

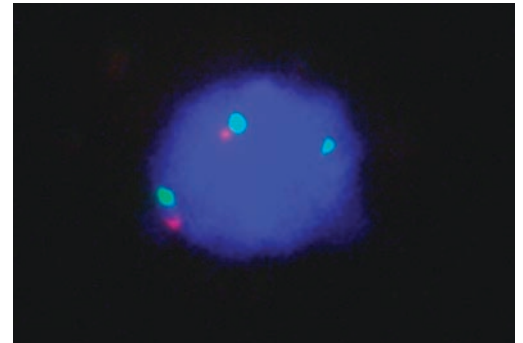


# henomena™

Laboratories ● 1-888-92-PHENO ● www.phenopath.com ● Spring 2011 ● Volume 14 No.2

## Now offering Myeloma FISH *expanded panel*

PhenoPath now offers an expanded panel of FISH assays to detect the major prognostically significant chromosomal alterations that occur in myeloma. Specifically, this panel detects the most common IgH translocations (involving the CCND1, FGFR3, and C-MAF genes), deletions of 17p (involving the p53 gene) and 13q, as well as hyperdiploidy involving chromosomes 3, 5, 7, 9, 11, and 15. IgH translocations involving the FGFR3 and C-MAF genes, and deletions involving 17p or 13q are associated with a worse prognosis. In contrast, IgH translocations involving the CCND1 gene and evidence of hyperdiploidy are associated with a favorable prognosis. As IgH translocations and hyperdiploidy are typically mutually exclusive, the myeloma FISH prognostic panel at PhenoPath is performed in a two-step reflexive approach in order to avoid unnecessary testing. In the first step, an IgH breakapart FISH probe that detects any generic translocations involving the IgH gene is performed along with FISH probes to detect deletions involving 13q and 17p. Based on the generic IgH FISH result, additional translocation-specific IgH probes are performed in order to determine the IgH translocation partner. If no IgH translocation is detected in the initial set of myeloma FISH studies, then the set of hyperdiploid probes is performed. This extensive panel approach for prognostic myeloma FISH has been validated for fresh specimens. A more limited prognostic FISH panel has been validated for paraffin-embedded myeloma specimens that detects the major IgH translocations only. Please contact Client Services at PhenoPath Laboratories for additional specimen requirement information.



CEP11 hyperdiploid FISH (green FISH signal)

*Bergsagel et al., J Clin Oncol. 2005 Sep 10;23(26):6333-8. ★ Fonseca et al., Blood. 2003 Oct 1;102(7):2562-7. ★ Gorczyca. Cytogenetics, FISH, and molecular testing in hematologic malignancies. Informa press, 2008, p162. ★ Chng et al., Leukemia 2006, 20, 807-813. ★ Swerdlow et al., WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, 2008, pp205-208.*

The diagnostic expertise of PhenoPath Laboratories pathologists is informed by ongoing clinical research studies.

In many cases, studies are performed in collaboration with outstanding pathologists and oncologists around the nation.

In this issue of Phenomena, we highlight three such recent publications.

Copies of these articles can be obtained by writing to Client Services at [lab@phenopath.com](mailto:lab@phenopath.com) or you can link to the articles using your smart phone (see bottom of page 2).

### HER2 Assessment in Breast Cancer via FISH and RT-PCR

Baehner FL, Achacoso N, Maddala T, Shak S, Quesenberry Jr. CP, Goldstein LC, Gown AM, Habel LA. JCO 28:4300-6, 2010.

As recognized by the recent American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) guidelines on HER2 testing in breast cancer, there is no “gold standard” methodology for assessing HER2 status in breast cancer. These guidelines also mandate that laboratories performing HER2 testing must demonstrate >95% concordance to another approved laboratory or methodology. While the “other” methodology in the case of fluorescence in situ hybridization (FISH) has typically been immunohistochemistry (IHC), in a recent study performed by PhenoPath pathologists Lynn Goldstein and Allen M. Gown, in conjunction with scientists and pathologists at the University of California San Francisco, Kaiser Permanente, and Genomic Health, the concordance of HER2 assessment by FISH (performed at PhenoPath Laboratories) with HER2 assessment by RT-PCR (performed at Genomic Health) was assessed in a series of 475 patients, all lymph node-negative and chemotherapy-

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untreated, derived from a large Kaiser Permanente case-control study. The percent positive agreement between the two methods was 98%, and percent negative agreement was 97%, with an overall HER2 concordance by FISH and RT-PCR of 97%. Twelve percent (67/568 patients) and 11% (60/568 patients) of patients were HER2 positive by RT-PCR and FISH, respectively, meaning that only one HER2 FISH-positive patient was RT-PCR negative. HER2-positive patients had increased odds of dying from breast cancer compared with HER2-negative patients, as assessed by either FISH or RT-PCR. Thus, a high degree of concordance, even greater than that mandated by the ASCO-CAP guidelines, exists between HER2 assessment of breast cancers by FISH and quantitative RT-PCR.

## Subclassifying Lung Carcinoma

Terry J, Leung S, Laskin J, Leslie KO, Gown AM, Ionescu DN. *AJSP* 34:1805-11, 2010.

The importance of correctly subclassifying carcinomas primary to the lung has never been more important, given the availability of targeted therapies such as EGFR tyrosine kinase inhibitors including erlotinib (Terceva™) and the VEGF-targeted bevacizumab (Avastin™). However, morphologic separation of poorly differentiated adenocarcinoma (ADC) from poorly differentiated squamous cell carcinoma (SCC) can be difficult, with low interobserver agreement even among experienced lung pathologists. Prior studies have documented that the accuracy and reliability of morphologic subclassification alone in small biopsies are low, with poor correlation between interpretation of the biopsies and subsequent resection specimens. Indeed, approximately 25% of tumors found in bronchoscopic biopsies cannot be subtyped based on morphology alone. With increasing frequency the latter is the only tissue obtained for diagnosis. In this study, performed by pathologists and oncologists at the University of British Columbia, Mayo Clinic, and PhenoPath Laboratories, using a series of 200 primary lung ADCs and 225 primary lung SCCs in a tissue microarray format to mimic small biopsy specimens from a potential pool of 9 immunohistochemical markers, the single best marker to separate ADCs from SCCs was found to be p63 (for SCC: sensitivity 84%, specificity 85%). Logistic regression analysis, however, identified p63, TTF1, CK5/6, CK7, napsin A, and mucicarmine as the optimal panel to separate ADCs from SCCs, with reduction of the panel to p63, TTF1, CK5/6, and CK7, marginally less effective, but perhaps the best compromise in the setting of limited tissue.



## TTF-1 Expression in Breast Cancer

Robens J, Goldstein L, Gown AM, Schnitt SJ. *AJSP* 34:1881-85, 2010.

The thyroid transcription factor (TTF-1) is a nuclear transcription factor, expression of which is critical to the development of both the thyroid as well as the lung. TTF-1 has also been employed for more than a decade as an organ-restricted marker to help determine the origin of carcinomas presenting at metastatic sites. While in normal tissues, TTF-1 expression is limited to lung and thyroid, and while in carcinomas TTF-1 expression has been demonstrated to be a highly sensitive marker of carcinomas (both non-neuroendocrine and neuroendocrine) of the lung and thyroid, over the years there have been published reports documenting TTF-1 expression in other carcinomas, albeit with much less frequency, including those arising in the colon, ovary, and endometrium. (It has also been widely documented that TTF-1 expression in the context of high-grade neuroendocrine carcinomas is by no means restricted to such tumors arising in the lung or thyroid.) However, previous publications have suggested that TTF-1 expression is vanishingly rare, if seen at all, in some carcinomas, including those primary to the breast. This is particularly important as recent studies have documented expression of some “breast-restricted” markers, such as estrogen receptor and GCDPF-15, in a subset of primary lung carcinomas. However, the true frequency with which TTF-1 expression is observed in breast carcinomas is unknown. To address this, a collaborative study involving pathologists from Beth Israel Deaconess Medical Center in Boston and PhenoPath was performed, in which we immunostained, with antibodies to TTF-1, a series of 546 primary breast carcinomas that had originally been submitted for routine estrogen receptor, progesterone receptor, and/or HER2 testing. TTF-1 expression was identified in 13 cases (2.4%). Expression varied from focal and weak to diffuse and strong and was seen in both invasive and in situ components. Thus, there exists a small proportion of breast carcinomas that can demonstrate TTF-1 expression, and, therefore, the presence of TTF-1 immunoreactivity in a carcinoma cannot by itself be used to exclude the possibility of a breast origin.



Go to [getscanlife.com](http://getscanlife.com) from your mobile phone browser to obtain the application needed to scan the barcodes in this issue of *Phenomena* and to link to the journal articles.



# MEET OUR PATHOLOGISTS AT THE FOLLOWING MEETINGS

For up-to-date information, visit our website: [www.phenopath.com](http://www.phenopath.com)

## CIQC/CAP-ACP Seminar in Diagnostic IHC & Molecular Pathology

6/1/11 - 6/2/11, Fairmont Hotel, Vancouver, BC

### Presentations

6/2/11, 8:05 AM: Allen M. Gown, MD presents "Antibody Validation: The Good, The Bad and The Ugly"

[www.ciqc.ca/ciqc-cap-acp-diagnostic-ihc-course-2011](http://www.ciqc.ca/ciqc-cap-acp-diagnostic-ihc-course-2011)



## ASCP Pathology Update, Chicago, IL: State-of-the-Art Diagnostic Approaches to Surgical Pathology

7/18/11 - 7/22/11, Hotel Inter-Continental Chicago

### Presentations

7/21/11, 8:00 AM to noon: Allen M. Gown, MD presents "Contemporary issues in Immunohistochemistry"

[www.ascp.org](http://www.ascp.org)



## 25th Contemporary Topics in Surgical Pathology XXV: Immunohistochemistry and Molecular Testing in Anatomic Pathology

Jointly sponsored by St. Thomas Pathology and Vanderbilt University Medical School Pathology Departments

9/17/11, St. Thomas Hospital, Nashville, TN

### Presentations

8:00AM: Harry C. Hwang, MD presents "Predictive and Diagnostic Testing in Anatomic Pathology"

9:00 AM: Allen M. Gown, MD presents "ER Testing in Breast Cancer: Current Techniques and Controversies"

10:15 AM: Allen M. Gown, MD presents "HER2 Testing in Breast and Gastric Cancers"

11:15 AM: Harry C. Hwang, MD presents "Emerging Molecular Technologies"

1:00 PM: Allen M. Gown, MD presents "Tumors of Unknown Origin"



## PhenoPeople Profile



**John Hinson**

PhenoPath Laboratories is pleased to announce the appointment of John Hinson as CEO on January 1, 2011. John had been working as an interim executive for the company since June of last year.

John believes that PhenoPath, as a physician-owned, customer-focused laboratory, is uniquely qualified to be the world's gold standard in pathology reference testing. He is excited about working with PhenoPath's pathologist and management teams to help the company realize this vision. With his help, PhenoPath will strengthen its ability to distinguish itself through definitive diagnosis, rigorous testing and outstanding service.

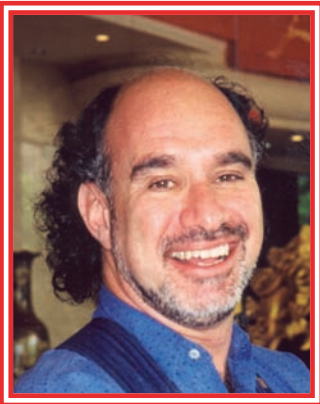
Prior to joining PhenoPath, John served as CEO, COO and CFO, as well as Board Director, for Cardiac Science, a medical device company. Prior to these roles, John served as an executive with DeCrane Aircraft Holdings, an aerospace electronics business, where his many roles included CFO and Vice President of Business Development. Earlier, John held positions in operations, finance and sales for Minimed Inc., another medical device company. And before that, he worked for Hewlett-Packard Company, a computer products company, for Bankers Trust, an investment bank, and served as an officer in the US Army (where he attained the rank of Captain).

John earned a B.A. in Economics, cum laude, from Claremont McKenna College and an MBA from the Anderson Graduate School of Management at UCLA. John currently serves on the Puget Sound Leadership Board of Medical Teams International, an organization providing humanitarian assistance to people affected by disaster, poverty and conflict around the world. In his free time, John enjoys hiking, biking, cross-country skiing and performing with the Sonic Matadors, a local cover band.

John's education and management experience are accompanied by an ability to build teams, inspire trust and confidence, focus on the big picture, and keep things in perspective. He is an important and welcome addition to PhenoPath's management team.

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## Dr. Adam Bagg Featured at Spring Conference



Adam Bagg, M.D., of the University of Pennsylvania, School of Medicine, Philadelphia, PA will present “Rational Use of Genetic Analysis in Lymphomas” at the Pathology/ Immunohistochemistry Conference on *Thursday, June 2, 2011*. The format of the conference is a social hour commencing at *6:30 p.m.*, followed by Dr. Bagg’s lecture at 7:30 p.m. A light catered dinner will be served during the social hour.

Dr. Adam Bagg is a Professor of Pathology and Lab Medicine at Penn, and divides his time between directing Hematology, attending in hematopathology (he also has a busy extramural consultation practice), teaching and translational research. He is Director of the Minimal Residual Disease Core Facility of the University of Pennsylvania and Children’s Hospital of Philadelphia Centre for Immunotherapy. In 2010, he was appointed Medical Director of the Cancer Cytogenetics Laboratory.

Dr. Bagg’s research is focused in 3 areas: 1) development of new assays, in particular molecular assays, to help diagnose and prognosticate hematologic malignancies; 2) minimal residual disease testing; and 3) developing new tools to facilitate the diagnosis of myelodysplastic syndromes (MDS). He was recently awarded a patent for a novel flow cytometry assay for diagnosing MDS.

Dr. Bagg is a renowned speaker who has lectured extensively nationally and internationally. He has over 110 publications, including peer-reviewed articles, invited reviews and textbook chapters, most in the realm of the molecular pathology of hematologic malignancies. He is an Associate Editor of the Journal of Molecular Diagnostics and on the Editorial Board of the American Journal of Clinical Pathology and Advances in Anatomic Pathology.

