The Newsletter of PhenoPath

Phenomena™

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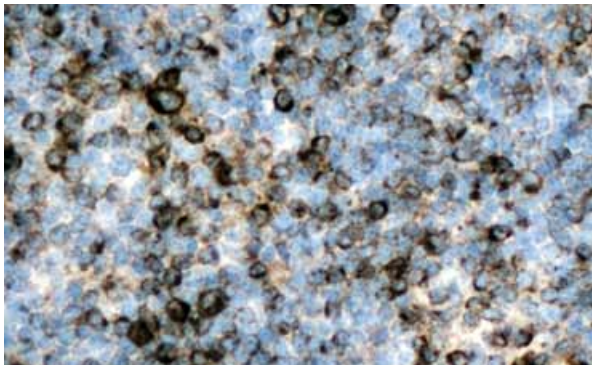
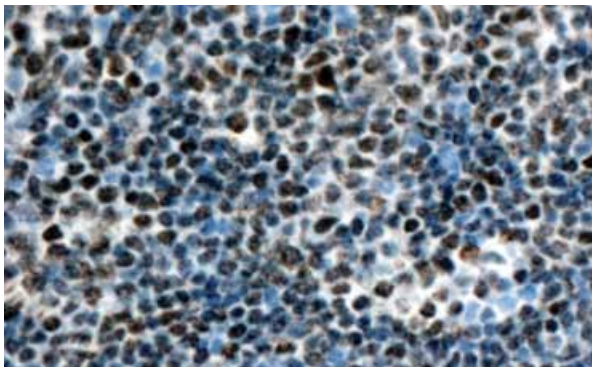
New Immunohistochemistry-Defined Subclassification of DLBCL



GCET1



FOXP1

In a 2004 paper by Hans and colleagues it was suggested that immunohistochemistry with antibodies to CD10, bcl-6, and MUM1 could be employed to stratify diffuse large B cell lymphoma (DLBCL) into prognostically distinct groups corresponding to the molecularly defined "germinal center B cell-like" (GCB) and activated B cell-like (ABC) subtypes. However, follow-up studies have been inconsistent in confirming these data, in part owing to the poor reproducibility of one or more of these markers, and likely because of the addition of rituximab to standard chemotherapy for DLBCL.

In a recent interinstitutional study of DLBCL stratification, Choi et al. have demonstrated a new immunohistochemical algorithm employing antibodies to CD10, bcl-6, MUM1 and two novel markers, GCET1 (germinal center B cell-expressed transcript 1) and FOXP1 (a transcription factor highly expressed in ABC-DLBCL). In a training set of 84 cases of CHOP-treated patients with DLBCL, use of this new algorithm closely approximated the subclassification of these same lymphomas by gene expression profiling (93% concordance vs. 86% concordance when the Hans algorithm was applied to the same data set). In a separate validation set of 63 DLBCL patients treated with CHOP-rituximab, the new algorithm was able to stratify patients into two distinct prognostic groups with 3-year survival rates of 87% (the GCB subset) and 44% (the ABC subset), simulating the predictive power of gene-expressing profiling of these same tumors.

PhenoPath Laboratories has recently validated both the GCET1 and FOXP1 antibodies, and is now pleased to offer this new IHC-based subclassification of DLBCL to our hematology/oncology colleagues for assistance in selecting the most appropriate therapy for their DLBCL patients.

References: Choi WWL et al., Clin Cancer Res 15:5494-502, 2009; Hans CP et al., Blood 103:275-82, 2004.

PhenoPath Profile

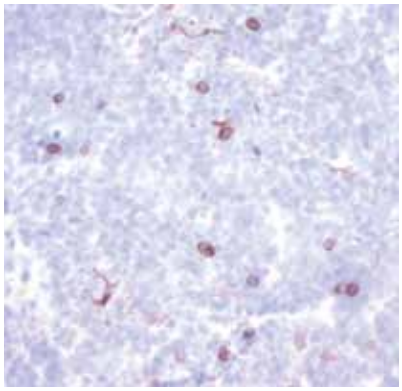
Sara M. Duesterhoeft, M.D.

PhenoPath Laboratories is pleased to announce the January 1, 2010 appointment of Sara M. Duesterhoeft, M.D. as a Pathologist and Associate Director of Hematopathology. Sara's duties involve the entire range of PhenoPath diagnostic hematopathology testing, including immunohistochemistry, flow cytometry, FISH, and PCR.

Sara attended the University of Minnesota – Twin Cities Medical School where she earned her M.D. She completed her residency in Anatomic Pathology and Laboratory Medicine at the University of Washington Medical Center. Following her residency, Sara fulfilled a Fellowship in Pediatric Pathology at Seattle Children's Hospital/University of Washington Medical Center, and a Fellowship in Hematopathology at the University of Washington Medical Center/Seattle Cancer Care Alliance. Sara is board-certified in Anatomic and Clinical Pathology, as well as Hematopathology.

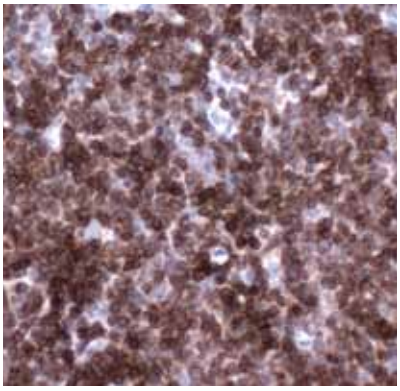
Sara's professional expertise and interest are in Hematopathology. In her spare time, she likes spending time with friends enjoying the amazing food, wine, and scenery of the Pacific NW, traveling, running, and following the Portland Trailblazers. Her interests also include art and architecture, and she aspires to claim amateur status in the realms of cooking and photography as well.

Anti-bcl-2 clone C2, newly validated *for PhenoPath Immunohistochemistry*



Negative expression of bcl-2 clone 124 in a case of follicular lymphoma

The majority of follicular lymphomas (FLs) contain the t(14;18) juxtaposing the *BCL2* gene on chromosome 18 with immunoglobulin heavy chain gene on chromosome 14. Germinal center B cells bearing this translocation express the bcl-2 protein at high level, leading to aberrant inhibition of apoptosis, and representing a critical step in lymphomagenesis. In the large majority of t(14;18)-positive FLs, strong cytoplasmic bcl-2 protein overexpression can be confirmed by immunohistochemistry with the most common anti-bcl-2 antibody in diagnostic use, clone 124 (raised against bcl-2 amino acids 41-54). However, there are rare cases of t(14;18)-positive FL that lack detectable bcl-2 protein with clone 124, but do show detectable bcl-2 by immunohistochemistry with the alternative clone C2 (raised against roughly the first 200 amino acids of bcl-2), presumably due to alteration in the clone 124 epitope in these cases. Therefore, we have validated clone C2 for use as an alternative anti-bcl-2 antibody in cases of probable FL that appear bcl-2-negative by initial immunohistochemistry with clone 124.



Positive expression of bcl-2 clone C2 in the same case of follicular lymphoma

Reference: Schraders M, de Jong D, Kluin P, Groenen P, van Krieken H. Lack of bcl-2 expression in follicular lymphoma may be caused by mutations in the BCL2 gene or by absence of the t(14;18) translocation. J Pathol 205(3):329-35, 2005

PhenoPath Laboratories *Retests Nearly 3,000 Breast Cancer Specimens* from Quebec Breast Cancer Inquiry

PhenoPath Laboratories served as the reference laboratory for a highly anticipated retesting of nearly 3,000 breast cancer specimens from the Province of Quebec, results of which were announced in December 2009 by Quebec Health Minister Yves Bolduc.

The review had been requested after Quebec's Association of Pathologists released a startling report in April 2009 of a limited study that had suggested a high error rate, of between 15% and 20%, in the determination of the estrogen receptor (ER) status, an important test for the determination of appropriate treatment of breast cancer patients. In recent years, there have been other disclosures of high error rates in breast cancer testing in other provinces of Canada, including Newfoundland several years ago.

All breast cancers from patients in North America are tested for the presence of ER, as patients with breast cancers that are ER positive generally have a more favorable outcome than those that are ER negative, and such patients can also be successfully treated with drugs such as tamoxifen.

PhenoPath Laboratories was selected to retest a total of 2,856 cases that had been originally analyzed at many laboratories in Quebec between April 1, 2008 and June 1, 2009. PhenoPath was involved in a landmark study published in December 2006 demonstrating that reagents employed for the identification of ER in breast cancer specimens at PhenoPath Laboratories were significantly more sensitive and specific than those widely used in the United States and around the world. PhenoPath's vast experience and expertise with IHC, and breast markers in particular, was a major factor in its selection by the Province of Quebec for this retesting.

In the re-analysis, a total of 87 women were found to have received a false-negative result from the original pathology laboratory tests in Quebec. Of this number, 39 were required to alter their treatment; five of the women had already died.

VISIT PHENOPATH AT USCAP 2010

United States & Canadian Academy of Pathology, 99th Annual Meeting
March 20-26, 2010, Marriott Wardman Park, Washington, DC www.uscap.org

The United States and Canadian Academy of Pathology's mission is to provide pathologists with high quality continuing medical education at the investigative and applied practice level and to reinforce and update attendees' knowledge of pathology in their area(s) of interest and need in the understanding of pathologic processes.

This annual week-long meeting regularly attracts over 3000 pathologists from the United States and Canada, as well as several hundred scientists from abroad.

Visit PhenoPath at Booth #220 to learn more about PhenoPath offerings.

Lectures by PhenoPath pathologists:

March 21, 2010, 1:30-5:30 PM:
ASIP/USCAP Companion Meeting: *"Molecular Markers for Diagnosis and Prognosis: What and When"*
Allen M. Gown, MD presents *"Breast Cancer, The New and The Old"*

March 22, 2010, 7:50 AM to 1:00 PM:
Special Course: Basic Principles and Practice of Molecular Pathology in Cancer
Allen M. Gown, MD presents *"Integration of the Molecular Classification of Breast Cancer into Current Practice"*

Posters including PhenoPath pahologists:

Monday, March 22, 2010, 9:30 AM, Poster Session I

Poster # 298: Stowell-Orbison/Surg Path/Autopsy Awards
Thyroid Transcription Factor (TTF-1) Expression in Breast Carcinomas
Authors: JN Robens, *LC Goldstein*, *AM Gown*, SJ Schnitt

Poster # 1017: Stowell-Orbison/Surg Path/Autopsy Awards
Aberrant Staining Patterns for Prostatic Adenocarcinoma (PCA) in Needle Biopsies Using Triple Cocktail Immunohistochemistry (IHC): An Experience of 469 Cases with Rationale for the Selective Inclusion of Novel Cancer Specific Nuclear Marker MYC
Authors: DE Westfall, DJ Luthringer, *AM Gown*, RS Parakh, M Vankalakunti, MB Amin

Monday, March 22, 2010, 1:00 PM, Poster Session II

Poster # 204: Markers of Metastatic Breast Cancer: Correlations between GCDFP-15 or Mammaglobin Expression and Tumor Grade, Hormone Receptor, and HER2 Expression
Authors: *AM Gown*, *LC Goldstein*, *PL Kandalaft*, *HC Hwang*, *SJ Kussick*, *CC Tse*

Poster # 82: Low Level MDM2 Gene Amplification and MDM2 Polysomy Are Found in Extra-Uterine and Uterine Leiomyosarcoma by Fluorescence In Situ Hybridization (FISH) Analysis
Authors: SJ Hwang, *HC Hwang*, *CH Tse*, *LC Goldstein*, *AM Gown*

Poster # 1008: Differential Immunohistochemical (IHC) Staining in Unusual and Morphologically Non-Classic Patterns of Testicular Germ Cell Tumors (GCT): Analysis with Traditional and Contemporary Markers
Authors: MP Venturina, RS Parakh, B Balzer, *AM Gown*, DE Westfall, *LC Goldstein*, MB Amin

Poster # 943: Sensitivity and Specificity of Novel and Contemporarily Used Immunohistochemical (IHC) Markers in the Histologic Typing of Germ Cell Tumors (GCT) of Testis: Implications for Creating a Best Practices Panel Approach
Authors: RS Parakh, M Venturina, B Balzer, *AM Gown*, DE Westfall, M Vankalakunti, MB Amin

Tuesday, March 23, 2010, 9:30 AM, Poster Session III

Poster # 1006: An Analysis of INI1 Nuclear Expression in Collecting Duct Carcinoma (CDC) and Renal Medullary Carcinoma (RMC): Diagnostic and Pathogenetic Implications
Authors: M Vankalakunti, *AM Gown*, R Gupta, RB Shah, RS Parakh, DE Westfall, M Amin, DJ Luthringer, *LC Goldstein*, MB Amin

Tuesday, March 23, 2010, 1:00 PM, Poster Session IV

Poster # 138: Can Pathologic Features and Immunophenotype of ER+, Node Negative Breast Cancers Identify High and Low Risk OncotypeDX Subgroups?
Authors: KH Allison, SM Dintzis, *PL Kandalaft*, *AM Gown*, *CH Tse*, *LC Goldstein*

Wednesday, March 24, 2010, 9:30 AM, Poster Session V

Poster # 1005: Immunohistochemical (IHC) Expression of Ulex Europaeus Agglutinin-1 (UEA-1) in the Spectrum of Adult Renal Epithelial Neoplasms – A Study of 165 Cases
Authors: M Vankalakunti, DE Westfall, RS Parakh, R Gupta, RB Shah, M Amin, *AM Gown*, *LC Goldstein*, MB Amin

Online Posters2View™ Session: Gynecologic & Obstetrics

Poster # 1209: Pax8 Expression in Uterine Adenocarcinoma: Immunohistochemical Analysis of 94 Cases
Authors: A Yemelyanova, *AM Gown*, BM Ronnett, R Vang

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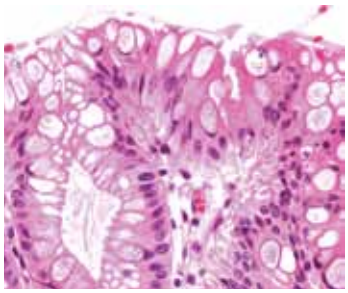
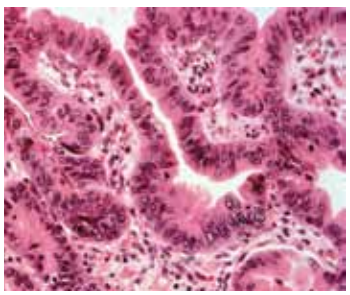
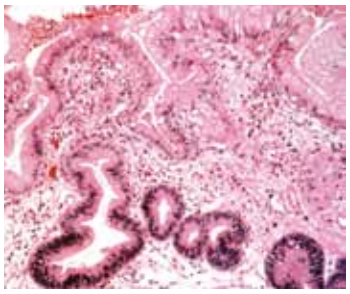
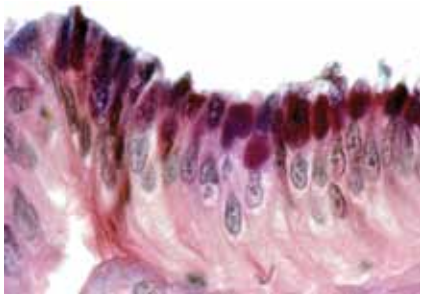






Featuring
Dr. John Goldblum
At Our Spring Conference



John Goldblum, M.D., of the Cleveland Clinic in Cleveland, OH, will present "Controversies in the Diagnosis of Barrett's Esophagus and Barrett's-Related Dysplasia" at the PhenoPath Spring Conference on ***Thursday, April 8, 2010***. The format of the conference is a social hour commencing at ***6:30 PM***, followed by Dr. Goldblum's lecture at 7:30 PM. A light catered dinner will be served during the social hour.

Dr. Goldblum is the Chair of the Department of Anatomic Pathology at the Cleveland Clinic. He specializes in the interpretation of biopsy and resection specimens in the fields of soft tissue pathology and gastrointestinal pathology for Cleveland Clinic and non-Cleveland Clinic patients throughout the U.S. and foreign countries. He is the co-author of the world's highest selling textbooks on soft tissue tumors with Dr. Sharon Weiss, and a GI pathology textbook with Dr. Robert Odze. In addition, he has published over 200 peer-reviewed articles. Dr. Goldblum is also a renowned speaker who has lectured extensively nationally and internationally in the field of anatomic pathology. A recipient of numerous awards, Dr. Goldblum was distinguished with The Arthur Purdy Stout Annual Prize Award in 2004.

Dr. Goldblum will also be giving a ***daytime lecture at 1:00 PM the same day***, entitled, "Useful Ancillary Diagnostic Techniques in the Evaluation of the Most Common Morphologic Patterns in Soft Tissue Tumors". All pathologists and residents are welcome to attend.