Intracystic papillary carcinoma (IPC) of the breast has traditionally been considered a variant of ductal carcinoma in situ (DCIS), characterized by a papillary carcinoma within a cystically dilated duct. In a recently published study performed in collaboration with Drs. Collins, Carlo and Schnitt at the Beth Israel Deaconess Medical Center and Harvard Medical School in Boston, MA, results were obtained that challenge this prevailing notion about the nature of these lesions and raise the possibility that at least some of such lesions may, in fact, represent invasive carcinomas. Twenty-two cases of IPC were studied for the presence of an outer myoepithelium using a panel of five markers (smooth muscle myosin heavy chain, calponin, p63, CD10, and CK 5/6); all cases showed a complete absence of myoepithelial cells at the periphery of the nodules of IPC, despite the presence of excellent internal controls around normal ductal and lobular structures. While it is possible that these still represent in situ lesions in which the delimiting myoepithelium has somehow become markedly attenuated to the point of nondetection, it is also possible that many or most of these lesions actually represent circumscribed, encapsulated nodules of invasive papillary carcinoma. Regardless of whether these lesions are in situ or invasive carcinomas, outcome data on IPC suggest that they have an excellent prognosis with adequate local therapy alone, and the study does not suggest a change in the way these patients are currently managed. Encapsulated papillary carcinoma, however, may represent a better term to describe these lesions.


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**FISH Studies Now Offered for Detection of Topoisomerase II Gene (TOP2A) Alterations as Predictors of Response to Anthracycline Chemotherapy in Breast Cancer**

We are pleased to announce that PhenoPath Laboratories is now offering fluorescence in situ hybridization (FISH) studies to assess the TOP2A gene status. This can be ordered as a stand-alone test, or as a follow-up test following HER-2/neu evaluation either by immunohistochemistry (IHC) or FISH. Results are reported with respect to the presence of both amplification and deletion of the TOP2A gene.

Chemotherapies incorporating anthracyclines, which are thought to act through the enzyme topoisomerase II in cancer cells, are commonly employed in the treatment of breast cancer. As the benefit from anthracycline-based adjuvant chemotherapy appears to be restricted to a subgroup of patients, a method of identifying these patients has long been sought. In the past, HER-2/neu amplification/overexpression has been associated with anthracycline sensitivity, and it has been suspected that in such patients HER-2/neu is actually a surrogate for amplification of the topoisomerase II-alpha gene (TOP2A) present on the same amplicon on chromosome 17. Strong corroboration of this hypothesis was presented in studies published recently (Knoop AS et al, *J Clin Oncol* 23:7483-90, 2005; Tanner M et al, *J Clin Oncol* 24:2428-36, 2006). In the latter study, investigators found that TOP2A was co-amplified in 37% of HER-2/neu amplified breast cancers, and only those HER-2/neu amplified patients with concomitant TOP2A amplification showed improved overall survival from individually tailored and dose-escalated adjuvant anthracycline chemotherapy. Continued on page two
Is Your Breast Tissue Being Fixed Long Enough

In the current epitope retrieval era of diagnostic immunohistochemistry (IHC), where most tissues are subjected to some form of heat-induced epitope retrieval (HIER or “antigen retrieval”) prior to the application of primary antibodies, the notion of overfixed tissue has become inoperative. Indeed, using epitope retrieval, IHC studies can be successfully employed on tissues fixed in formalin for days, weeks, months, and possibly years. The problem of underfixation is a more serious one, however, as tissues that are inadequately fixed and processed into paraffin may lose antigenicity that cannot be brought back. As shown in a study published by Neal Goldstein and colleagues from William Beaumont Hospital (Goldstein NS et al., Am J Clin Pathol 120:86-92, 2003), estrogen receptor (ER) is an example of an antigen that can be lost (i.e., result in false-negative immunostaining) if tissue is inadequately fixed. Dr. Goldstein’s study suggests that breast biopsies – even needle core biopsies – need a minimum of 6 to 8 hours of fixation to ensure reliable IHC ER results. This is longer than is currently employed in many pathology laboratories, where there is great pressure to have results of breast biopsies out the day following surgery. Further evidence that inadequate fixation can clearly lead to false-negative ER IHC results was presented in a more recent study (Mann GB et al., J Clin Oncol 23:5148-54, 2005), in which the ER IHC results obtained in needle core biopsies and corresponding resection specimens were compared in 100 cases. In almost 10% of cases, a false-negative ER IHC was obtained in the larger resection specimen, presumably from inadequate fixation, compared with the corresponding needle core biopsy. These authors also suggested that ER IHC is more reliably performed in needle core rather than resection specimens of breast cancer.

B and T Cell Clonality Assessment by PCR

Features
- Molecular report integrating PCR results with Anatomic and immunophenotypic data
- Ongoing clonal T cell receptor-gamma chain gene (half arrows indicate site of binding for PCR primers)
- Assessed for monoclonal, polyclonal, or mixed population
- Fast turnaround time
- Preferred T cell clonality in a 45 year old breast
- Clonal TCR-gamma chain rearrangement identified in PCR

PhenoPath Laboratories is proud to offer PCR testing for both B cell and T cell clonality, that can be applied to fresh, frozen, or formalin-fixed, paraffin-embedded tissue sections, also available for fresh or frozen material.

Check out our website (www.phenopath.com) or give us a call (888-92-PHENO) for your copy of our newest flier on PCR studies offered at PhenoPath Laboratories.

Oncodiagnosics

Identifying the Targets of Targeted Therapies in Tissue Sections

Features
- Staff pathologists with high levels of expertise, extensively published in peer-reviewed journals
- Accurate and comprehensive diagnostic and prognostic testing with therapeutic impact for the patient
- On the technological forefront of diagnostic pathology
- Ongoing clinical research collaborations with recognized experts in the pathology, oncology and pharmaceutical fields
- Fast turnaround time
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Continued from page one

In the former study, published by the Danish Breast Cancer Cooperative Group, investigators found that patients with TOP2A amplification had significantly increased recurrence-free and overall survival when treated with anthracycline-based chemotherapy; in this study, however, a nearly identical hazard ratio was found in patients with either TOP2A deletions or TOP2A amplification. The conclusion of these studies is that TOP2A amplification and possibly deletion seem to be predictive markers of response to anthracycline containing breast chemotherapy.
Meet PhenoPath Pathologists and/or representatives at the following upcoming meetings:

Dr. Allen M. Gown is a featured speaker at the 6th Annual Update Course in Surgical Pathology, held in Columbus, Ohio from October 8-10, 2006. Dr. Gown will be presenting the following lectures:

**Sunday, October 8, 2006, 2:00-3:00 PM:**
- Immunohistochemical Approaches to Carcinomas Presenting at Metastatic Sites (with Emphasis on Newer Markers)

**Sunday, October 8, 2006, 3:00-4:00 PM:**
- Current Issues Regarding ER and HER2 Testing in Breast Cancer

[http://ccme.osu.edu/index.cfm](http://ccme.osu.edu/index.cfm)

Dr. Todd S. Barry is a featured speaker at the ASCP 2006 Annual Meeting, held at the Flamingo Las Vegas from October 18-22, 2006. Dr. Barry, along with Dr. Hadi Yaziji of Ancillary Pathways in Miami, FL, will be presenting the following lecture:

**Saturday, October 21, 2006, 2:00-5:30 PM:**
- Most Common Pitfalls in Diagnostic Immunohistochemistry

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

Colorado Society of Pathologists Meeting

Dr. Todd S. Barry is a featured speaker at the Colorado Society of Pathologists Meeting, held in Denver, CO on October 28, 2006. Dr. Barry will be presenting the following lecture:

- **7:15 AM:** Use of Immunophenotypic and Molecular Studies to Make Difficult Diagnoses in Hematopathology

Drs. Todd S. Barry and Steven J. Kussick are featured speakers at the Fall Conference of the Washington State Society of Pathology (WSSP), held at the Glaser Auditorium, Swedish Hospital, Seattle, WA on November 11, 2006. Drs. Kussick and Barry will be presenting the following lectures:

- **2:10 PM:** Use of Immunophenotypic and Molecular Studies to Make Difficult Diagnoses in Hematopathology
- **3:30 PM:** Hematopathology in a Post WHO World

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

Dr. Steven J. Kussick is a featured speaker at the Beckman Coulter Symposium 2006, held at the University Place Conference Center in Indianapolis, IN on November 16, 2006. Dr. Kussick will be presenting the following lecture:

- **4:00-5:00 PM:** Multi-Color Flow Cytometric Immunophenotyping of Leukemia & Lymphoma: 2006 Update


PhenoPath will be presenting an abstract describing concordance of FISH and IHC HER2 studies in breast cancer at the San Antonio Breast Cancer Symposium, held December 14-17, 2006 at the Henry B. Gonzalez Convention Center in San Antonio, TX.

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

Dr. Allen M. Gown is a featured speaker at the Harvard Medical School Combined Pathology Grand Rounds, held in Boston, MA on January 22, 2007. Dr. Gown will be presenting the following lecture:

- **12:30-1:30 PM:** Immunohistochemistry as a Window onto the Molecular Biology of Tumors

[http://labmed.bwh.harvard.edu/pathology/Calendar/HMS_grand_round.htm](http://labmed.bwh.harvard.edu/pathology/Calendar/HMS_grand_round.htm)

Dr. Todd S. Barry is a featured speaker at the First International Course on Applied Immunohistochemistry and Molecular Morphology presented by the Society of Applied Immunohistochemistry, held January 23-26, 2007 in Duck Key, Florida. Dr. Barry will be presenting the following lecture on Friday, January 26, 2007

- **9:30-10:20 AM:** FISH-Lymphoid and Mesenchymal Lesions

[www.pathlearning.com/Pages/schedule.php](http://www.pathlearning.com/Pages/schedule.php)

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**PhenoPeople Profile**

**Harold Lane**

At PhenoPath Laboratories we recognize how important it is that you, our clients, receive your materials back in a timely manner when the studies you request are completed. Working “behind the scenes” to ensure this happens is Harold Lane, one of PhenoPath’s greatly valued office assistants. On a daily basis, Harold uses his highly organized system of records and material maintenance to monitor which clients’ specimens need to be shipped and takes steps to guarantee that the slides and blocks are handled safely, quickly and accurately. You may be assured that all materials processed by Harold will be treated with the utmost care.

When you find your send-out department running short of PhenoPath shipping supplies, it is Harold who responds to your requests. He also coordinates the send out of materials for consultation, when our pathologists seek expert assistance from one of their colleagues in the Seattle area or throughout the U.S. Harold’s other responsibilities include back-up front desk duties as needed during the day, and each night until closing.

Harold has many interests that he pursues during his free time, including a strong interest in astronomy. He enjoys science fiction movies and literature as well, and can be counted on to be a ready and willing participant in a discussion of a wide range of philosophical or political issues.
Dr. David Bostwick of Bostwick Laboratories in Glen Allen, Virginia, will present “Diagnostic Problems in Prostatic Adenocarcinoma” at the Quarterly Pathology/Immunohistochemistry Conference on Thursday, November 2, 2006. 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 light catered dinner will be served during the social hour.

Dr. Bostwick is an internationally renowned pathologist, with more than two decades of experience and interest in prostate cancer, bladder cancer, and urologic diseases. He has authored 13 books, more than 25 book chapters, and more than 400 papers. His textbook, *Urologic Surgical Pathology* (WB Saunders, 1997), is the best selling book in Uropathology.

Formerly a Professor of Pathology and Urology at the Mayo Clinic (1991-1999), Dr. Bostwick left in June 1999 to found Bostwick Laboratories, where he currently serves as Chief Medical Officer and Chief Executive Officer. He is a member of the editorial boards of 10 journals and is a past president of the International Society of Urological Pathology.

The fall Quarterly Conference will be co-sponsored by DAKO.