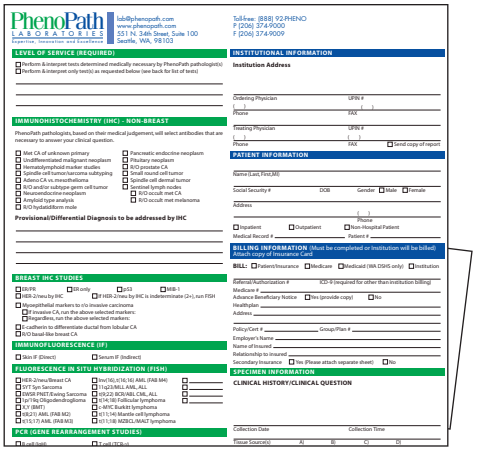
In addition to the clinical aspects of the flow cytometry service, PhenoPath has an active research flow cytometry service. For example, we are working with a Seattle-area biotechnology company in a study of immunologic function in several cohorts of patients. As part of this research collaboration, we developed a highly versatile, single-tube, flow cytometric assay to evaluate immunologic activation in these patients. For both research and clinical endeavors, the PhenoPath flow cytometry service is committed to designing flow cytometry panels which meet our clients' needs in the most efficient and cost-effective manner possible.



Precursor B-All (neoplastic cells colored light blue)

PhenoPath's new requisition form is now available.

The form has been significantly expanded for ease in ordering our new services (flow cytometry and expanded molecular offerings). To obtain forms with your institution's name, address, phone number, and FAX number preprinted, contact a member of our Client Services Staff, or simply request requisition forms the next time you submit a case. If you have any questions regarding the new form, contact a member of our Client Services Staff at 888-92-PHENO (888-927-4366), and we'll be happy to help.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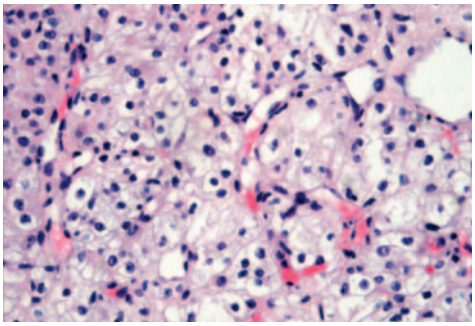
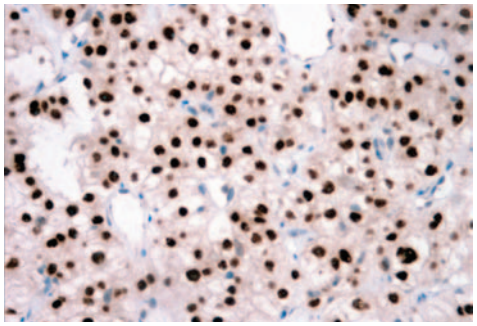


H&E of metastatic renal cell carcinoma



PAX-2 positive metastatic renal cell carcinoma

Renal Cell Carcinoma Marker: PAX-2

Renal cell carcinomas have often been difficult to identify, particularly in the metastatic setting, due to a lack of sensitive and specific markers. Despite initial enthusiasm, markers such as the proximal tubule protein, gp100 ("RCC"), and CD10 have not been particularly useful owing to their low sensitivity and/or specificity. However, PAX-2, a nuclear transcription factor instrumental in renal development, has recently been shown to be an excellent marker of renal cell carcinoma. In a recently published study (Mazal PR et al, Mod Pathol 18:535-40, 2005), PAX-2 was demonstrated to show a sensitivity of 88% in clear cell variants of renal cell carcinoma (but considerably lower in papillary renal cell variants), and studies performed here at PhenoPath Laboratories and presented at the February 2006 meeting of the United States and Canadian Academy of Pathology (see pages 1 and 2) have demonstrated the very high specificity of PAX-2 for carcinomas of renal origin. (A subset of ovarian carcinomas was the only non-renal carcinoma found to be positive.) PAX-2 joins a lengthening list of organ-specific transcription factors (e.g., TTF-1 for lung, CDX-2 for colorectum) that can serve as critical markers for the identification of carcinomas of unknown primary site.

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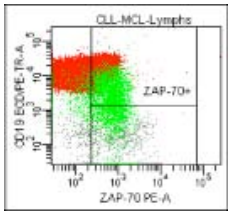
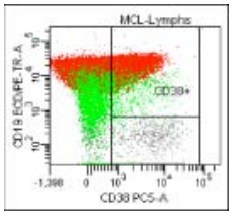
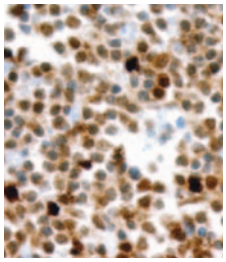


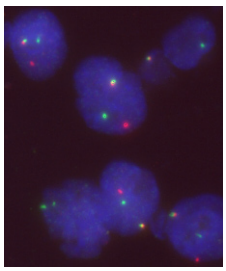




Winter Quarterly Conference

Todd S. Barry, MD, PhD and Steven J. Kussick, MD, PhD of PhenoPath Laboratories will present ***"Hematopathology in the Post-WHO World: What the Practicing Pathologist Needs to Know"*** at the Quarterly Pathology/Immunohistochemistry Conference on Thursday, March 2, 2006 at PhenoPath Laboratories. The format of the conference is a social hour beginning at 6:30 pm, lecture at 7:30 pm, and sharing of interesting cases at 8:30 pm **(note new times)**.

Dr. Barry has been with PhenoPath since 2002 and has substantial experience in leukemia and lymphoid immunophenotyping. He is board-certified in hematopathology, as well as anatomic and clinical pathology. Prior to joining PhenoPath, Dr. Barry completed anatomic and clinical pathology residency training as well as fellowships in hematopathology and immunohistochemistry at the University of Washington, and subsequently completed two additional years of fellowship training in hematopathology with Dr. Elaine Jaffe. Since joining PhenoPath, Dr. Barry has acquired national prominence for his skills in immunohistochemistry and hematopathology. Dr. Barry has also been spearheading PhenoPath's molecular pathology endeavors.



Dr. Kussick, Pathologist and Director of Flow Cytometry of PhenoPath Laboratories, has extensive experience in the use of morphologic, immunophenotypic, and molecular methods in the diagnosis of hematolymphoid neoplasms. He arrived at PhenoPath in April 2005 after nearly seven years as an attending hematopathologist and the Associate Director of Hematopathology in the University of Washington Department of Laboratory Medicine. He is board-certified in both anatomic pathology and hematopathology, having trained in these areas at the University of Washington.

This Quarterly Conference presentation, rather than reviewing the WHO classification of hematolymphoid neoplasms in detail, will focus on advances in hematopathology practice since this classification was introduced in 2000. Dr. Barry will focus on lymphoid neoplasms, and Dr. Kussick on myeloid neoplasms.