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

Universal Screening for Lynch Syndrome
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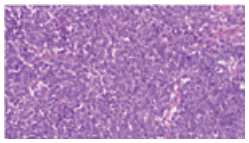

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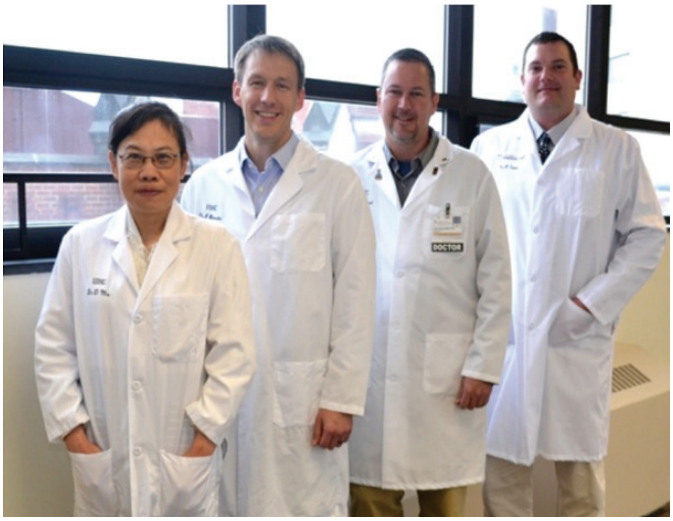
PathBeat

The Newsletter of the Department of Pathology
University of Iowa Carver College of Medicine

No. 14 Winter 2013

Laboratory Focus

Expansion of Test Development Capability – UIHC Molecular Pathology Lab



Molecular Pathology Faculty Team:
Deqin Ma, MD, PhD, Aaron Bossler, MD, PhD (Director), Jonathan Heusel, MD, PhD, and Anthony Snow, MD (Fellow)

"We are witnessing a revolution in the way we practice medicine—from what we understand about pathogenesis to how we predict, diagnose, and treat diseases. The challenge is to find that right balance between the molecular information we can collect against the information that is most beneficial to our individual patients." –Jon Heusel, MD, Ph.D., UIHC Molecular Pathologist. This is the guiding principle that drives new test development in the UIHC Molecular Pathology Laboratory.

Along with the recent addition of Dr. Deqin Ma to the Molecular Pathology (and Surgical Pathology) faculty Molecular Pathology has also hired a full-time Research Scientist, Natalya Guseva, Ph.D., to provide assistance in molecular test development.

Dr. Guseva has over 20 years experience in molecular oncology and immunology research, and has been instrumental in the validations of many molecular tests that have arrived on the Molecular Pathology testing menu over the last year (see list of recently added tests on page 6 of this issue). The Molecular Pathology Laboratory Director, Dr. Aaron Bossler, credits the entire laboratory staff led by Jon Pruessner, Lead Scientist, with a 'unified, focused effort to expand our testing while maintaining a very high degree of daily clinical testing service. These people are incredibly dedicated.'

The UIHC Molecular Pathology Laboratory has emphasized expansion of testing for targeted mutations in oncology (e.g., BRAF and KRAS mutation detection in colorectal cancer, and melanoma, quantitative BCR-ABL transcript detection for CML, CEBPA sequencing in AML, KIT sequencing for AML, melanoma and GIST, and NRAS mutation detection in melanoma) in part through ongoing dialogue with the Holden Comprehensive Cancer Center clinicians and investigators. The idea is to provide the tests that UIHC and regional Iowa physicians need most, and to assist in directing reference laboratory testing for those tests that are not provided on the current Molecular Pathology testing menu.

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University of Iowa Health Care Launches Universal Screening for Lynch Syndrome in Colorectal Cancer

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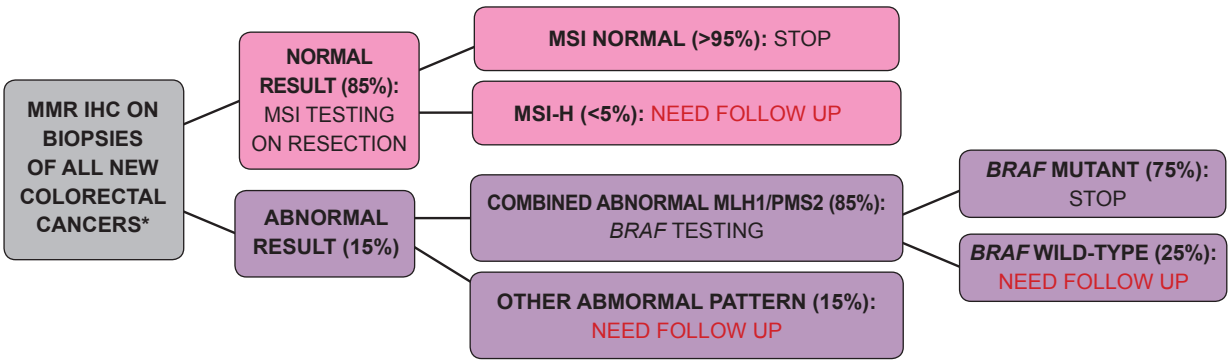
Lynch Syndrome Defined:
Lynch syndrome (LS) is the most common cause of hereditary colorectal cancer (CRC), accounting for 2-4% of all CRC. This highly penetrant autosomal dominant cancer syndrome is usually due to germline inactivating mutation in a DNA mismatch repair (MMR) gene (*MLH1, PMS2, MSH2, MSH6*), rarely due to *EPCAM* deletion, and exceptionally due to *MLH1* or *MSH2* epimutation (i.e., soma-wide, allele-specific promoter methylation). The LS phenotype is characterized by early onset CRC, increased cancer risk at a defined set of extracolonic sites (i.e., endometrium, stomach, small intestine, ovary, upper urinary tract, brain, and skin [sebaceous tumors and keratoacanthomas]), and tendency for multiple tumors. Two-thirds of LS-associated CRC's are right-sided, and tumors may demonstrate one or more characteristic histologic features including mucinous, medullary, or signet-ring-cell differentiation; a prominent tumor-associated lymphoid response; and a pushing tumor front.

DNA Mismatch Repair and Microsatellite Instability:
The DNA MMR apparatus recognizes and repairs mispaired bases and insertion-deletion loops. Cancers in LS are associated with silencing of the wild-type allele, resulting in loss of expression of one or more of the mismatch repair proteins (see Image). Immunostains for MLH1, PMS2, MSH2, and MSH6 are commercially available, and MMR immunohistochemistry (IHC) has been shown to detect >90% of LS-associated CRC's. Microsatellites are simple repetitive DNA sequences scattered throughout the genome. During DNA replication they are especially apt to form the insertion-deletion loops normally repaired by an intact DNA MMR apparatus. Microsatellite instability (MSI) is thus a phenotypic consequence of deficient MMR (dMMR) function, and polymerase-chain-reaction-based MSI testing is similarly sensitive in detecting LS.

Clinical Relevance:
Patients with CRC in whom LS is diagnosed may be counseled to undergo a subtotal colectomy (as the risk of a second CRC in these patients is as high as 40%), and mutation-positive individuals benefit from intensive colonoscopic surveillance. They may also be entered into surveillance for other LS-associated tumors, especially endometrial and urothelial cancer.

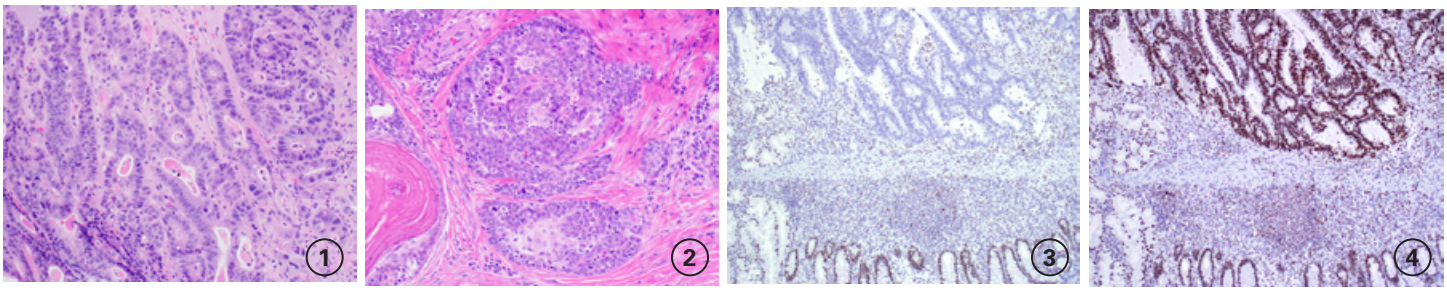
Testing Strategies:
A variety of approaches to identify potential LS cancers have been employed, ranging in intensity from passive strategies (i.e., relying on clinicians to request testing) to universal ones (i.e., testing all CRC's). Other strategies take advantage of the characteristic clinical and/or pathologic features of LS-associated tumors. Unfortunately, the most widely publicized clinical criteria, the revised Bethesda guidelines and the Amsterdam criteria II, are relatively insensitive in population-based screening. There is increasing momentum for universal screening, which has been officially endorsed by the Evaluation of Genomic Applications in Practice and Prevention Working Group and the Association for Molecular Pathology. Universal screening has been shown to have an incremental cost-

Figure. Iowa Lynch Syndrome Screening Algorithm in Colorectal Cancer



Key: MMR IHC, mismatch repair protein immunohistochemistry; MSI, microsatellite instability; MSI-H, high-level microsatellite instability

**If clinically compelling, may refer to Cancer Genetics at any point in algorithm*



Mismatch Repair Protein Immunohistochemistry in Lynch–Associated Neoplasms
(Image 1) Duodenal cancer detected in the follow up of a patient with (Image 2) sebaceous carcinoma (hematoxylin-and-eosin, each 200x). The patient had a colectomy 17-years prior for colon cancer, and there was a strong family history of colon cancer. (Image 3) Absent MSH2 (and MSH6) expression in the associated duodenal adenoma, with intact expression in stroma, a lymphoid aggregate, and non-neoplastic crypts and Brunner glands; (Image 4) Intact MLH1 (and PMS2) expression (immunoperoxidase, each 100x). This pattern of expression is most in keeping with Lynch syndrome (LS) due to a *MSH2* mutation. The occurrence of sebaceous neoplasms in LS is referred to as Muir-Torre syndrome.

effectiveness ratio on the order of that seen with screening colonoscopy for CRC. MMR IHC and MSI testing, either alone or in combination, may be employed in LS screening.

Sporadic Tumors with dMMR Function:
Fifteen (15) % of CRC's are characterized by transcriptional silencing of *MLH1* due to acquired promoter methylation. These tumors are also identified by MMR IHC or MSI testing. It is advantageous to identify this larger group of tumors because dMMR function is prognostically favorable and is associated with reduced sensitivity to 5-fluorouracil-based chemotherapy. Given these facts, medical oncologists are increasingly using the results of MMR IHC and/or MSI testing to help decide whether to recommend adjuvant chemotherapy in patients with stage II CRC. Additional testing is useful in separating sporadic dMMR tumors from LS-associated ones. Up to three-quarters of sporadic dMMR CRC's have a *BRAFV600E* mutation, which essentially does not occur in *MLH1*-associated LS. *MLH1* promoter methylation testing may also be used.

University of Iowa Health Care Testing Algorithm:
There was support for LS screening in CRC from Gastroenterology, Surgery, Medical Oncology, and Cancer Genetics, represented at the Holden Comprehensive Cancer Center Colorectal Cancer Tumor Board. Given reasonable cost-effectiveness, a strong desire to detect as many LS patients as possible, and the added benefit of identifying additional sporadic dMMR tumors, a universal screening strategy was adopted (see Figure). MMR IHC, with the advantages of rapid turnaround time and ready application in biopsy material (without the need for matched normal DNA), was selected as the first screening test. Most tumors (~85%) have normal MMR protein expression. To maximize the sensitivity of LS detection, in these cases MSI testing is performed on a resection specimen. Very rare MSI-H tumors with preceding normal MMR IHC are likely LS due to a missense mutation in a MMR gene that silences MMR function without altering protein expression. Approximately 15% of tumors will have an abnormal MMR IHC result. Usually, this is absent expression of MLH1 and PMS2. In these cases *BRAF* mutation testing is pursued to distinguish sporadic dMMR tumors from LS. *BRAF* wild-type tumors require follow up (*MLH1* promoter methylation testing and/or referral to Cancer Genetics). Tumors with other patterns of abnormal protein expression (isolated absence of MSH6 or PMS2 or combined absence of MSH2/MSH6) are likely due to LS and need referral to Cancer Genetics.

Additional Applications:
The lifetime risk of endometrial cancer (EC) in women with LS is similar to the CRC risk. As such, there is surging interest in screening EC's for LS. The National Comprehensive Cancer Network clinical practice guideline for uterine neoplasms recommends consideration of LS screening in EC patients <55-years-old, although the median age of patients detected in population-based screening is 60-years-old. Pathology and Gynecologic Oncology at Iowa are currently working together to develop the best screening strategy for our patient population. MMR IHC is fairly sensitive (~67%) and highly specific for identifying LS in colorectal adenomas. Screening for LS is also reasonable in other Lynch-associated tumors (e.g., sebaceous neoplasms, small intestinal cancers), especially in cases with a suspicious family history in which a CRC or EC is not available for testing.

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Merkel Cell Carcinoma is Caused by a Polyomavirus, Which can be Detected by Routine Immunohistochemistry

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Clinical Background:
Merkel cell carcinoma (MCC) is the designation for primary high-grade neuroendocrine carcinoma (HGNEC) of the skin. It is a clinically aggressive tumor with 33-50% mortality at 5-years. 1600 cases are diagnosed in the United States annually, a 400% rise over the last 25 years (attributed to improved disease recognition and to an aging population that is more frequently immune suppressed). The diagnosis of MCC is often clinically delayed. In an attempt to improve diagnosis, Heath and colleagues analyzed the clinical features in 195 MCC's.(1) They coined the acronym AEIOU, which captures the disease's key presenting features: Asymptomatic (i.e., non-tender), seen in 88%; Enlarging rapidly, 63%; Immunosuppression (chronic lymphocytic leukemia, transplant, HIV), 8%; Older than 50, 90%, and UV-exposed areas, 81%. Also of note, 98% of patients were white. In addition to surgery, sentinel lymph node biopsy and radiation are often important components of patient treatment. Chemotherapy is reserved for patients with high-stage disease, and it is not especially effective.

Historical Background:
In 1972 Cyril Toker reported 5 cases of "trabecular carcinoma of the skin."(2) Patients had a median age of 65, and tumors had been noted for 3 months to 2 years before biopsy. Two patients experienced local recurrences, 3 had nodal metastases, and 1 died of disease. Three cases had originally been diagnosed as "cutaneous metastases from anaplastic visceral cancers." Toker subsequently reported the presence of neurosecretory granules seen on electron microscopy in these tumors and suggested a relationship with Merkel cells (mechanoreceptors within the epidermis). "Merkel cell carcinoma" entered the lexicon in 1980. In 1985 Moll and Franke identified the protein that would soon come to be known as cytokeratin 20, which in addition to being expressed by intestinal epithelium was found in 9 of 9 MCC's and 0 of 17 pulmonary neuroendocrine tumors (NET's).(3)

Histologic Features:
MCC is a dermal-based tumor that is generally recognizable on the H&E as a HGNEC. Some cases resemble small cell carcinoma of the lung but tumors are especially apt to show "intermediate cell" morphology (i.e., slightly larger cell size, more open chromatin, inconspicuous but identifiable nuclei) (see Image 1). Most cases are pure NEC's but around 5% are "combined" with another non-melanoma skin tumor (i.e., overlying actinic keratosis or squamous cell carcinoma [SCC] in situ; admixed with SCC or basal cell carcinoma; or with intratumoral squamous differentiation) (see Image 2). The principal differential diagnosis is cutaneous metastasis from a visceral HGNEC, especially from lung, and diagnosis can be difficult in crushed small biopsies (where a distinction from lymphoma, for example, can be challenging).

Immunohistochemical Features:
Routine immunohistochemistry (IHC) is helpful on both of these fronts. MCC's mark with antibodies to broad spectrum keratins and general neuroendocrine markers. In addition, approximately 95% of tumors express CK20, which is often perinuclear/dot-like (see Image 3). TTF-1 expression in MCC is seen in less than 1% of cases. Pulmonary HGNEC's, on the other hand, are nearly always TTF-1-positive/CK20-negative. There is very little data on the immunophenotype of non-pulmonary, visceral HGNEC's, although primary parotid HGNEC's are known to often express CK20 (60-80%), while HGNEC's of the uterine cervix occasionally do (10-20%). CK20 expression by non-MCC HGNEC's and CK20-negative MCC's are challenges, and additional diagnostically useful immunostains would be welcome.

Merkel Cell Polyomavirus Causes Merkel Cell Carcinoma:
In 1994 Drs. Yuan Chang and Patrick Moore identified a herpesvirus (human herpesvirus 8; Kaposi-sarcoma-associated herpesvirus) in Kaposi sarcoma. They hypothesized that MCC, a tumor that typically affects the elderly and with a very large relative risk in the immune suppressed, would also be associated with an oncovirus. Utilizing a technique they termed "digital transcriptome subtraction" in which they sequenced cDNA libraries constructed from 4 tumors, aligned the resulting sequences against NCBI human genome reference sequences, and searched for an infectious agent among the rare non-aligned sequences, they discovered a single sequence with high homology to the large T (LT) antigen of monkey and human polyomaviruses.(4) They subsequently identified the virus, which they termed Merkel Cell Polyomavirus (MCPyV), by polymerase chain reaction (PCR) in 8 of 10 (80%) MCC's and only 9 of 84 (11%) control tissues. In tumor samples, MCPyV was clonally integrated into host DNA. The group next demonstrated a characteristic mutation pattern in the LT antigen of the integrated virus, which abolished the virus's ability to productively replicate (and thus destroy the host cell) without affecting the oncogenic properties of its RB-binding domain.(5) Since the initial description, MCPyV has been detected by PCR in MCC by ~20 groups in ~600 tumors,

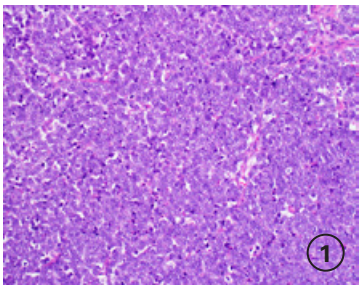

Image 1. Merkel cell carcinoma (MCC): high-grade neuroendocrine carcinoma with "intermediate cell" differentiation.

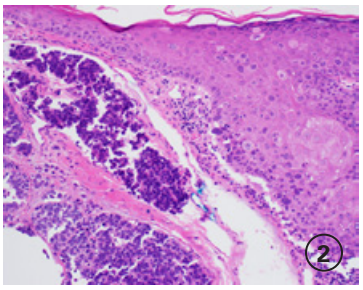

Image 2. "Combined" MCC: MCC associated with overlying squamous cell carcinoma in situ

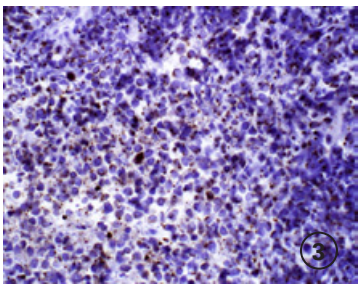

Image 3. Typical CK20 perinuclear/dot-like expression in MCC

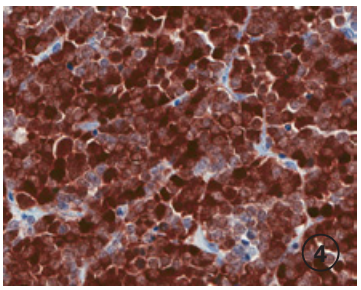

Image 4. Large T antigen expression in MCC detected by Ab3 immunohisto-chemistry

generally in the 80% range reported by Chang and Moore. A notable outlier was a group of Australian tumors, in which virus was detected in only 5 of 21 (24%).(6)

Epidemiology of Merkel Cell Polyomavirus:

About 60% of the population demonstrates MCPyV seropositivity. Schowalter et al were able to detect full-length, wild-type MCPyV genomes from skin swabs of 14 of 35 (40%) healthy adult volunteers.(7) Infection is believed to be asymptomatic. Although MCPyV is prevalent in the population, MCC is rare because it requires both clonal integration of the virus and the characteristic mutation in the LT antigen described above.

Merkel Cell Polyomavirus Immunohistochemistry:

In an effort to lend additional support to the etiopathogenic role of MCPyV in MCC, Chang and Moore's group developed a monoclonal antibody (MoAb) to the virus's LT antigen (clone CM2B4).(8) They detected LT protein expression in 21 of 30 (70%) CK20-positve MCC's and 0 of 4 pulmonary HGNEC's, 0 of 142 hematolymphoid neoplasms, and 0 of 31 non-neoplastic lymphoid tissues. Similar to the MCPyV PCR data, LT antigen has been detected by CM2B4 IHC in ~80% of MCC's. Interestingly, the few dozen "combined" MCC's tested to date have been uniformly negative. Other skin cancers are also negative, and other HGNEC's, including 7 primary parotid tumors, have been negative in most groups' hands. Again, a cohort of Australian tumors is the outlier, with Paik and colleagues reporting LT antigen expression in 19 of 89 (21%) MCC's.(9) The CM2B4 antibody is commercially available from Santa Cruz Biotechnology (Santa Cruz, CA).

A New Monoclonal Antibody Improves Detection of Merkel Cell Polyomavirus:

I recently had the opportunity to participate in the evaluation of a new monoclonal antibody to the LT antigen of MCPyV. This project intersected with my interests in gastrointestinal (GI) neoplasia, NET's, and diagnostic IHC. The antibody Ab3, raised against the N-terminal 260 residues of LT, was produced in the MoAb core facility of the Dana-Farber Cancer Institute, directed by my former colleague James DeCaprio. Dr. DeCaprio is a virologist whose laboratory focuses on the polyomavirus SV40. He hypothesized that >80% of MCC's are caused by MCPyV and that a better MoAb would improve the detection rate. While LT antigen expression as detected by CM2B4 was found in 81% (46/57) of MCC's, the rate of positivity with Ab3 was 97% (56/58) (see Image 4).(10) Ab3 IHC was negative in 10 GI HGNEC's, 8 small cell lung cancers, and 7 non-neoplastic lymphoid tissues. Interestingly, *TP53* mutations were detected in both Ab3-negative MCC's.

Summary:

MCC is an aggressive neuroendocrine skin tumor, increasing in incidence. Most cases are associated with MCPyV, which is clonally integrated and contains LT antigen truncating mutations. MCPyV LT antigen can be detected by IHC, which may be useful to confirm the diagnosis of MCC in rare CK20-negative tumors and to either confirm or argue against the diagnosis in CK20-positive tumors in which a non-MCC HGNEC is a reasonable possibility. Using the new MoAb Ab3, LT antigen expression was found in 97% of 58 MCC's. It will be interesting to see the results of Ab3 staining in Australian cases, which up to now appear to largely represent a closely related but distinct tumor type.

Finally, there are likely other tumors or inflammations out there just waiting to be "solved" with pathogen discovery by genomic subtraction.

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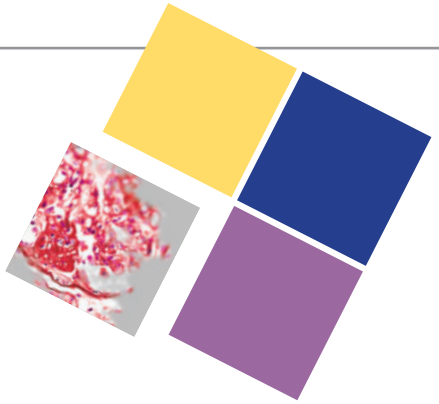

UIDL Corner

Test Updates

UIDL
UI Diagnostic Laboratories

1-866-844-2522

Please visit our website and test directory for more detailed test information and to download forms at:
www.healthcare.uiowa.edu/uidl

NEW: ALK FISH

The Vysis ALK Break Apart FISH is a qualitative test to detect rearrangements involving the ALK gene via fluorescence in situ hybridization (FISH) in non-small cell lung cancer tissue specimens to aid in identifying those patients eligible for treatment with XALKORI® (crizotinib).

NEW: BCR/ABL Quantitative

The BCR/ABL gene rearrangement is observed in CML, ALL, and, rarely, AML. A positive result indicates the presence of the Philadelphia chromosome, but the diagnosis of CML or ALL should be based on the presence of characteristic cellular abnormalities in bone marrow. In patients with ALL, the BCR/ABL rearrangement is associated with poor prognosis. Serial monitoring of assay values may provide a quantitative measure of tumor burden and response to therapy. Increasing levels of BCR/ABL are associated with clinical progression. Testing is performed on RNA from peripheral blood or bone marrow specimens using real time PCR. Results are calibrated and reported relative to the WHO International Standard as the percent international standard or %IS.

NEW: CEBPA Mutation Analysis

Somatic mutations of CEBPA are among the most common in acute myelogenous leukemia ranging from 5-14% of cases particularly in the former FAB M1 and M2 subtypes. Along with having a normal karyotype, the majority of CEBPA-mutated cases have two distinct CEPBA mutations affecting different functional domains of the protein. In the absence of other unfavorable mutations that mitigate CEBPA double-mutations, there is an associated favorable prognosis as measured by overall and disease-free survival.

NEW: Dysferlin Gene Sequence Analysis

Mutations in the dysferlin gene (DYSF) on chromosome 2p13, are at the origin of dysferlinopathies, a heterogeneous group of rare autosomal recessive inherited neuromuscular disorders. The main clinical presentations are the distal-onset muscular dystrophy called Miyoshi myopathy and the proximal-onset form LGMD2B, both characterized by progressive muscle weakness, usually appearing in the second decade, and highly elevated serum creatine kinase (CK) levels. Mutational analysis of DYSF is complicated by the large mutational spectrum and a high proportion of "private" mutations, with the recurrent difficulty of interpreting novel DYSF sequence variants, in particular putative splicing and missense variants.

The 55 coding exons and the flanking intronic regions of the DYSF gene are amplified by PCR and sequenced in both directions. The reference sequence with which patient sequences are compared is NM_003494.3 (in some case with alternative exons HGVS recommended).

NEW: Epstein Barr Virus (EBV) by Quantitative PCR

This test is intended for use in conjunction with clinical presentation and other laboratory markers as an indication of an EBV-related tumor. This test is also used as an aid in accessing viral response to treatment as measured by changes in EBV DNA levels. Testing is performed using real time PCR. Results are calibrated to the WHO International Standard and will be reported in international units (IU)/ml and the log transformed values. EBV PCR should not be used to diagnose or confirm primary or reactivated mononucleosis; serology should be requested for those situations.

NEW: Hepatitis E Virus PCR

Hepatitis E virus (HEV) causes sporadic and epidemic forms of acute hepatitis. It is responsible for waterborne hepatitis epidemics in developing countries, while in the United States, it is usually diagnosed in recent travelers to endemic areas (India, Asia, Africa, and Central America). It can infect animals, and pigs are an important reservoir. One clinical concern is the development of chronic HEV infection in solid organ transplant patients. Hepatitis E IgG antibodies can be detected particularly during the acute phase, but in most patients IgG antibodies are short lived. Molecular testing for the viral RNA may be used if there is concern for chronic HEV infection.

NEW: KIT Mutation Analysis (GIST and melanoma)

The principle use of this test is to detect mutations in patients with gastrointestinal stromal tumor (GIST) and melanoma. For acute myeloid leukemia (AML) testing, please order KITAML Mutation Analysis (LAB7659). This test is not intended to detect D816 mutation in bone marrow for mast cell disease or minimal residual disease, see KITMAST Mast Cell Disease (LAB7567).

NEW: KIT AML Mutation Analysis

KIT (also known as c-KIT) belongs to a family of type III receptor tyrosine kinases. Activating KIT mutations are seen in 70–80% of gastrointestinal stromal tumors (GISTs), ~95% mastocytosis, 25% germ cell tumor, 2% melanoma and a subset of acute myeloid leukemia (AML). The location and type of KIT mutations are associated with prognosis and response to imatinib therapy.

Testing of KIT mutations can be utilized:
1. To assist in diagnosis of GIST, melanoma and AML.
2. To assist in therapy selection for GIST and melanoma.
3. To assist in prognosis of GIST and AML.

KIT AML Mutation Analysis detected exons related to patients with AML. If patient has GIST or melanoma, order KIT Mutation Analysis (LAB7660). This is a sequence-based assay. This test is not intended to detect D816 mutation in bone marrow for mast cell disease or minimal residual disease (see KIT Mutation (D816V) Mast Cell Disease (LAB7567).

NEW: KIT Mutation (D816V) MAST Cell Disease

Activating point mutations at codon 816 in the KIT receptor tyrosine kinase are seen in the majority of patients with systemic mast cell disease and can help in diagnosis of this disorder.

NEW: ISPD (Isoprenoid synthase domain containing)

Mutations in the isoprenoid synthase domain containing (ISPD) gene (HGNC 37276) have been shown recently to cause Walker-Warburg syndrome (WWS). WWS is characterized by congenital muscular dystrophy, hydrocephalus, agyria, retinal dysplasia, with or without encephalocele.

NEW: MatBA® – CLL Array – CGH Assay

Loss of specific chromosomal loci is associated with prognostic information for CLL patients. MatBa–CLL Array–CGH Assay provides for a more comprehensive panel of chromosomal loci information not available in a single test.

NEW: NRAS Mutational Analysis

The presence of an oncogenic mutation in codons 12, 13, or 61 of NRAS is indicative of a tumor that may respond to drugs targeted at genes downstream of NRAS in the mitogen activating protein kinase (MAPK) signaling cascade, as in malignant melanoma cases. In contrast, mutations in NRAS can inhibit therapeutic response to EGFR-targeted therapies in patients with metastatic colorectal cancer. NRAS mutations are found in the more aggressive variant of chronic myelogenous leukemia (CMML) and may predict response to farnesyl transferase inhibitors therapy in acute myeloid leukemia (AML).

Faculty
RESEARCH PUBLICATIONS

Evaluation of the Bruker Biotyper and Vitek MS matrix-assisted laser desorption ionization-time of flight mass spectrometry systems for identification of nonfermenting gram-negative bacilli isolated from cultures from cystic fibrosis patients.
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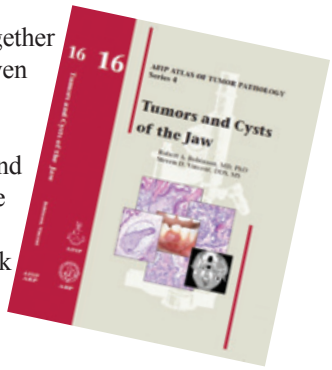
Robert A. Robinson, MD, PhD Publishes 2nd Pathology Textbook

Robert Robinson, MD, PhD

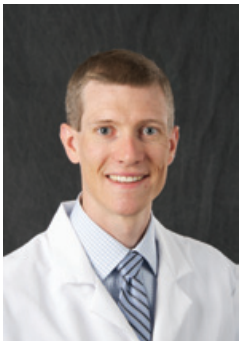
Dr. Robert A. Robinson, Professor of Pathology and Oral Pathology, Radiology and Medicine, and Medical Director of the University of Iowa Diagnostic Laboratories has co-authored a second textbook "AFIP ATLAS of TUMOR PATHOLOGY Series 4: Tumors and Cysts of the Jaw".



Authored together with Dr. Steven Vincent, Department Head of Oral Pathology, Radiology and Medicine, University of Iowa College of Dentistry, this book follows Dr. Robinson's first book "Head and Neck Pathology: Atlas for Histologic and Cytologic Diagnosis".

New Faculty Join Our Team

Please join us in welcoming our two newest faculty members **Dr. Bradley Ford**, Clinical Assistant Professor, Associate Director of Microbiology and **Dr. Megan Samuelson**, Clinical Assistant Professor, Surgical Pathology and Cytopathology, Subspecialty – Obstetrics and Gynecologic Pathology. We are very pleased to have them join our team in serving the physicians and patients of UIHC as well as our UI Diagnostic Laboratories outreach clients.



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Outstanding Educator Award 2012

Congratulations to **Dr. Krasowski** for his recent receipt of the 2012 Carver College of Medicine, Department of Pathology, Outstanding Educator Award. Dr. Krasowski received this award due to his significant contributions to medical student education during the past year. Dr. Barry Deyoung, Interim Department Head, comments on Dr. Krasowski's award:

Matthew Krasowski, MD, PhD
Clinical Associate Professor of Pathology

Dr. Krasowski has significantly contributed to medical student education at the Carver College of Medicine. He serves as the clerkship director for the "Laboratory Medicine in Clinical Practice" (for M3 and M4 students) which not only involves approximately 50 hours of direct student contact, but also significant administrative work.

He has led a major overhaul of this course with significant improvement in student evaluations. He also lectures to M2 medical students in the Medical Pathology course. In addition, in the past year, he served on one of the Mechanisms of Health and Disease (MOHD) work groups for the curriculum revision process. He is a constant advocate for medical student education and an excellent role model in this regard."

USCAP 2012 Features UI Department of Pathology

The University of Iowa Department of Pathology was featured in a video presentation at the 2012 United States & Canadian Academy of Pathology (USCAP) meeting held in March in Vancouver. The five-minute video was part of USCAP-TV, an innovative initiative to raise the visibility of best practices in the field. Our feature video entitled "Balanced Leadership – University of Iowa Pathology" can be viewed online on YouTube.

Expansion of Test Development Capability

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The lab also develops new tests in the areas of genetics and infectious disease, such as ISPD and DYSF gene sequencing for patients with suspected inherited neuromuscular disease, and a qualitative PCR test for hepatitis E virus (HEV). Details about these and other molecular tests now available are provided in this issue. More new tests are in development—stay tuned.

George D. Penick Award Presented to Outstanding Pathology Residents

The George D. Penick Award for Excellence in Education had two recipients in 2012: **Michael Gailey, DO** and **John Blau, MD**. The Penick award is given annually to a pathology resident who displays excellence in and commitment to the education and teaching of medical students, peers and clinical colleagues.

The awards were presented to Dr. Gailey and Dr. Blau by Leslie Bruch, MD, Vice Chair of Educational Affairs.

John Blau, MD and Leslie Bruch, MD

Michael Gailey, DO and Leslie Bruch, MD

2012-2013 Co-Chief Residents Selected

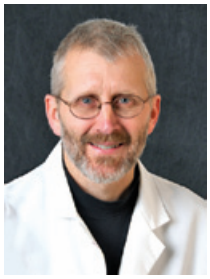
Congratulations are extended to the 2012-2013 Co-Chief Residents: **Bryan Steussy, MD** and **Thomas Wilson, MD**. A special thank you goes to Drs. Michael Gailey and Joel Miron for serving as the 2011-2012 Co-Chief Residents.

Resident Teaching Award 2012

The 2012 recipient of the Resident Teaching Award is **Frank Mitros, MD**. This award is given each year to a faculty member in the Department of Pathology who displays exemplary teaching and mentoring skills while working with the residents. Bryan Steussy presented Dr. Mitros an award certificate at the Farewell Dinner for Pathology Residents and Fellows held on June 8, 2012. His name will also be added to the teaching award plaque displayed in Pathology Administration.

Pictured: Dr. Frank Mitros, Dr. Bryan Steussy.

RESIDENCY LEADERS



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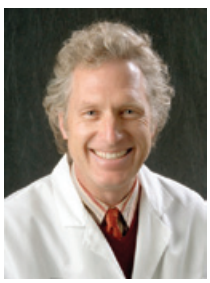

Assistant Residency Program Director
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For more information about our residency program, please contact:

Pathology Residency Coordinator
Janet Delwiche, MA
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UNIVERSITY OF IOWA
CARVER COLLEGE
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A Letter from UI Foundation

Partners in Supporting the Department of Pathology

It has almost been over 2 years since my appointment as the Development Officer for the Department of Pathology. I have had the pleasure of meeting many engaging faculty, staff, alumni and friends of the department and I have discovered a common thread they all share, a thread that is simply referred to as "the Iowa way." Whether it was a kind welcome, a dedicated faulty member or help in the lab, the Iowa way makes you feel like you are always in the right place and among friends. There are many more stories to be told and memories to be revisited. I welcome the opportunity to have you share with me your personal experience with "the Iowa Way."

As you start to prioritize your year-end donations, or think about your future ones, please consider supporting the UI Department of Pathology. Private support is as important as ever right now. What areas would be most meaningful for you to support? Is it the brilliant, young students? Cutting edge research or dedicated faculty? Dedicated faculty?

Below are some of the most common ways you can support the UI Department of Pathology, often while realizing tax benefits. No matter how – or how much – you give, your generosity will make a difference in the lives and work of UI students, educators, and all whom the University serves.

Annual Giving – Ongoing, sustaining gifts that enable UI areas to embrace opportunities and meet challenges

Planned Giving – Gifts carefully planned to help you meet your philanthropic and financial goals

Corporate and Foundation Relations - Relationships with corporations and foundations that result in philanthropic benefit for The University of Iowa

Matching Gifts – A way to multiply your generosity through your employer's matching gift program

Honorary and Memorial Gifts – Honoring someone special with a gift supporting the UI

Stock Gifts – Supporting the UI with gifts of appreciated stocks and mutual funds

Cash gifts – Outright gifts made via cash, check, credit card, or other means

Real and personal property – Real estate and marketable items of personal property

Online giving – Gifts made through www.givetoiowa.org

To learn more about The University of Iowa Foundation, and how gifts from alumni and friends support students and faculty in the UI Department of Pathology, please visit www.uifoundation.org or contact me at shelly-mott@uiowa.edu, (319) 467-3668 or toll-free 800-648-6973.

Shelly J. Mott
Director of Development, Roy J. and Lucille A. Carver College of Medicine/ University of Iowa Hospitals and Clinics, The University of Iowa Foundation

No matter how or how much you give, your generosity will make a difference...