IOWA DEPARTMENT OF PATHOLOGY, UNIVERSITY OF IOWA CARVER COLLEGE OF MEDICINE

PATHOLOGYBEAT

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UI Pathology Now Offering 10-color Flow Cytometry

The accuracy and ability of detecting such combinations is dramatically enhanced by the ability to measure more and more markers on the same individual cell

Diagnostic multiparameter flow cytometry allows rapid measurements of multiple phenotypic characteristics of tens of thousands of individual cells in an aligned fluid stream. Flow cytometry can be used to identify and quantify various cell types in specimens containing a complex mix of cells, such as bone marrow, lymph nodes, blood, body fluids or other tissues. It is often applied to analyze the combination and levels of molecules expressed on the cell surface or within cytoplasm or nucleus.

Multiparameter flow cytometry is now the standard of care in the diagnosis, classification, staging and monitoring of hematolymphoid neoplasia (leukemia, lymphoma and myeloma) as well as various non-neoplastic immune disorders. Normal or reactive myeloid and lymphoid cells exhibit a generally predictable combination of cellular "markers." This information can be used to detect abnormally or aberrantly expressed marker combinations to detect and diagnose neoplastic populations.

The accuracy and ability of detecting such combinations is dramatically enhanced by the ability to measure more and more markers on the same individual cell. In particular, there is tremendous strength of this approach in the detection of low-level disease, delineation of subtle aberrant immunophenotypic features or evaluation of paucicellular specimens.

Therefore, we at UI Pathology are very excited to bring on board the cutting-edge 10-color flow cytometer, BD FACSCanto, in our clinical laboratory. With our new 10-color data, the pathologists and technologists will employ both "gating" and "cluster analysis" strategies to maximize the sensitivity and accuracy of the test. We are excited to offer this cutting-edge technology for better patient care.

University of Iowa Carver College of Medicine
University of Iowa Health Care

Updates in Diagnostic Immunohistochemistry: Additional Offerings from the University of Iowa Immunopathology Laboratory

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Introduction:

The purpose of this column is to discuss and illustrate the 9 diagnostic immunohistochemical tests validated by the Immunopathology Laboratory since the last issue of PathBeat (see Table). Many of these markers were discovered by gene expression profiling (glypican-3, GATA-3, MUC4, TLE1) or are surrogates for molecular genetic events (beta-catenin, c-Myc) and are thus exemplars of so-called "next generation immunohistochemistry."

New Immunohistochemical Stains Validated in the UIHC Immunopathology Laboratory

Marker	Principal Diagnostic Application(s)	Comments, Additional Applications, Potential Pitfalls
Glypican-3	• Hepatocellular carcinoma (60-90% sensitive) • Yolk sac tumor (95%)	• Stains up to 30% of melanomas and squamous cell carcinomas and occasional adenocarcinomas • Severely active hepatitis may stain positively • Reportedly positive in Wilms tumor and some neuroblastomas
Beta-catenin	• Desmoid fibromatosis (70-90%) • Solid-pseudopapillary neoplasm (95%) • Pancreatoblastoma (95%) • BCAT-activated hepatocellular adenoma • Fetal-type lung adenocarcinoma	• Nuclear and cytoplasmic staining is the abnormal result • Second-line colon cancer marker • Nuclear accumulation in 10-20% of adrenal cortical carcinomas
Napsin A	• Lung adenocarcinoma (70-80%)	• Also expressed by papillary renal cell carcinomas (70-80%) • Expressed by a smaller number of clear cell renal cell carcinomas • Has been suggested as a Müllerian clear cell carcinoma marker
GATA-3	• Urothelial carcinoma (75-90%) • Breast carcinoma (70-90%)	• Reportedly less sensitive in ER-negative breast cancers • Also expressed by most paragangliomas, parathyroid tumors, cutaneous basal cell carcinomas, skin adnexal tumors, and trophoblastic tumors • Also may be expressed by squamous cell carcinomas, salivary gland tumors, yolk sac tumors, mesotheliomas, and pancreatic ductal adenocarcinomas • Biocare Medical antibody appears less specific for urothelial and breast origin than Santa Cruz Biotechnology antibody
MUC4	• Low-grade fibromyxoid sarcoma (100%) • Sclerosing epithelioid fibrosarcoma (75%)	• Also broadly expressed by epithelia • Has been suggested as a pancreatic ductal adenocarcinoma marker
c-Myc	• Burkitt lymphoma (>95%) • c-Myc-activated diffuse large B-cell lymphoma	• Diffuse, strong nuclear staining is considered positive
CD163	• Monocyte/macrophage-lineage marker (histiocytes and neoplasms with histiocytic differentiation)	• More specific than CD68
TLE1	• Synovial sarcoma (>95%)	• Diffuse, strong nuclear staining is considered positive • Other sarcomas, in particular malignant peripheral nerve sheath tumor, demonstrate lesser amounts of staining • TLE1 is often positive in carcinomas
SSTR2A	• Predicts response to octreotide therapy in neuroendocrine neoplasms	• Membranous staining in >10% of tumor cells is considered positive • Staining in 1-10% of cells is considered indeterminate

Glypican-3:

Background: Glypican-3 (GPC3) is an oncofetal protein highly expressed in embryonic liver and re-expressed in most hepatocellular carcinomas (HCCs). Compared to other "HCC markers" (e.g., Hep Par 1, pCEA) that are expressed in benign and malignant hepatocytes, GPC3 is only expressed in HCC. Thus, this marker is used to distinguish well-differentiated HCC from benign mimics (Figure 1). Another significant advantage is its retained expression/superior sensitivity in poorly differentiated HCCs. GPC3 is also a sensitive and specific marker for yolk sac tumor (superior, in fact, to AFP) (Figure 2). Potential pitfalls include GPC3's frequent expression in squamous cell carcinoma and melanoma (each ~30%)

Key Reference: Kandil DH, Cooper K. Glypican-3: a novel diagnostic marker for hepatocellular carcinoma and more. *Advances in Anatomic Pathology.* 2009;16(2):125-9.

Beta-catenin:

Background: Beta-catenin (BCAT) performs two sets of functions. In the cell membrane it participates in cell-cell adhesion, and in the nucleus it interacts with TCF/LEF family transcription factors to mediate the expression of target genes. The BCAT nuclear fraction is tightly regulated. Physiologic Wnt signaling, *CTNNB1* (the gene that encodes BCAT) activating mutations, and inactivating mutations affecting BCAT regulatory proteins (e.g., APC) lead to BCAT nuclear accumulation.

In normal cells, the BCAT membrane-associated fraction predominates, which manifests immunohistochemically as crisp membranous staining. BCAT-activation, generally due to CTNNB1 mutation, leads to a shift in staining from the cell membrane to the nucleus.

Thus, BCAT immunohistochemistry functions as a surrogate for *CTNNB1* mutation status. The detection of nuclear BCAT expression has become a "gold-standard" immunohistochemical marker for several tumor types including especially desmoid fibromatosis (Figure 3), solid pseudopapillary neoplasm, pancreatoblastoma, hepatoblastoma, BCAT-activated hepatocellular adenoma, and fetal-type lung adenocarcinoma.

Key Reference: Montgomery E, Folpe AL. The diagnostic value of beta-catenin immunohistochemistry. *Advances in Anatomic Pathology.* 2005;12(6):350-6.

Napsin A:

Background: Napsin A is an aspartic proteinase that is highly expressed by type II pneumocytes (staining is also seen in alveolar macrophages, likely due to ingestion of pneumocyte debris), where it is believed to participate in the processing of surfactant, and in the renal proximal tubules, where it is involved in protein catabolism. Napsin A has emerged as a key

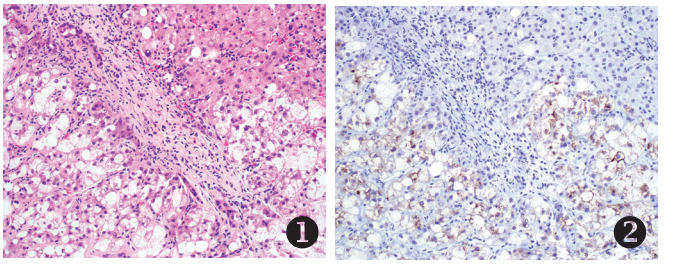


Figure 1: Glypican-3 Staining in Well-Differentiated Hepatocellular Carcinoma. An 80-year-old man with a past history of "gastrointestinal stromal tumor" had a small liver lesion detected on surveillance CT examination. It has grown to 1.7 cm over 3 years. A. Image from a core biopsy showing the transition from the possible lesion, characterized by prominent hepatocyte ballooning, and background liver with mild steatosis (H&E, 200x). The differential diagnosis included focal fat, hepatocellular adenoma, and well-differentiated hepatocellular carcinoma. B. Robust granular cytoplasmic staining with membranous accentuation in lesional cells and not in background liver supports a diagnosis of well-differentiated hepatocellular carcinoma (200x).

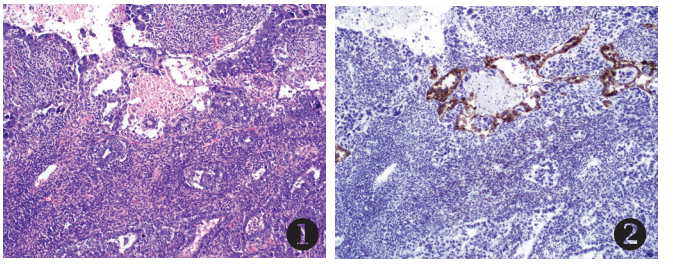


Figure 2: Glypican-3 Staining in Yolk Sac Tumor. A 21-year-old man presents with a testicular mass. A. Sections show predominantly embryonal carcinoma in a tubular arrangement admixed with a cellular teratomatous stroma (H&E, 100x). Serum AFP is elevated (330 ng/ml) and, thus, a yolk sac component is sought. B. Glypican-3 is strongly expressed in the yolk sac component; it is also weakly expressed in the teratomatous stroma (100x).

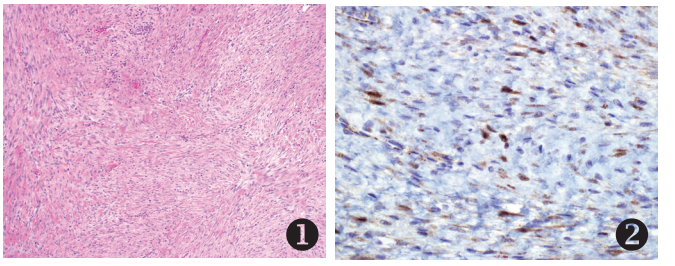


Figure 3: Beta-catenin Staining in Desmoid Tumor. A 29-year-old pregnant woman had an arm mass excised 2-years ago, diagnosed as "lipoma with scarring." The mass has recurred and has rapidly grown to 8 cm over the course of the pregnancy. A. Modestly cellular spindle cell tumor arranged as loose fascicles with no significant atypia (H&E, 100x). B. Nuclear staining for beta-catenin supports a diagnosis of desmoid fibromatosis (400x).

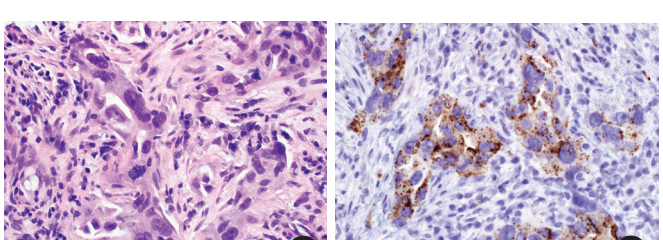


Figure 4: Napsin A Staining in Lung Adenocarcinoma. A 58-year-old woman with a remote history of breast cancer presents with diffuse metastatic disease. Core biopsy of a supraclavicular lymph node is performed. A. High-grade gland forming carcinoma (H&E, 400x). A panel of immunostains was performed, and the tumor was found to express CK7, CK20, TTF-1, and napsin A and not GATA-3 or PAX8, supporting a lung origin. B. Napsin A immunostain demonstrates strong granular cytoplasmic staining (400x).

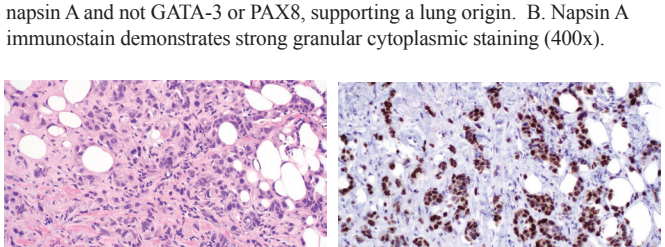


Figure 5: GATA-3 Staining in Urothelial Carcinoma. A 61-year-old man with a history of muscle invasive bladder cancer status post cystectomy presents with peritoneal carcinomatosis. A. Peritoneal biopsy demonstrates involvement by a high-grade malignant epithelioid neoplasm (H&E, 200x). B. The tumor expresses GATA-3 (pictured) and CK7 and not p63, PSA, or ER, supporting a diagnosis of urothelial carcinoma (200x). p63 is only 80-90% sensitive for urothelial carcinoma, with poorly differentiated examples less likely to be positive. GATA-3 is especially helpful in these cases.

maker of lung adenocarcinoma (Figure 4). It is also frequently expressed by renal cell carcinomas, especially papillary type.

In the lung, the distinction of adenocarcinoma from squamous cell carcinoma and small cell carcinoma is therapeutically critical. TTF-1 is the "gold standard" lung adenocarcinoma marker, but it is only ~75% sensitive and is also expressed by 85% of small cell lung cancers.

Napsin A is similarly sensitive in lung adenocarcinoma, but it is not expressed by small cell lung cancer. Neither of these markers are significantly expressed in squamous cell carcinomas. The addition of Napsin A staining to TTF-1 may lead to an incremental increase in the frequency of "immunopositive" lung adenocarcinomas, perhaps approaching 85%.

Key Reference: Napsin A expression in lung and kidney neoplasia: a review and update. *Advances in Anatomic Pathology*. 2012;19(1):66-73.

GATA binding protein 3 (GATA-3):

Background: GATA-3 is a GATA family transcription factor that was demonstrated in gene expression profiling

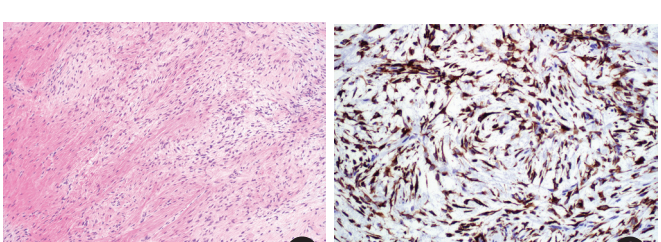


Figure 6: MUC4 Staining in Low-Grade Fibromyxoid Sarcoma. A 37-year-old woman was found to have a 6 cm soft tissue mass in the pelvis, superficial to the obturator internus muscle. It was excised. A. Sections show a low-grade spindle cell lesion with densely collagenized and more myxoid areas (H&E, 100x). B. Diffuse, strong cytoplasmic expression of MUC4 supports a specific diagnosis of low-grade fibromyxoid sarcoma, obviating the need for FUS FISH (200x).

experiments to be highly expressed in breast cancer, where it was shown to correlate with ER-positivity and favorable prognosis and in urothelial carcinoma (Figure 5), in which expression distinguishes this tumor type from renal and prostatic carcinomas.

GATA-3 immunohistochemistry has emerged as a "cutting edge" marker in the diagnosis of breast cancer and urothelial carcinoma. It is at least as, if not more, sensitive than the traditional breast cancer markers ER and PR, with the advantage that it is not expressed in Mullerian tract tumors. It is nearly twice as sensitive as the similarly specific marker GCDFP-15. In urothelial carcinoma, sensitivity is on par with p63, with the advantage that GATA-3 is less frequently expressed by squamous cell carcinomas. Compared to other urothelial-specific markers (uroplakin III, thrombomodulin) that have gained relatively little traction, GATA-3 performs at nearly twice the sensitivity.

Key Reference: Ordonez NG. Value of GATA3 immunostaining in tumor diagnosis: a review. *Advances in Anatomic Pathology*. 2013;20(5):352-60.

Mucin 4 (MUC4):

Background: MUC4 is mucin core protein that was found, through gene expression profiling, to be upregulated in low-grade fibromyxoid sarcoma (LGFMS) and not in other morphologically similar mesenchymal tumors (Figure 6). LGFMS is characterized by a recurrent translocation (7;16) that results in *FUS-CREB3L2* fusion.

MUC4 immunohistochemistry has emerged as an incredibly sensitive and specific marker for this tumor type, which, although unusual, is a differential diagnostic consideration with many more common spindle cell tumors including perineurioma, myxofibrosarcoma, cellular myxoma, solitary fibrous tumor, desmoid fibromatosis, neurofibroma, schwannoma, and dermatofibrosarcoma protuberans, among others. Doyle et al demonstrated MUC4 expression in 100% of 49 LGFMSs, with expression typically diffuse and strong. Of 240 other tumors, expression was detected in only 6 (2%),

all of which were monophasic synovial sarcomas (30% of 20 examples of this tumor type; expression in these tended to be weak and patchy). Of note, LGFMS and synovial sarcoma can be readily distinguished based on keratin and TLE1 expression in the latter (see below). MUC4 is also detected in 70% of sclerosing epithelioid fibrosarcomas (SEF) and all hybrid LGFMS-SEFs.

Key Reference: Doyle LA, Moller E, Dal Cin P, Fletcher CD, Mertens F, Hornick JL. MUC4 is a highly sensitive and specific marker for low-grade fibromyxoid sarcoma. *The American Journal of Surgical Pathology.* 2011;35(5):733-41.

c-Myc:

Background: The transcription factor c-Myc is dysregulated in many human cancers. Translocations involving the *c-Myc* locus are detected in ≥90% of Burkitt lymphomas and 5-15% of diffuse large B-cell lymphomas. Immunohistochemistry for c-Myc has emerged as a surrogate for c-Myc activation (Figure 7). In lymphomas, although that activation usually occurs due to a translocation (historically necessitating FISH or karyotyping for detection), it is increasingly recognized that post-transcriptional regulation (e.g., by mircoRNAs) may be responsible.

Diffuse, strong nuclear staining correlates with c-Myc activation. c-Myc immunohistochemistry is useful to support a diagnosis of Burkitt lymphoma (including occasional translocation-negative cases) and to suggest the presence of a *c-Myc* translocation in a diffuse large B-cell lymphoma (prognostically adverse). Non-c-Myc-activated lymphomas are characterized by lower level protein expression.

Key Reference: Ruzinova MB, Caron T, Rodig SJ. Altered subcellular localization of c-Myc protein identifies aggressive B-cell lymphomas harboring a c-MYC translocation. *The American Journal of Surgical Pathology.* 2010;34(6):882-91.

CD163:

Background: CD163, a scavenger receptor for hemoglobin-haptoglobin complexes, is highly expressed by cells of monocyte/macrophage lineage. CD163 immunohistochemistry is useful to highlight tissue macrophages (Figure 8), as well conditions/tumors with histiocytic differentiation including Rosai-Dorfman disease, histiocytic sarcoma, littoral cell angioma, tenosynovial giant cell tumor, and a subset of dermatofibromas. Staining is membranous and cytoplasmic/granular.

CD163 has emerged as a favored histiocytic marker over CD68 due to superior specificity. CD68 is a lysosome/phagosome-associated antigen. Although it is thus highly expressed by macrophages, CD68-positivity is also frequently seen in melanoma, benign nerve sheath tumors, and (depending on the clone) myeloid leukemias and is occasionally seen in mast cell disease, non-histiocytic sarcomas, carcinomas, and lymphomas. In myeloid leukemias, CD163 expression is limited to those with monocytic differentiation, though the rate of positivity by immunohistochemistry (compared to that by flow cytometry) is low.

Key Reference: Nguyen TT, Schwartz EJ, West RB, Warnke RA, Arber DA, Natkunam Y. Expression of CD163 (hemoglobin scavenger receptor) in normal tissues, lymphomas, carcinomas, and sarcomas is largely restricted to the monocyte/macrophage lineage. *The American Journal of Surgical Pathology*. 2005;29(5):617-24.

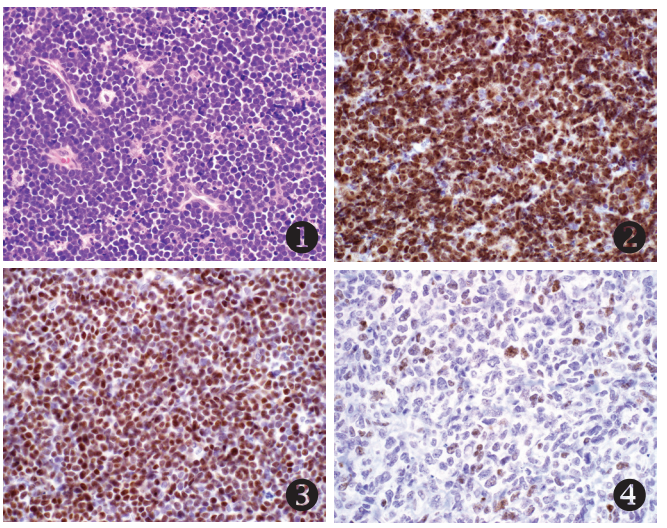


Figure 7: c-Myc Staining in Burkitt Lymphoma. A 10-year-old boy presented with fatigue and pallor. Pill endoscopy revealed active bleeding from the distal small intestine. Laparoscopy was performed, and a large, firm abdominal mass fixed to the mesentery and adherent to intestines was biopsied. 1. High-grade round cell neoplasm with monomorphous cytomorphology; note the frequent tingible body macrophages (H&E, 400x). The tumor was found to express CD20, CD10, and Bcl-6 and not Bcl-2, TdT, or CD34. 2. The Ki-67 proliferation index approaches 100% (400x). 3. Although c-Myc FISH was negative, the tumor shows diffuse, strong c-Myc staining, in keeping with c-Myc activation (400x). A diagnosis of Burkitt lymphoma was made, and the patient has responded to therapy. 4. c-Myc staining in a non-c-Myc-activated diffuse large B-cell lymphoma is weak and patchy (400x).

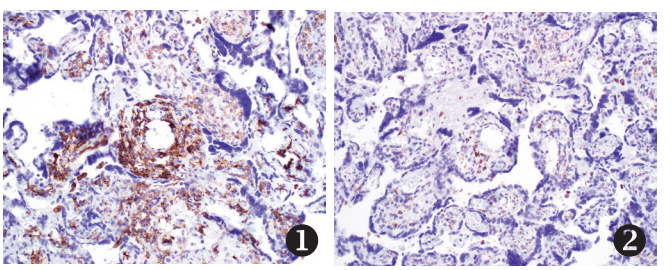


Figure 8: CD163 Staining in Cells of Monocyte/Macrophage Lineage. A. CD163 immunostain highlights Hofbauer cells in placental villi (200x). B. CD68 immunostain performed on a serial section (200x).

Transducin-like enhancer protein 1 (TLE1):

Background: Transducin-like enhancer of split 1 (TLE1), a transcriptional co-repressor that inhibits cell fate determination, was shown by gene expression profiling to be upregulated in synovial sarcoma (SS).

Synovial sarcoma represents up to 10% of all sarcomas, and although biphasic examples are readily recognized on the H&E, the differential diagnosis of monophasic and poorly differentiated examples includes an array of spindle cell and round cell tumors. Diagnosis rests on the detection of focal broad-spectrum keratin of EMA expression and/or on the demonstration of the characteristic t(X;18) by FISH or RT-PCR.

Immunohistochemistry for TLE1 has emerged as a diagnostic marker of SS, with diffuse, strong nuclear staining (Figure 9A-B) distinguishing SS from histologic mimics including malignant peripheral nerve sheath tumor (Figure 9C-D), solitary fibrous tumor, fibrosarcomatous transformation of dermatofibrosarcoma protuberans, and Ewing sarcoma.

Key Reference: Terry J, Saito T, Subramanian S, Ruttan C, Antonescu CR, Goldblum JR, et al. TLE1 as a diagnostic immunohistochemical marker for synovial sarcoma emerging from gene expression profiling studies. *The American Journal of Surgical Pathology.* 2007;31(2):240-6.

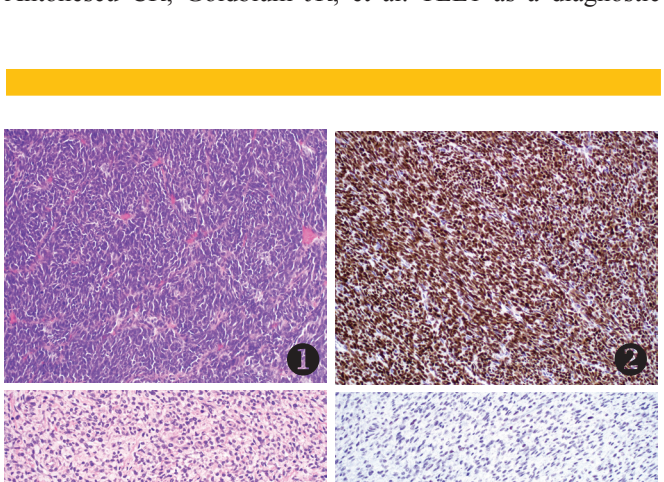


Figure 9: TLE1 Staining in Synovial Sarcoma and Mimics.
A 64-year-old man presents with a recurrence of a primary lung tumor. A. Cellular spindle cell lesion with high nucleus:cytoplasm ratio, hyperchromatism, and numerous mitotic figures (H&E, 200x). B. Diffuse, strong nuclear staining supports a diagnosis of synovial sarcoma, in this instance, poorly differentiated (200x). A 12-year-old with neurofibromatosis type I presents with a large retroperitoneal tumor involving the femoral nerve. C. Cellular spindle cell lesion with moderate atypia and scattered mitotic figures consistent with malignant peripheral nerve sheath tumor (H&E, 200x). D. Weak, patchy TLE1 staining may be seen in this tumor type (200x).

Somatostatin receptor type 2A (SSTR2A):

Background: Somatostatin is an inhibitory peptide hormone produced in regions of the brain and by D cells in the gastroenteropancreatic system. Somatostatin receptors (SSTR) are highly expressed by neuroendocrine neoplasms, especially well-differentiated tumors (Figure 10). This high-level expression is the basis of nuclear medicine imaging of neuroendocrine tumors (e.g., OctreoScan) and, perhaps more importantly, anti-secretory and anti-proliferative therapy with the somatostatin analogue octreotide. Of the various receptor subtypes, a positive scan is most closely related to expression of SSTR2A.

Octreotide therapy is only approved in the face of a positive OctreoScan or a positive SSTR2A immunohistochemical result. Unfortunately, the OctreoScan is usually negative in tumors <2 cm, and occasionally tumors are resected before their neuroendocrine nature is known.

If >10% of tumor cells stain, the tumor is very likely to express high levels of somatostatin receptors, and the patient may benefit from somatostatin-analogue therapy. If 1-10% of cells stain, the result is indeterminate. Patients with weak staining in this indeterminate group and patients with no staining at all are unlikely to benefit from octreotide.

Key Reference: Korner M, Waser B, Schonbrunn A, Perren A, Reubi JC. Somatostatin receptor subtype 2A immunohistochemistry using a new monoclonal antibody selects tumors suitable for in vivo somatostatin receptor targeting. *The American Journal of Surgical Pathology.* 2012;36(2):242-52.

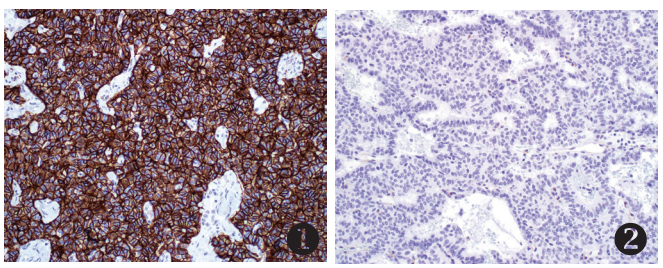


Figure 10: SSTR2A Staining in Neuroendocrine Neoplasms.
A. Strong, complete membranous staining in a well-differentiated pancreatic neuroendocrine tumor (200x). B. Complete absence of staining in another well-differentiated pancreatic neuroendocrine tumor; this patient had an insulinoma (200x).

OUTREACH Update

MOLECULAR ONCOLOGY: EGFR TESTING PERFORMED WITH DNA EXTRACTED FROM FNA PREPARATIONS

Specimen type: Both Diff Quik and Pap stained slides can be used.

Ideal slide(s): Please use slide(s) with the highest percentage of tumor cells and lowest percentage of non-neoplastic cells/mucin/pigment, etc.

Minimum number of tumor cells required: Depending on the test requested: 2,000 tumor cells for EGFR and KIT; 500 cells for BRAF/KRAS/NRAS. If the number of tumor cells is lower (but not significantly lower), please send the slides for review. Sometimes part of the test can be performed; e.g., we may sequence the two most important exons instead of all 4 exons of EGFR.

PLEASE NOTE: The slide sent for testing will be sacrificed. Please keep a diagnostic slide for your record. If only one slide is available and the testing is still desired, you may photograph the slide. We may only need a portion of the slide and the slide can be re-coverslipped and returned to you.

We will greatly appreciate if you could mark the areas with tumor cells. If you have any questions, please feel free to contact Client Services toll-free at 1-866-844-2522.

For additional test information, EGFR Test Directory page: **http://www.healthcare.uiowa.edu/path_handbook/rhandbook/test2711.html**

UIDL
UI Diagnostic Laboratories

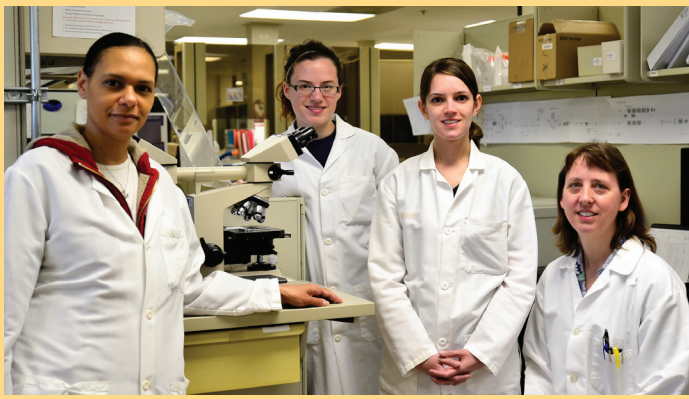
New
Client Services Hours:
Monday – Friday:
7:30 am – 7:00 pm
Saturday:
8:00 am – 1:00 pm

Client Services:
Toll-free: (866) 844-2522
Local: (319)-384-7212

Website and Test Directory:
www.healthcare.uiowa.edu/uidl

At your service! The UI Flow Cytometry Medical Laboratory Scientist Team

Our highly trained and educated MLS are dedicated to producing consistent, accurate work of the highest quality.



Sabrina Bonde, MLS (ASCP); Monica Smith, MLS (ASCP); Laura Didier, MLS (ASCP); Angie Rummelhart, MLS (ASCP)

The UI diagnostic flow cytometry laboratory is staffed by 4 Medical Laboratory Scientists, who have all undergone specialized technical training and are board certified by the American Society for Clinical Pathology. They function as the front line for lab technical service for all types of specimens, and can answer questions concerning proper specimen collection, preservation, viability and testing. These skilled professionals work very closely with the pathologists to screen patient history and evaluate submitted specimens. The pathologists use this information to make decisions concerning appropriate antibody panels for testing, which are then carried out by the MLS team through a series of technical steps involving the specimen processing and staining with numerous antibodies conjugated with distinct fluorochromes. These stained cell preparations are placed onto a flow cytometer which uses 3 different lasers to identify and characterize cell populations of interest. The flow cytometer software uses the information collected by the lasers to generate abundant numerical data that is then presented in graphical report format. The MLS staff continuously monitor the performance of the flow cytometers and also help perform a preliminary analysis of the data, which is then submitted to the pathologist for review, edits and sign out.

BRAF/RAS Mutation Analysis for Thyroid Nodules on Cytology Smears

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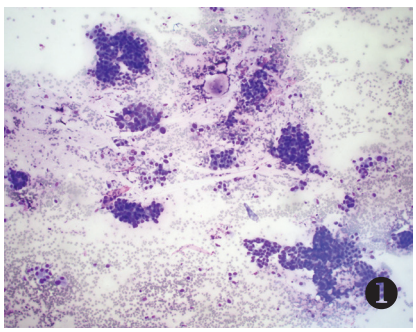
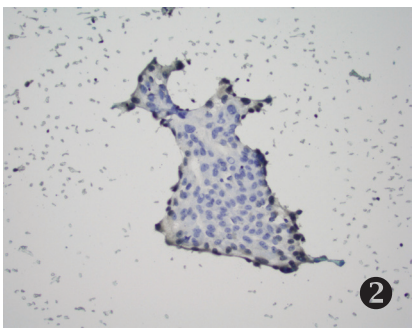
Fine needle aspiration (FNA) is the first line workup for thyroid nodules. Up to one-third of aspirated nodules fall into the category of indeterminate follicular lesion. These patients may first undergo lobectomy, followed by completion thyroidectomy if necessary. Recent studies have shown the presence of *BRAF* V600E mutation to be highly specific for papillary thyroid carcinoma. *RAS* mutations carry a 74% to 87% positive predictive value for malignancy, although these mutations can also be seen in benign conditions (1-3). *BRAF/RAS* testing on FNA smears maximizes the utility of cytology materials. It may help with a patient's management and save the patient from an additional procedure.

While formalin-fixed paraffin-embedded cell blocks from FNA's are routinely used for molecular oncology testing, a pitfall of their use is the inability to assess cellularity before preparation. This can result in insufficient tumor cells for testing and require additional procedures. The Molecular Pathology Laboratory at the University of Iowa has developed a method of extracting genomic DNA directly from cytology smears using a matrix capture method that allows lifting of aspirated tissue directly from smears. Using a two-tube multiplex PCR followed by single nucleotide primer extension assay, we are able to simultaneously detect 52 mutations including V600E and K601Q/E of the *BRAF* gene, mutations in codons 12, 13 and 61 of the *KRAS* and *NRAS* genes, and codon 61 of the *HRAS* gene. Both Romanowsky-type (Diff-Quik) and Papanicolaou (Pap) stained slides are accepted. The assay has a 5% limit of detection with a minimum of 1000 tumor cells needed depending on the percentage of tumor cells present in the specimen.

Below are some examples: Figures 1 and 2. The combined Diff Quik and pap-stained slide were combined and the cells were used for BRAF testing (in duplicate) in a papillary thyroid carcinoma.





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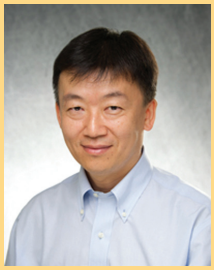
NEW FACULTY

JOHN LARRY BLAU, MD

Dr. Blau received his MD in 2008 from the University of Colorado. He then entered the combined Anatomic and Clinical Pathology Training program here at the University of Iowa, and completed his residency in 2012. During residency, he contributed to the department in a unique and impactful manner using his extensive computer skills and knowledge, which include writing code and programming. His expertise on two projects, the gross room photography data management program, and the antimicrobial sensitivity program, has markedly enhanced departmental operations. He just completed a two-year fellowship in the Pathology Informatics Program at the University of Michigan and joined us here at University of Iowa Hospitals and Clinics at the end of June.

Dr. Blau will expand the Department's capabilities in all three aspects of the tripartite mission; Teaching, Research, & Exceptional Patient Care.

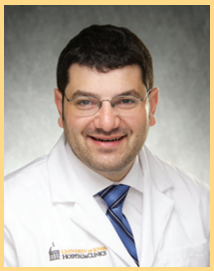
CHEN ZHAO, MD, PhD



Dr. Zhao received his MD and initial pathology training in China, followed by a move to Tokyo where he pursued his PhD training at Keio University School of Medicine. After receiving his PhD in 2002, he remained at Keio University as an assistant professor in the Department of Immunology and Microbiology where he published several high profile papers in the area of bone metabolism and homeostasis. In 2004 he moved to Duke University to work in the laboratory of Tannishtha Reya, focusing on stem cells and cancer, and Chen again proved to be productive with a number of high impact papers including reports in *Nature* and *Cancer Cell*. After 5 years as a post-doctoral fellow, Dr. Zhao elected to resume his medical training and performed his pathology residency at the University of Rochester (2009-2013). He finished a Hematopathology Fellow at the University of Pennsylvania (2013-2014).

Dr. Zhao's recruitment is part of an ongoing effort to increase the number of physician-scientist investigators in the Department and further enhance our cancer biology research program. Although the majority of Chen's time will be dedicated to establishing a competitive research program, approximately 25% of his effort will be spent on the Hematopathology service.

MUNIR- ZAKARY TANAS, MD



Dr. Tanas received his B.S. degree in Biochemistry from Whitworth College in Spokane, and his MD degree from the University of Washington in Seattle. Munir remained in Seattle to perform his Anatomic Pathology Residency and Surgical Pathology Fellowship at the University of Washington Medical Center. During his last year at the University of Washington, he also served as Chief Resident. In 2007, Dr. Tanas left the west coast and moved to Cleveland to perform a fellowship in Bone and Soft Tissue Pathology at the Cleveland Clinic under the mentorship of Dr. Brian Rubin and Dr. John Goldblum.

At Cleveland Clinic, Munir worked on both applied and basic projects with an emphasis on soft tissue cancers. On the clinical side, he and Dr. Goldblum evaluated the utility of FISH in the diagnosis of mesenchymal neoplasms. Upon completion of his bone and soft tissue subspecialty training, Dr. Tanas embarked on a post-doctoral research fellowship in Dr. Rubin's laboratory. During his post-doctoral fellowship, Munir identified the presence of a *WWTR$_1$-CAMTA$_1$* gene fusion in 90% of epithelioid hemangioendothelioma, a rare vascular cancer. This finding was published in *Science Translational Medicine*. He followed up on this discovery by showing that WWTR1-CAMTA$_1$ transforms cells by constitutively activating the WWTR$_1$ (also called TAZ) portion of the fusion and is submitting the manuscript for publication.

Munir plans to take his insights into TAZ and YAP (TAZ paralogue) activation from his post-doctoral training experience and apply them to more common solid tumors, including breast cancer. There is a range of faculty in the College of Medicine who have shared interests with Munir indicating strong potential for collaboration and multi-investigator grants.

ANTHONY SNOW, MD

Dr. Snow received his B.S. degree in Chemistry from Marquette University in Milwaukee, and his MD degree from Creighton University in Omaha. He completed his residency in anatomic and clinical pathology at Wake Forest University Baptist Medical Center in Winston-Salem, North Carolina where, during his last year he served as Chief Resident. He has just completed a fellowship in surgical pathology with an emphasis in GI pathology at Brown University.

Anthony is just beginning his career, but has had a range of experiences in molecular pathology across a spectrum of next generation technologies; having used microarray technology in medical school and having been instrumental in the development of a melanoma targeted next generation sequencing research panel last year here at the University of Iowa. During his MGP fellowship he was a critical driver on a number of projects including multiple improvements to tissue processing for molecular oncology testing, a critical component in moving forward with personalized molecular testing. To date, he has published six peer reviewed manuscripts. Dr. Snow was highly regarded by the pathology residents during his MGP fellowship and it is clear that he has the potential to be a highly effective teacher. His mentors at Brown praise him for his work ethic and knowledge in surgical pathology fellowship.

Dr. Snow's recruitment is part of an ongoing effort to enhance the bridge between the dual clinical activities of molecular and surgical pathology in the Department of Pathology. Anthony's fellowship training in both has prepared him well for this position and he will bring unique understanding for moving the field forward. Equally important, there is a range of faculty in the College of Medicine who share interests with Dr. Snow indicating potential for collaboration.

ACTIVE RESEARCH AWARDS

Dr. Aaron Bossler has a new research contract negotiated with Cepheid for a research project titled *Analytical Validation Study of the Cepheid Xpert BCR-ABL Monitor Assay*. The contract total is $32,206. This contract is for the period of August 30, 2013 through August 30, 2014.

Stephanie Condotta, a Postdoctoral Fellow in Dr. Vladimir Badovinac's research lab, was awarded an American Heart Association, Midwest Affiliate, Winter 2013 Postdoctoral Fellowship. The title of this project is *Sepsis induced changes in naïve and memory CD8 T cell responses to newly encountered infections*. The award total is $95,224 and is for the period of July 1, 2013 through June 30, 2015.

Dr. Marina Ivanovic received one of the first small Thoracic MOG research grants at the University of Iowa. The title of this project is *Metastasis-Associated Protein 1 Expression in lung adenocarcinoma*. The award is in the amount of $15,000.

Dr. Siegfried Janz received a SPORE Career Development Award through the Holden Comprehensive Cancer Center. The title of this project is *Preclinical validation of the newly emerging lymphoma drug, piperlongumine (PL)*. This funding total is $59,874 and is for the period of September 1, 2013 through June 30, 2014.

Dr. C. Michael Knudson received a Donald D. Dorfman Research Award from the Holden Comprehensive Cancer Center at the University of Iowa Health Care. This award is for the best research paper in lymphoma published in 2012 or 2013. The title of the paper is *2-deoxyglucose-induced toxicity is regulated by Bcl-2 family members and is enhanced by antagonizing Bcl-2 in lymphoma cell lines*. The award is in the amount of $2,500.

Dr. Kevin Legge received grant funding from the National Institutes of Health/National Institute of Alcohol Abuse and Alcoholism (NIH/NIAAA). The title of this project is *Chronic Ethanol Consumption and Pulmonary Immune Suppression*. This funding total is $396,376 and is for the period of September 5, 2013 through August 31, 2015.

Dr. Deqin Ma received research funding from the Carver College of Medicine, Holden Comprehensive Cancer Center at the University of Iowa. The title of this project is *Molecular Studies of Leiomyosarcoma – Identification of Potential Targets for Personalized Medicine*. The award is in the amount of $10,000.

Dr. Andrean Simons-Burnett received a second year of American Cancer Society Institutional Research Grant (ACS-IRG) seed grant funding from the Holden Comprehensive Cancer Center at the University of Iowa. The title of the project is *Chronic ER-stress and inflammasome activity in HNSCC tumor response to EGFR inhibition*. The amount of this award is $30,000. The period for this project is November 1, 2013 through October 31, 2014.

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FACULTY AWARDS AND RECOGNITIONS

Marcus Nashelsky, MD, Appointed as the Johnson County Chief Medical Examiner

Dr. Nashelsky was appointed Johnson County Chief Medical Examiner by the Johnson County Board of Supervisors to a two-year term effective January 2, 2014. He previously served as a Johnson County Deputy Medical Examiner and continues in his appointment as an Iowa Assistant State Medical Examiner. As County Medical Examiner, Dr. Nashelsky appoints Deputy Medical Examiners. The Deputy Medical Examiners include Dennis Firchau, MD, Clinical Assistant Professor of Pathology. This appointment will enhance the existing productive collaboration between Johnson County and the Department of Pathology, University of Iowa Health Care.

C. Michael Knudson, MD, PhD Received the Donald D. Dorfman Research Award

Left to right: George Weiner, MD, Jonathan Dorfman, Lorraine Dorfman and Michael Knudson, MD, PhD

The Donald D. Dorfman Research Award recognizes one investigator in basic research and one investigator in clinical/population research in leukemia and lymphoma. The award was presented by Jonathan and Lorraine Dorfman at a recognition event held on Friday, October 25, 2013.
C. Michael Knudson, MD, PhD, was selected for this year's Donald D. Dorfman Award for Basic Research for his paper entitled "2-deoxyglucose-induced toxicity is regulated by Bcl-2 family members and is enhanced by antagonizing Bcl-2 in lymphoma cell lines." published in *Oncogene*. This paper examined novel approaches to the treatment of lymphoma using 2-deoxyglucose, a drug that targets the abnormal metabolism that is prevalent in lymphoma cells. This award includes support for research on lymphoma that will be utilized by Dr. Knudson and Dr. Siegfried Janz to study the role of metformin in mouse models of lymphoma.

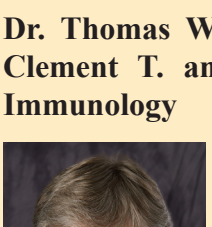
Dr. Nashelsky Elected President of the National Association of Medical Examiners

Marcus Nashelsky, MD, has been elected as President of the National Association of Medical Examiners. The one year term will begin on January 1, 2015.

Dr. Nashelsky is a Clinical Professor of Pathology and directs the UI Hospitals and Clinics Autopsy Service; his clinical work is centered on forensic and general autopsy pathology. He is a Johnson County Chief Medical Examiner and an Assistant State Medical Examiner for Iowa.

The National Association of Medical Examiners (NAME) is the professional organization of physician medical examiners (most of whom are board certified forensic pathologists) and medicolegal death investigators who perform the official duties of medicolegal death investigations in the United States and elsewhere. NAME's activities are centered on professional education, development of practice standards and accreditation of medical examiner offices to maximize contributions to public health and the civil/criminal judicial systems. The official journal of NAME is *Academic Forensic Pathology*.

Dr. Thomas Waldschmidt Reappointed as the Clement T. and Sylvia H. Hanson Chair in Immunology



Thomas Waldschmidt, PhD, has been reappointed as the Clement T. and Sylvia H. Hanson Chair in Immunology. This is a five year appointment effective July 1, 2013. The Hanson Chair was established through gifts from the Hanson family to support the academic pursuits of a faculty member who has a distinguished research program in Immunology. Dr. Richard Lynch, former chair of Pathology, was the original Hanson Chair and Dr. Waldschmidt was first appointed in 2008.

Dr. Waldschmidt is recognized for his research in B lymphocytes and adaptive immunity, academic achievements, teaching and contributions to the Department and College.

Department of Pathology Receives Excellence in Quality Award.

The Pathology Clinical Laboratory Team was presented the Excellence in Quality Award at the Annual University of Iowa Physicians (UIP) Fall meeting on October 21, 2013. The award is given to an individual or team in recognition of outstanding quality of care provided to patients. Recipients will have demonstrated excellence in reportable measures of quality, benchmarked patient outcomes, or improvements in internally measured outcomes.

The Pathology Clinical Laboratory Team received a recognition plaque that will be displayed in Pathology Administration. This is a testament to all managers, techs, medical directors, pathology faculty, support staff, IT professionals and a whole host of other individuals who help the pathology operation run smoothly for our patients.

Dr. Matthew Krasowski pictured, holding the Excellence in Quality Award plaque

EXCERPTS FROM THE NOMINATION FORM INCLUDED:

"I am greatly impressed by the high standard of quality and the culture of continuous improvement that pervades the laboratory."

"Personnel in every area are dedicated and enthusiastic contributors 'in the background' to facilitate excellent patient care."

"We are very lucky as an institution to have high quality leadership as medical directors."

"Multi-disciplinary efforts in tackling over- and multi-utilization of laboratory testing."

"Development of formulary and formal approval protocol for expensive mailout testing."

"Development of IRL clinical laboratory and phlebotomy team using Disney model."

Dr. Meyerholz will serve on the Editorial Board of *The American Journal of Pathology*

David Meyerholz, DVM, PhD has accepted an invitation to serve on the Editorial Board at *The American Journal of Pathology* for a three-year renewable term, starting August 1, 2013. The American Journal of Pathology is known as the premier journal in investigative pathology and is the most cited journal in the field of research pathology.

Dr. Meyerholz is an Associate Professor of Pathology and serves as Director of the Division of Comparative Pathology. Dr. Meyerholz's research efforts are currently focused on the study of cystic fibrosis and other lung diseases.

The American Journal of Pathology, official journal of the American Society for Investigative Pathology (ASIP) seeks to publish high-quality, original papers on the cellular and molecular biology of disease. The editors accept manuscripts that advance basic and translational knowledge of the pathogenesis, classification, diagnosis, and mechanisms of disease, without preference for a specific analytic method. High priority is given to studies on human disease and relevant experimental models using cellular, molecular, animal, biological, chemical, and immunological approaches in conjunction with morphology.

Posters Receive Best in Class Awards at the UIHC Quality and Patient Safety Symposium

Process Improvement Committee – As the laboratory provides vital information upon which diagnostic and treatment algorithms are determined, the UIHC surgical pathology laboratory formed a process improvement committee (PIC) composed of technical leaders from several laboratories within anatomic pathology, including cytology, histology, immunopathology, the surgical pathology gross room, and quality assurance. The committee meets once weekly to discuss and define system weaknesses that can be improved to provide better clinical service. The PIC's main objectives are: (1) to increase cross-talk between sections of the department, (2) to better define processes, (3) to improve system efficiency, (4) to streamline workflow, and (5) to provide accurate diagnostic results with faster turn-around-time (TAT).

Results of process improvements initiated by the PIC:

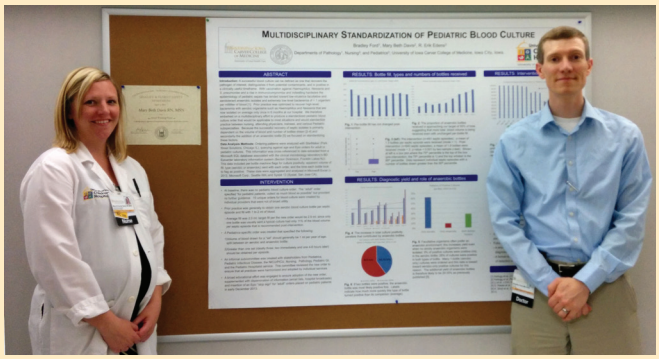
- 37.5% of IHC tests available on same day they are ordered
- Tissue processing reduced 22% for GI biopsy cases and number of cassettes per part significantly reduced
- TAT for 88307/88309 cases reduced by more than one day

Kent Becker, Quality and Operational Improvement Engineer, would like to acknowledge the contributions made by Melissa Jans, CLSIII, Histology; Emily Fuller, Pathologist Assistant; Debbie Jacobsmeier, CLSIII, Cytology; Lisa Horning, CLSIII, Immunopathology; Heidi Nobiling, RN, MA, MBA, NEA-BC; Bryan Steussy, MD; Michael Gailey, DO; Patricia Kirby, MD; and Robert A. Robinson, MD, PhD.

Michael Gailey, DO; Emily Fuller, MS, PA(ASCP); Kent Becker, MT(ASCP); Melissa Jans, HTL(ASCP); Robert A.Robinson, MD, PhD

Pediatric Blood Culture – Prior pediatric blood culture practice at UIHC was to send a single aerobic blood culture bottle with a small inoculum of blood per septic episode, often less than 1 ml. This led to low yield, apparent culture-negative sepsis, and failure to obtain a microbiologic diagnosis that might guide therapy. A multidisciplinary effort was undertaken to promote the adoption of a new pediatric blood culture protocol that emphasizes delivery of higher blood volumes (ideally, a total of 3 ml per year of age, divided across 6 bottles) and inclusion of matched aerobic/anaerobic bottle pairs instead of reliance on only the aerobic bottle.

This effort led to an increase in the overall rate of blood culture positivity from 5% pre-intervention to 7% post-intervention (a 40% increase). Compared to a pre-intervention baseline,



Left to right: Mary Beth Davis, RN and Bradley Ford, MD, PhD.

this was associated with receipt of twice as many bottles on average, almost half of which were anaerobic culture bottles. The increase in yield was almost entirely due to positive anaerobic bottles: 10% of cultures were positive only in the anaerobic bottles, and where both bottles were positive (30% of total episodes) the anaerobic bottle was most likely positive first and 8.5 hours before its aerobic mate. This has led to more rapid and effective diagnosis of sepsis in our pediatric patients, and in recognition of this effort and its success a poster by Bradley Ford, MD PhD; Mary Beth Davis, RN; and Erik Edens, MD, received a best-in-class award at the UIHC Quality and Patient Safety Symposium.

left to right: Frank Mitros, MD and Nancy Rosenthal, MD

Frank A. Mitros Excellence in Teaching and Clinical Service Award

Nancy Rosenthal, MD, Clinical Professor of Pathology was presented with the "Frank A. Mitros Excellence in Teaching and Clinical Service Award" at a recent faculty meeting. This award is presented annually to a clinical faculty member who provides outstanding performance in both the clinical and educational missions of the Department after nomination by peers.

During the nominating process, one of Dr. Rosenthal's nominators wrote:
"I nominate Nancy Rosenthal for this award. She is the perfect blend of knowledge, patience, and directivity that we should all strive for with our clinical teaching. Furthermore, she has worked tirelessly for the path department in the realm of medical student education."

The award was presented to Dr. Rosenthal by Dr. Frank Mitros himself, who said "Now, as to some of the reasons why Nancy has been recognized for carrying on this departmental tradition. She has one of the cardinal skills of an anatomic pathologist, the ability to teach at the scope effectively, with the gift of being able to engage all the various members of the multi-leveled group gathered there. She has the knack of recognizing those people who are learning and those who are not. She can adjust her approach in response to the situation and do this efficiently. She has been said to have excellent timing, allowing her to hit the "sweet spot" when those whom she is teaching are most receptive.

Her clinical acumen is clear; when there is a tough marrow, she is recognized to be a superb "go-to" person, and our clinical colleagues recognize that. She is excellent at communicating her findings. It has been reported that on many an occasion such notoriously curmudgeonly clinicians {who shall remain nameless} have been known to charge into the lab as a roaring lion and leave as a gentle lamb!"

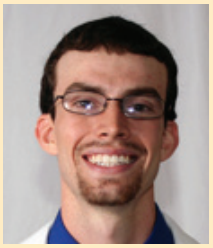
We are thankful and honored to have such a valued clinician and teacher working alongside us.

Congratulations, Dr. Rosenthal!

Special Achievement in Pathology Award

Kaleigh Lindholm received the **2014 Special Achievement in Pathology Award**, given by the University of Iowa Department of Pathology in conjunction with the Iowa Association of Pathologists (IAP). This achievement is awarded to a senior medical student for meritorious participation throughout the four-year curriculum in programs related to Pathology. Kaleigh received a monetary award from IAP and her name will be added to the award plaque displayed in Pathology Administration.

Sophomore Medical Student Award in Pathology



Andrew Baldwin received this year's **Sophomore Medical Student Award in Pathology**. This award is given by the University of Iowa Department of Pathology in conjunction with the Iowa Association of Pathologists (IAP) to the student who had the highest scores in the sophomore Pathology curriculum. Andrew received a monetary award from IAP and his name has been added to the award plaque displayed in Pathology Administration.

RESIDENCY PROGRAM **UPDATE**

New Co-Chief Residents 2014-15

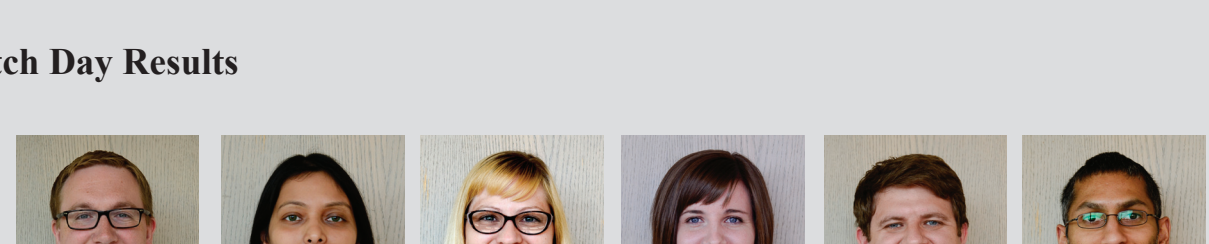
Dr. Stephanie Stauffer and Dr. Carly Rysgaard

We are pleased to announce that **Carly Rysgaard** and **Stephanie Stauffer** have been selected and agreed to serve as Co-Chief Residents for 2014-2015. They will assume duties of the Co-Chief residents beginning April 1, 2014. We asked Steph and Carly what they most look forward to in taking on this new role:

Steph: "I am honored and excited to begin my year as a co-chief for the UIHC pathology residency program. I have had an outstanding educational experience while at UIHC, and I hope to use this year to give back as much as possible. As a department, I believe that we consistently strive to provide the best quality patient care as possible, while also constantly challenging ourselves to improve our processes and provide a unique and well-rounded education to our residents, externs, and fellows. I most look forward to working as a team with my co-residents this year to meet those goals."

Carly: "I'm honored to be chosen as one of the 2014-2015 chief residents and will do my best to live up to the great examples set by our predecessors. I feel fortunate to be part of such a strong and collaborative team where everyone's input is valued. Looking ahead to the coming year, I am excited to work with faculty and my fellow residents to continue to make University of Iowa one of the best places to train!!"

Match Day Results



Chris Jensen, MD, Director, Pathology Residency Program: "I am delighted to announce our newest class of incoming residents. Thank you to everyone who participated in the recruitment process! We had a successful year because of all your collective efforts. I see tremendous potential in this group and know they will be a terrific addition to our resident cohort and our department as a whole."

Eric Destrampe, DO
AT Still University – Kirksville College of Osteopathic Medicine

Sarika Gupta, MD
Maulana Azad Medical College

Natalie Malvik, MD
Southern Illinois University

Kendra Palmer, MD
University of Arizona

Jon Thomason, MD
University of Kansas

Sagar Vishal, MD
University of Arkansas

2014 RESIDENCY PROGRAM **AWARDS AND RECOGNITION**

George D. Penick Award for Excellence in Education Presented to Brittany Pakalniskis

Brittany Pakalniskis, MD, is the 2014 recipient of the **George D. Penick Award for Excellence in Education**. This award is presented annually to a Pathology Resident who displays excellence and commitment to the education and teaching of medical students, peers, and clinical colleagues. Pictured above are Brittany Pakalniskis, MD, receiving the award from Leslie Bruch, MD, Vice Chair of Education and Faculty Development. Congratulations, Brittany!

Brittany Pakalniskis (left); Leslie Bruch (right)

Stephanie Stauffer (left); Matthew Krasowski (right)

Dr. Krasowski receives 2014 Resident Teaching Award

Congratulations to Matthew Krasowski, MD, PhD, recipient of the **2014 Resident Teaching Award**. Each year, residents select a faculty member in the Department of Pathology who they believe has been an outstanding teacher and mentor. Co-chief resident Stephanie Stauffer presented the award to Dr. Krasowski at the Resident and Fellow Farewell Dinner, held June 5, 2014.

In the words of one Pathology resident: "Dr Krasowski does a great job in making residents understand their roles as upcoming pathologists in chemistry and lab management. I've learned so much and enjoyed working with him. I really appreciated how he gets residents involved in all lab-related discussions. I am looking forward to undertaking a management project with Dr. Krasowski."

Frank A. Mitros Residents' Visiting Professor Award

The **2014 Frank A. Mitros Residents' Visiting Professor Award** was presented to Michelle Hirsch, MD, PhD, Associate Professor of Pathology, Harvard Medical School. During her visit to the program on April 10, 2014, Dr. Hirsch held a special slide analysis conference with the residents, a highlight of this annual educational experience. She also delivered a Department of Pathology Grand Rounds presentation entitled: "Updates in Renal Epithelia Neoplasia: From Morphology to Molecular Genetics."

Carly Rysgaard (left), Michelle Hirsch (right)

Thank you!

Please join us in thanking **Michelle Kurt-Mangold** and **Brittany Pakalniskis** for their service over the past year as Co-Chief Residents. They have had numerous roles, including recruiting and scheduling, and have been active behind the scenes in maintaining and improving the quality of the program. We hope that the leadership skills they gained during this past year will serve them well in their future careers.

Chris Jensen, Director, Pathology Residency Program
Leana Guerin, Assistant Director, Pathology Residency Program

2014-15 PATHOLOGY HOUSE **STAFF ROSTER**

PATHOLOGY RESIDENTS

R4
Anna Dolezal, M.D
Omar Jaber, MD
Marisa Jacob, MD
Carolyn Rysgaard, MD, Co-Chief Resident
Stephanie Stauffer, MD, Co-Chief Resident
Stephanie Wood, MD

R3
Deema Alkapalan, M.D
Ava Bhattarai, MBBS
Gagan Mathur, MBBS

R2
Craig Dunseth, MD,
Amelia Fierro-Fine, MD
Matthew Keeney, MD
Katie Schouweiler, MD
Angela Wu, M.D

R1
Eric Destrampe, DO
Sarika Gupta, MBBS
Natalie Malvik, MD
Kendra Palmer, MD
Jon Thomason, MD
Sagar Vishal, MD

PATHOLOGY FELLOWS

Cytopathology
Michael Kyle, MD
Thomas Wilson, MD

Hematopathology
Bryan Steussy, MD

Molecular Genetics
Jacqueline Lekostaj, MD

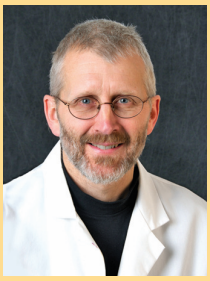
Surgical Pathology
Omar Jabar, MD
Michelle Kurt-Mangold, MD
Brittany Pakalniskis, MD
Erica Savage, MD
Johanna Savage, MD

Transfusion Medicine
Keith Smith, DO

PATHOLOGY EXTERNS

Matthew Braithwaite M3
Nate Camden M2
Michael Jorgensen M2
Kevin Pettit M2
Heather Schopper M2
Brennan Tesdahl M2

RESIDENCY **LEADERS**



Residency Program Director
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Clinical Professor
Surgical Pathology
Director of Cytopathology

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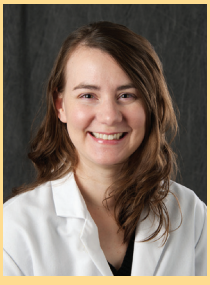

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Assistant Residency Program Director
J. Stacey Klutts, MD, PhD
Assistant Professor
Clinical Pathology

Ssacey-klutts@uiowa.edu
319-338-0581

Faculty Focus: *Chris Jensen, MD*

What is your hometown?
New Hampton, Iowa

What interested you to pursue a career in Pathology?
I was drawn to Pathology because it gave me a view into what was happening behind the scenes in medicine. I have always been interested in how things work.

In Pathology, I could see what was happening at the tissue and cellular level. Pathology also dealt with solving problems. I enjoy helping patients and physicians understand how things work or more often, why they are not working the way they should.

Is there a teacher or mentor who helped shape your career?
There are many teachers who shaped me along the way.

My parents, both teachers, instilled a love of learning at an early age which is one of the greatest gifts you can give your children. My father was my high school chemistry and physics teacher and helped give me the foundation to pursue a career in science.

Fred Dee, Charlie Platz, Michael Cohen, and Kent Bottles were just a few of the major influences during my residency and fellowship training at Iowa.

When I came back to Iowa as a faculty member, Frank Mitros was a great mentor as well, by showing me day in and day out how true excellence in clinical service and education could coexist and thrive together, and actually were inseparable.

How or why did you choose the University of Iowa?
For me, joining the faculty, in 1999, here was coming back home.

Iowa had been home for most of my life and coming to the University of Iowa was an opportunity to connect further to the state of Iowa and give something back as well.

The University of Iowa's faculty members are united to provide exceptional patient care while advancing innovations in research and medical education.

What kinds of professional opportunities or advantages does being a faculty member at an academic medical center provide?
I enjoy being able to interact with outstanding physicians from many diverse specialties every day. In addition, interacting with and learning from students and residents enriches my practice.

Please describe your professional interests.
I am a surgical pathologist and cytopathologist. I have specific subspecialty interests in fine needle aspiration and gastrointestinal pathology.

How does working in a collaborative and comprehensive academic medical center benefit your work?
I love the opportunity to interact with experts and collaborators from across the spectrum of medical specialists. These colleagues teach me so much and enhance my practice.

Do you have an insight or philosophy that guides you in your professional work?
Although I don't meet most of my patients, I always try to think about the patient (and physician) behind each biopsy. I know that the patient and physician need the best possible information to make an informed decision about treatment and care.

If you could change one thing about the world (or the world of medicine/science), what would it be?
Equal access to quality health care seems a good place to start.

What is the biggest change you've experienced in your field since you were a student?
Perhaps the biggest change is the pace of change. Just the volume of information is one of the biggest challenges (and opportunities) for physicians today.

What one piece of advice would you give to today's students?
Choose a career or specialty because it is what you like to do or find interesting, not based on what someone else thinks will be needed in the future.

What do you see as "the future" of medicine/science?
I always say that anyone who can tell you what will happen five years from now in medicine should be treated with a great deal of skepticism. That being said, molecular diagnostics are already changing the way we think about and make diagnoses in pathology. I know that trend will continue.

In what ways are you engaged with the greater Iowa public (i.e., population-based research, mentoring high school students, sharing your leadership/expertise with organizations or causes, speaking engagements off campus, etc.)?
I see my involvement with medical students and resident education as perhaps my most important form of engagement with the citizens of Iowa.

Our role is not only to provide excellent health care but to train the next generation of physicians. I believe that some day when I look up from a bed in the emergency room, I will see one of my former students and smile because I know I am in good hands. In that way I am confident I am giving something back to Iowans.

UNIVERSITY OF IOWA
CARVER COLLEGE
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University of Iowa Health Care

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A Letter from UI Foundation

Partners in Supporting the Department of Pathology

Greetings from the University of Iowa Foundation! In my new role as director of development for the Department of Pathology, I look forward to working with committed donors to ensure the department has the financial resources necessary to develop and meet their goals. My role is something of a matchmaker—I help the department's alumni and friends align their philanthropic passions and interests with the department's needs. The result is a stronger department that is better able to improve lives, make vital discoveries, and train first-rate pathologists.

Although new to the foundation, I am quite familiar with the university and Iowa City. A native Iowan, I received my B.A. at the University of Iowa and my M.S. at the University of Kansas. Prior to joining the Iowa Foundation, I worked at Coe College in Cedar Rapids and Pennington & Company in Kansas City, Kansas.

Private support has always been important but it is nothing short of critical in today's funding environment. Hundreds of donors express their loyalty to the Department of Pathology through an annual gift. We appreciate those who have done so, and we welcome new givers to join the effort!

Other donors make larger contributions establishing an endowed fund through an outright gift or estate planning. These are the gifts that make new chairs, professorships, and funds for scholarships and research available. The foundation has several endowment opportunities available that you can arrange now, with cash and securities, or later through a will or trust. Estate gifts allow us to look ahead and plan with confidence, providing financial light for future generations

As the department's representative for the UI Foundation, I would love to hear your Iowa story and be a resource to you as you shape your philanthropic legacy. I encourage you to support the Department of Pathology by giving online at **https://www.givetoiowa.org/pathology.** If you have any questions, regarding giving opportunities or the department's needs, feel free to contact me by sending an email to anne-m-barber@uiowa.edu or calling (319) 467-3756. Thank you again for your interests in and support of the Department of Pathology.

Anne Barber

Associate Director of Development

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