Implementing whole slide imaging in surgical pathology

By Thomas W. Bauer, MD, PhD, Renee J. Slaw and A. Scott Mackie

Only a few years ago the term “digital pathology” implied a static snapshot obtained from a digital camera mounted on a conventional microscope, and “telepathology” implied remotely viewing a microscope slide via an analog camera. Technological advances now allow high resolution scanning of whole microscope slides (“whole slide images” or WSI) and the use of secure web-based viewing applications can link those images to clinical information to facilitate remote interpretation on a computer monitor.

These technological advances have been paralleled by an increasing demand for digital pathology information in general throughout health care networks with the expectation by some for eventual integration of digital pathology images and information with the laboratory information system and electronic medical record. The use of WSI for interpreting routine surgical pathology cases (primary interpretation) is currently neither cost effective nor FDA-approved, but the technology offers an immediate opportunity for the remote interpretation of surgical pathology consultation cases (secondary interpretation) and frozen sections. It also holds promise as a way of improving workload distribution and automated image analysis, but implementing digital pathology for cost-effective patient care requires careful attention to work flow, validation, security and recognition of its limitations.

In 2010, in anticipation of an increasingly important role of digital imaging in pathology, Walter Henricks, MD, and the administration of the Robert J. Tomsich Pathology & Laboratory Medicine Institute (RT-PLMI) established a section of “ePathology” within the Department of Anatomic Pathology. The section was initially supported by a single, high-resolution scanner and an associated server (Fig. 1).

Figure 1: Diagram of ePathology infrastructure in 2009.
Early activities focused on education and research, leading to the development of a Digital Education Library (DEL) that now consists of more than 4,000 images. In the past year images from the DEL have been distributed to 15 residents and fellows, and have been used to support 21 internal and 22 external educational conferences. In addition, changing from glass to digital “recuts” has saved patient tissue for future testing and clinical trials.

One of the most obvious attributes of digital pathology is to facilitate the interpretation of surgical pathology cases at a distance. This has the potential of helping distribute workload within a complicated health care system, as well as the ability to provide subspecialty pathology interpretations to regions of the world that currently lack optimal pathology services. With those long-term goals in mind, we started by validating the use of WSI for optimal pathology services. With those long-term goals interpretations to regions of the world that currently lack well as the ability to provide subspecialty pathology workload within a complicated health care system, as at a distance. This has the potential of helping distribute

Our ePathology infrastructure has evolved significantly to support these activities (Fig. 2). As an overview, the digital slide system runs on an HP ProLiant DL360 GL7 Windows 2008 server with 2 quad core xenon E5620 processors and 16 GB RAM. This platform hosts eSlideManager (Leica Biosystems) software that performs the function of web server (user access), database server (SQL), image server and application server for the web-based SQL viewer.

Digital slides are captured on Aperio AT Turbo scanners, capable of 20x and 40x magnification scanning at resolutions of 49um and 24um, respectively, with a load capacity of 400 slides. Images are stored in a proprietary format and viewed via a “bits on demand” type stream, similar to Google Earth. Barcoded slides are interfaced with and accessible from the Anatomic Pathology Laboratory Information System (LIS), CoPath, and case and demographics are populated. Typical 20x images range in size from 350 to 700mb per slide; 40x images can be as large as 2.4Gb. Images are streamed using a 1Gb local network and stored on an EMC VNX5400 network attached storage array (NAS) at the Cleveland Clinic datacenter offsite and backed up to a mirrored file system. Additionally, slides may be captured at 60x or 100x on an Olympus VS-120 scanner. These slides are converted and imported into the Aperio eSlideManager for general use. We currently have 59,000 individual images that occupy...

![Diagram of ePathology infrastructure in 2015. See text for details and abbreviations.](image-url)
a total of 18 terabytes storage. In addition to the NAS located offsite, older images are stored on an Isilon storage area network (SAN) array. Smaller subsets of images can be downloaded to portable hard drives, primarily for resident and fellow educational use.

Outside consult cases are obtained via two cloud-based platforms; one offshore, one domestic. The system provides email notification and workflow management between main campus and our international clients. Additional in-network consultations (Weston and Abu Dhabi) and eventually frozen section interpretation (affiliated regional hospitals and ambulatory surgery centers – Fig. 3) will be performed by directly accessing eSlideManager. Users log into a web front end that controls access to the database. Access to whole slide images is controlled by individual or group permissions that are configured by the ePathology Manager. Slides are organized into cases, courses and research projects within the application database.

Tissue Microarray (TMA) and image analysis algorithms are supported, and access to the system for authenticated users outside the Cleveland Clinic firewall is provided through a Bluecoat reverse proxy. This allows off-site pathologists to temporarily view a designated subset of images. For example, if a Cleveland Clinic pathologist is giving an invited lecture on soft tissue tumors, then WSI of unknown cases can be made available to conference participants before and after the conference, no matter where the lecture takes place.

The FDA has not yet approved the use of WSI for primary diagnosis in the United States, but several manufacturers have clinical studies under way and hope to achieve clearance in the relatively near future. Already used for primary diagnosis in Europe and Canada, we hope Cleveland Clinic will be well positioned to utilize digital pathology in a cost-effective way for primary diagnosis of selected types of cases once it is cleared by FDA, and we anticipate continued growth of digital pathology for consultation cases as well as for education and research.

References:
About the Authors

**Thomas W. Bauer, MD, PhD**

Dr. Bauer has been a pathologist at Cleveland Clinic since 1983. He specializes in orthopaedic pathology, especially biomaterials, and in that context has published more than 235 peer-reviewed publications and 32 book chapters. He is the Deputy Editor for Research for the *Journal of Bone and Joint Surgery*, the co-editor-in-chief of *JBJS Case Connector*, has been a consultant to orthopaedic device manufacturers, and is a frequent speaker at orthopaedic and biomedical engineering meetings. He has been the Medical Director for the Center for ePathology since 2011, and along with a highly capable team of scanning technologists, managerial and IT specialists, has helped validate the use of digital whole slide images for patient care, research and education. Dr. Bauer is a member of the Digital Pathology Advisory Committee to the College of American Pathologists and one of his publications concerning validation is currently promoted by the FDA as a template for future similar studies. In his spare time during the last 10 years he has completed more than 40 marathon races, five 50K races, six 50-mile and nine 100-mile ultramarathons. Dr. Bauer can be reached at bauert@ccf.org or 216.444.6830.

**Renee J. Slaw**

Renee Slaw currently serves as the Manager of ePathology (Digital Pathology). She received her BA in Biology from Wittenberg University and her MBA at Cleveland State University. Ms. Slaw has worked in a laboratory setting for 25 years and has been at Cleveland Clinic for eight years. She has been responsible for the development of the ePathology Department, coordinating multiple validations, and managing education sessions and partnerships with other institutions involved with digital pathology. She has co-authored three peer-reviewed publications and has been a member of American College of Healthcare Executives (ACHE) for eight years. Ms. Slaw can be reached at slawr@ccf.org or 216.445.8739.

**A. Scott Mackie**

A. Scott Mackie studied computer science and electronics at Cuyahoga Community College and Hickock Technical Institute. He is currently a technical specialist embedded in the ePathology Department in the Center for Pathology Informatics at Cleveland Clinic. He has been involved with the evaluation, implementation and support of telepathology and pathology imaging systems since 2001. Prior to joining Cleveland Clinic in 1999 he was a quality control manager in a manufacturing environment and involved in ISO 9000 implementation. Mr. Mackie can be reached at mackies@ccf.org or 216.445.9990.
Celiac Review Update

By Thomas Daly, MD

Background
Celiac disease is one of the most common autoimmune diseases, with an estimated prevalence of roughly 1% in the United States and Europe. The disease is characterized by an autoimmune response to gluten, a protein commonly found in wheat and related grains. Exposure to this antigen in sensitive patients can lead to progressive villous atrophy in the small bowel, resulting in malabsorption. A wide spectrum of gastrointestinal (GI) symptoms can be associated with celiac disease, including diarrhea and abdominal pain. Systemic findings such as iron deficiency anemia and fatigue can also occur in patients with active disease. Accurate recognition and diagnosis of celiac disease can be challenging because of the non-specific nature of many symptoms, but is important because the implementation of a gluten-free diet can ameliorate many of these findings. If left untreated, celiac disease can be associated with increased mortality in adult life from a range of causes, including autoimmune diseases and malignancy.

Testing
Laboratory testing for the workup of celiac disease can be broadly divided into two categories: serologic assays that measure autoantibodies directed against various disease-associated antigens, and genotyping assays of the HLA-DQ locus to identify variants known to be associated with celiac disease. Serologic assays are classified by the target of the autoantibody and the immunoglobulin isotype. The most widely used serologic assays target IgA autoantibodies against tissue transglutaminase (TTG), deamidated gliadin (dGDN) or endomysial tissue (EMA). IgG versions are also available for use in IgA-deficient patients (a disorder often associated with celiac disease). TTG and dGDN assays are routinely measured using immunassay techniques that provide semi-quantitative results, while EMA testing is done using immunofluorescence analysis on slides containing endomysial tissue. The diagnostic characteristics of celiac serology tests have been well described in many populations, and have shown analytical performance sufficient for use as a screening test. In general, tTG-IgA and EMA-IgA assays have shown the best diagnostic performance in most studies, with pooled sensitivities of 89-90% and specificities of 98-99% in a recent systematic review of the literature.

HLA-DQ haplotype analysis can also be used in the diagnostic workup of celiac disease. The HLA-DQ2 and/or HLA–DQ8 haplotypes are found in the vast majority of patients with confirmed celiac disease. However, these haplotypes are also present in a large percentage of the general population (roughly 30%), most of whom will never develop celiac disease. As a result, stand-alone genetic testing is most often used to “rule out” disease. This can be useful in patients who fall into a group with an increased clinical risk of developing celiac disease (such as family members of an affected individual) or patients where serologic testing may be compromised (ie, patients who have been on a gluten-free diet prior to testing).

Algorithms
Serologic testing has been recommended as the primary screening method by many groups, including the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHN), the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), and American College of Gastroenterology (ACG). Anti–TTG IgA is routinely recommended as the best serologic test for initial screening, coupled with the measurement of total IgA to rule out the possibility of concurrent IgA-deficiency that could lead to false-negative results in the TTG IgA assay. A variety of different algorithms have been suggested for how to follow up a positive screening result. Although most algorithms are largely similar, there are slight variations in the choice of confirmatory laboratory testing and the stage at which one moves to duodenal biopsy. Many of the distinctions between algorithms are based on the pretest probability of the patient having celiac disease, which is determined largely from the clinical presentation.
References:


About the Author

Thomas Daly, MD

Thomas Daly, MD, is the Medical Director of Cleveland Clinic Laboratories and Head of the Center for Test Development, a translational laboratory within the Robert Tomsich Pathology and Laboratory Medicine Institute of Cleveland Clinic. He received his medical degree from Washington University in St. Louis, and trained in clinical pathology at Barnes-Jewish Hospital, specializing in clinical chemistry. He has previously held positions as a Medical Advisor at Eli Lilly and Company supporting biomarker development for the oncology portfolio and Section Head of Clinical Chemistry at the University of Alabama-Birmingham. His research interests are in the development and application of emerging biomarkers to clinical practice, and the challenges associated with translating the minutiae of analytical performance into clinically meaningful advice for clinicians.
New approaches to molecular pathology testing in advanced lung cancer

By Roger D. Klein, MD, JD

Lung cancer is the leading cause of cancer mortality both in the United States and worldwide. Historically, lung cancer was classified as non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC) and carcinoid tumors. NSCLC represents greater than 85% of lung cancers. More recent categorization of these tumors have emphasized further subtyping of NSCLC into adenocarcinoma, the most common form that accounts for 50% of NSCLC, squamous cell carcinoma and large cell carcinoma (NCCN guidelines).

Patients diagnosed with lung cancer usually present at advanced stages. Most patients who present with metastatic adenocarcinoma continue to be treated with conventional chemotherapy and fare poorly, with an overall survival of less than 20%. However, over the past several years great advances have been made in our understanding of the molecular basis for NSCLC. This increased awareness of the biological underpinnings of NSCLC has in turn revolutionized the management of a subset patients who have been diagnosed with lung adenocarcinoma.

For these patients, information obtained from mutational analysis of specific oncogenes within their tumors has identified them as candidates for treatment with "personalized" therapies. Recent data suggest that such patients may derive significant benefit from treatment with drugs targeted to their particular mutations, often with much better side effect profiles than conventional chemotherapy. Further, our ability to undertake these molecular analyses on small biopsies and cytology specimens obtained through minimally invasive techniques has resulted in substantial reductions in morbidity for lung cancer patients.

Nevertheless, despite the enormous progress that has been made over the last decade, we have merely scratched the surface of what can potentially be accomplished through molecular profiling of lung and other cancers. Consortia like The Cancer Genome Atlas (TCGA) and the International Cancer Genome Consortium (ICGC), along with other research groups, have generated large amounts of genomic data that have revealed many potential future drug targets. Next generation sequencing allows us to rapidly and inexpensively interrogate multiple gene targets in a single reaction, ushering in a new era of comprehensive molecular profiling.

Current guidelines for mutation testing in patients with advanced lung adenocarcinoma include testing for mutations in the epidermal growth factor receptor (EGFR) gene and rearrangements involving anaplastic lymphoma receptor tyrosine kinase (ALK). However, the field is moving rapidly, and many institutions test for a broader range of mutations and rearrangements for both clinical trial selection and off-label use of approved therapies.

At Cleveland Clinic, routine mutation profiling of patients with metastatic lung adenocarcinoma currently includes upfront mutation analysis for mutations in EGFR, the Kirsten rat sarcoma viral oncogene homolog gene (KRAS), ALK rearrangements, and in those patients' tumors that lack demonstrated ALK rearrangements, testing for rearrangements in ROS proto-oncogene 1, receptor tyrosine kinase (ROS1) and the ret proto-oncogene (RET). In addition, patients may be tested for mutations in B-Raf proto-oncogene, serine/threonine kinase (BRAF) and erb-b2 receptor tyrosine kinase 2 (HER2). These latter emerging biomarkers, ROS1, RET, BRAF and HER2, appear to predict responsiveness to targeted therapies, but have been less extensively studied than EGFR and ALK. The following paragraphs provide additional information about each of the genes profiled in the tumors of Cleveland Clinic patients with metastatic lung adenocarcinoma.

**EGFR**

EGFR encodes a receptor tyrosine kinase that is a member of the ERBB family. Receptor dimerization activates the downstream RAS/RAF/MEK and PI3K/AKT/mTOR pathways.
pathways, which promote cellular growth and survival. EGFR mutations are identified in approximately 16% of lung adenocarcinomas and are most commonly found in Asians, women and non-smokers. In-frame deletions within exon 19 and the Leu858Arg mutation in exon 21 account for 90% of EGFR mutations. Exon 19 deletions and mutations in exons 18 and 21 typically predict responsiveness to reversible small molecular EGFR tyrosine kinase inhibitors such as gefitinib and erlotinib, as well as irreversible inhibitors such as neratinib, dacomitinib and afatinib, while exon 20 insertions and the T790M mutation are associated with resistance to EGFR tyrosine kinase inhibitors.

**ALK**

ALK rearrangements are detected in approximately 3–8% of lung adenocarcinomas, usually in younger patients who are non-smokers. The majority of these involve fusions with a portion of the echinoderm microtubule associated protein like 4 (EML4) gene, and result in constitutive activation of the ALK pathway. ALK rearrangements predict responsiveness to crizotinib as well as ceritinib, which is active in crizotinib-resistant tumors. ALK inhibitor resistance occurs via mutations that alter the drug-binding site (e.g. Leu1196Met, Gly1269Ala), ALK gene amplification and activation of bypass pathways.

**ROS1**

ROS1 encodes a receptor tyrosine kinase that is related to the insulin receptor. ROS1 rearrangements, which can involve multiple fusion partners, are found in approximately 1.5% of lung adenocarcinomas, predominantly in never or former light-smoking younger patients. Rearrangements of ROS1 were first identified in NSCLC. The ALK inhibitor crizotinib also has activity in patients with ROS1-positive tumors.

**RET**

Rearrangements in RET are identified in approximately 1.7% of patients' lung adenocarcinomas, most commonly in younger, non-smokers. RET is a receptor tyrosine kinase that is involved in cell proliferation, differentiation and migration, in addition to neuronal navigation. Fusions most often involved kinesin family member 5B (KIF5B), and less frequently coiled-coil domain containing 6 (CCDC6), and result in constitutive activation of the RET kinase. RET-rearranged tumors may respond to tyrosine kinase inhibitors such as vandetanib and cabozantinib.

**BRAF**

BRAF encodes a serine threonine kinase that is part of the mitogen-activated protein kinase (MAPK) signaling pathway, which promotes cellular growth and survival.
Mutations of **BRAF** codon 600 in exon 15 are present in 1–5% of lung adenocarcinomas, and result in constitutive activation of the enzyme. In addition, mutations may be seen in exons 11 and 15. The V600E mutation, which describes the substitution of glutamic acid (E) for valine (V) at position 600, represents approximately 50% of codon 600 mutations in lung cancer, and is associated with light or never-smoking women whose tumors have micropapillary histology. Other **BRAF** mutations are found in former or current smokers, and have an adverse prognosis. **BRAF** V600 inhibitor therapy is approved for patients with malignant melanoma, and appears to be active in lung adenocarcinoma patients whose tumors have **BRAF** V600 mutations (Hyman D. et al. *N Engl J Med* 2015:726-36).

**KRAS**

Activating mutations of the **KRAS** gene, a member of the RAS family of oncogenes, is mutated in 20–25% of lung adenocarcinoma, with the majority found in codons 12 and 13 in exon 2, and less frequently in codon 61 in exon 3. **KRAS** mutations are more often found in smokers, and less commonly in Asians. Mutations in **KRAS** are rarely found in combination with other driver mutations such as **EGFR**, **BRAF**, **HER2**, **ALK** and **ROS1** rearrangements. Activating **KRAS** mutations may be an adverse prognostic marker in lung adenocarcinoma, and appear to predict non-responsiveness to anti-**EGFR** tyrosine kinase inhibitors.

**HER2**

**HER2**, now known as **ERBB2** (erb-b2 receptor tyrosine kinase 2), encodes a receptor tyrosine kinase that lacks a known ligand. The **HER2** receptor is activated by homo- or heterodimerization with other ERBB receptor family members including **EGFR**. **HER2** receptor dimerization activates downstream signaling through the PI3K/AKT/ **mTOR** and MEK/ERK pathways, promoting cellular proliferation, differentiation and migration, and mediating sensitivity of **EGFR**-mutant lung tumors to anti-**EGFR** therapy. Activating mutations in **HER2** are present in approximately 2–4% of lung adenocarcinoma patients, most commonly in women, never smokers. They are typically mutually exclusive with **EGFR**, **KRAS** and **ALK** mutations. **HER2** gene mutations in NSCLC typically occur in exons 18-21 of the tyrosine kinase domain, with an in-frame insertion in exon 20 most frequently identified. **HER2** mutations in NSCLC may predict response to anti-HER2 inhibitor therapies such as traztuzumab or afatinib. (Mazieres J, et al. *J Clin Oncol* 2013;31:1997-2003; Zimmerman S, Peters S. *Ann Oncol* 2012;23(September Suppl. 10)):x197-2030. Pao W, Girard N. *Lancet Oncol* 2011;12:175-80) refs 16, 22.)

**Alternative Specimens**

Most lung cancers are diagnosed at advanced stages, generating a reliance on small biopsies and cytology specimens for diagnosis and ancillary studies. Fine needle aspiration biopsy (FNAB), which can be performed through the airways or chest wall, has increased in importance due to advances in biopsy tools and biopsy techniques, low risk of serious complications, and increased experience of cytopathologists in interpreting aspirate specimens.

Thanks to technological advances in imaging, such as CT and endobronchial ultrasound, 100 to 500 cells are adequate for DNA sequencing-based assays.

FNAs are an advantageous and effective means to obtain diagnostic cellular material by sampling a wide area of the target lesion and by acquiring tumor cells with lower contamination by background stromal connective tissue elements.

Although cell blocks are the traditional cytopathology specimen tested, problems with assay failure due to insufficient cellularity have prompted a search for alternative methods. Testing on direct smears can be effective of PCR analysis, as nucleic acids obtained are generally of high quality, and specimens can be immediately assessed for cellular adequacy. Moreover, the cancer cells of interest can be directly visualized on the direct smear and selected for analysis. Because fixation is alcohol rather than formalin-based, the effects of formalin crosslinking can be avoided.

**NGS**

Next generation sequencing (NGS), also known as “massively parallel sequencing” represents a revolutionary advancement in genotyping. NGS allows for the accurate, rapid sequencing of large regions of DNA, with exponential decreases in per base sequencing costs relative to
previously used Sanger methods. Thus, it confers the ability to sequence multiple genes simultaneously and comprehensively at an affordable cost, with superior analytical sensitivity (lower limit of detection of minor allele populations) and acceptable turnaround times. Moreover, NGS allows for quantitation of mutation proportion. NGS has ushered in a new era of mutation profiling of lung and other tumors that is already offering great benefits to patients, and promises even more dramatic improvements in our management of cancer patients.

References:


About the Author

Roger D. Klein, MD, JD

Dr. Klein is Medical Director of Molecular Pathology at the Robert J. Tomsich Pathology and Laboratory Medicine Institute at Cleveland Clinic, where he focuses on the clinical implementation of molecular pathology assays for oncologic and heritable disorders.

Dr. Klein is a national leader in the advancement of policies related to the implementation of genetic and genomic testing. He is Chair of the Association for Molecular Pathology’s (AMP) Professional Relations Committee, and plays a key leadership role in the development of AMP’s advocacy agenda, policies and interactions with government agencies, legislators, and other professional and trade organizations. He also serves on the AMP Board of Directors, Economic Affairs Committee and Strategic Opportunities Committee, and has been a member of the Whole Genome Analysis Working Group and the Task Force on MGP Fellow Training in Genomics.

Dr. Klein pursued his undergraduate and medical degrees as well as an internship in internal medicine at Case Western Reserve University. He completed residency training in laboratory medicine along with a fellowship in molecular genetics at Yale Medical School, followed by a fellowship in molecular genetic pathology at Mayo Clinic. He is board-certified in clinical pathology and molecular genetic pathology, and is licensed to practice medicine in Ohio and Florida.
Alumni Connect

We are thrilled to feature one of our distinguished alumni, Emily Volk, MD, MBA, in this installment of Alumni Connect. Dr. Volk did her anatomic and clinical pathology residency (1993-97) and her surgical pathology fellowship with emphasis in gastrointestinal pathology at Cleveland Clinic from 1993-97 and 1997-98, respectively.

We invited Dr. Volk to tell us about her current position, reflect on her training at Cleveland Clinic, and provide current residents and fellows with valuable advice.

Dr. Volk:

“In my current role as the Chief Quality Officer for the Baptist Health System in San Antonio, I am responsible for clinical initiatives related to quality and safety opportunities throughout the Baptist Health System. I am expected to serve as a catalyst for the development of clinical initiatives such as practice guidelines and care protocols that lead to the achievement of quality outcomes and cost efficiencies. In addition, I am responsible for continuous quality improvement and regulatory readiness and provide input into risk management as they relate to our hospitals. Previously I served as medical director of laboratories and pathology for the Baptist Health System. The past 22 years in pathology prepared me well for this opportunity as laboratory medicine touches so many aspects of the hospital and larger health care system. Pathologists are central to patient care and yet, to my chagrin, often remain unseen to many healthcare administrators.

Happily, pathologists were never just part of an “ancillary” service during my training at Cleveland Clinic. My mentors – including, but not limited to, Drs. Jonathan Myles, John Goldblum, Gerald Hoeltge, Ronald Domen, Carol Farver, Tom Bauer, Wilma Bergfeld and Bruce Sebek – taught me the influence that an interventionist pathologist could have through their enthusiastic clinical engagement. Their service ethic and their impact on patient care were highly visible and appreciated by their patients and colleagues. The staff was involved in organized medicine through work with the AMA, USCAP, ASCP, OSP and CAP. Their volunteer spirit left an indelible mark and I have no doubt help drive my interest in serving the membership of the CAP and that of my state medical and pathology societies.

My advice to residents is to learn as much as possible during the training years. Do not differentiate too early. Disease knows no anatomical or clinical bounds that correlate to chapter headings in textbooks. It is impossible to predict what skills you may need to nurture for your future. Enthusiastically embrace advocating for your profession for doing so serves patients well. Strive to understand how things work not just in histology and the clinical chemistry laboratory, but also in the boardroom and in the C-suites. Understand and embrace your important place at the table in the practice and business of medicine. The more savvy and engaged pathologist physician leaders we have, the more our patients will benefit.”

We want to hear from you

Please send us your news and accomplishments to be featured in this “Alumni Connect” section in future issues of Pathology Innovations. If you prefer to receive an electronic version, please let us know by providing your preferred email address to ClientServices@ccf.org.

Fadi W. Abdul-Karim, MD, MEd
Vice-Chair, RT-PLMI
Center for Pathology Education

Jonathan L. Myles, MD
Pathology and Laboratory Medicine Specialty Director

Alumni Connect Steering Commitee

Drs. Abdul-Karim and Myles, Daniel Kelly, Kathy Leonhardt, Emily Lopick, Paul Suchy, PhD, and Karl Theil, MD.
Cleveland Clinic represented at CAP

The annual meeting of the College of American Pathologists (CAP), Oct. 4–7, in Nashville, Tennessee, saw participation from many Cleveland Clinic staff members as well as representation with a booth from Cleveland Clinic Laboratories. With more than 18,000 board-certified pathologists, CAP serves patients, pathologists and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide.

Cleveland Clinic participants in CAP’s course presentations and abstracts are listed below.

**Course Presentations**

“A journey from glomerulus to urethra through interesting cases along the GU tract” by Leah Herlitz, MD, and Christopher Przybycin, MD.

“Implementing whole slide imaging for clinical use: what to do and what to avoid” by Walter Henricks, MD, and other faculty.

“CPT coding and Medicare physician fee schedule 101: history, evolution and future” by Jonathan Myles, MD, and other faculty.

“Critical differential diagnoses in soft tissue pathology” by Steven Billings, MD, and Brian Rubin, MD, PhD.

“Frozen section evaluation in ovarian and pelvic lesions: an interactive and practical approach with real cases” by Fadi Abdul-Karim, MD, and Andres Roma, MD.

“A potpourri of common diagnostic challenges in gastrointestinal pathology” by Deepa Patil, MD.
“Common diagnostic challenges in gastrointestinal pathology – a special focus on current management guidelines” by John Goldblum, MD, and Deepa Patil, MD.

“Empowering pathology in the electronic health record era” by Walter Henricks, MD, and other faculty.

“Establishing good test utilization practices” by Gary Procop, MD, and other faculty.

“Frozen section evaluation in ovarian and pelvic lesions: interactive approach to a correct interpretation” by Fadi Abdul-Karim, MD, and Andres Roma, MD.

“IVM Reimbursement for Pathologists” by Jonathan Myles, MD.

Abstracts
Cleveland Clinic also was well represented in the CAP ’15 Abstract program, designed to promote a broad range of research in pathology. The competition allows pathologists and research scientists the opportunity to submit original research to their peers in a poster presentation format.

“Interobserver Agreement Study on Diagnosing Serrated Polyps With Stromal Changes” by Juliana Kissiedu, MD; Rish Pai, MD, PhD; Daniela Allende, MD; and Xuili Liu, MD, PhD.

“New Proposed Terminology for Anal Squamous Lesions: Its Application and Interobserver Agreement Among Pathologists in Academic and Community Hospitals” by Andres Roma, MD; Xiuli Liu, MD, PhD; Deepa T. Patil, MD; Hao Xie, MD, PhD; and Daniela Allende, MD.

“Hemophagocytic Lymphohistiocytosis as a Harbinger of Undetected NK/T-Cell Neoplasms” by Basma M. Basha, MD, and Megan O. Nakashima, MD.

“Cross-Reactivity of Treponema pallidum Immunohistochemistry With Intestinal Spirochetes” by Sory J. Ruiz, MD, and Gary W. Procop, MD, MS.

“Histology Laboratory Paraffin Waste Disposal: A Cost Reduction Opportunity” by Kelsey E. McHugh, MD; Linda G. McDonald, HT; and Ilyssa O. Gordon, MD, PhD.

“High Yield of Oncogenic Drivers in Lung Adenocarcinomas With Psammoma Bodies: Comprehensive Molecular Profiling of 10 Resected Cases Using Next-Generation Sequencing” by Kelsey E. McHugh, MD; Sanjay Mukhopadhyay, MD; Vamsidhar Velcheti, MD; and other faculty.

“Biohazard Waste Reduction in the Cytopathology Laboratory” by Amber L. Smith, MD; Yvonne Foster, CT(ASCP)CM; and Ilyssa O. Gordon, MD, PhD.

“Radial Scars in Breast Core Biopsies Are Infrequently Associated With Carcinoma and May Not Require Excision” by Alana R. Donaldson, MD; Leah K. Sieck, MD; Christine N. Booth, MD; and Benjamin C. Calhoun, MD, PhD.

“Discordance in the Diagnosis of Metaplastic Breast Carcinoma on Core Biopsy and Surgical Excision” by Alana R. Donaldson, MD; Charles M. Leyer, MD; Camille A. Berriochoa, MD; Shree Agrawal, BS; Robyn Stewart, MD; Halle C. Moore, MD; Rahul D. Tendulkar, MD; Benjamin C. Calhoun, MD, PhD.

“Used in the Diagnosis of Anal Squamous Intraepithelial Lesions: New Guideline Application and Interobserver Agreement Results” by Andres Roma, MD; Xiuli Liu, MD, PhD; Deepa T. Patil, MD; Daniela Allende, MD; and other faculty.

*The abstracts can be found at www.archivesofpathology.org.

New Staff

Jennifer Ko, MD, PhD
Dermatopathology
Biorepository Medical Director

Scott A. Robertson, MD, PhD
Gastrointestinal Pathology

Gabrielle A. Yeaney, MD
Neuropathology
Ocular Pathology
Clinical Biochemistry at 2015 AACC Annual Conference

The Clinical Biochemistry Department was well represented at the 2015 American Association for Clinical Chemistry (AACC) Annual Meeting and Vendor Expo in Atlanta in July. Six staff members comprised of a medical technologist, a senior research technologist, a quality specialist, a manager, and two medical staff presented research findings as 12 posters, which received significant attention from meeting attendees. Sihe Wang, MD, Medical Director and Section Head of Clinical Biochemistry, also was involved in leadership activities for the Pediatric Fetal and Maternal Division, Clinical and Translational Division, and Commission on Accreditation in Clinical Chemistry.

Attendees were able to experience education sessions, such as a talk by Martin Makary, MD, titled “Art, Assassination, and America: How Transparency Disrupts an Industry and Changes a Nation,” and scientific and management seminars to learn of new developments in the clinical sciences and the changing healthcare environment. The Clinical Biochemistry group also connected with other clinical laboratorians for information exchange and potential future collaboration.

In addition, the Clinical Biochemistry group had extensive interactions with the in vitro diagnostic industry and were provided updates on new developments. For example, they learned about the advance in automation from vendors, such as Roche and Siemens. Some also explored future opportunities with informatics vendors, such as Orchard. They also had the opportunity to meet with current vendors, such as Roche, ThermoFisher, Tecan and Sunquest, through both meetings and instrument demonstrations, as well as visiting Cleveland Clinic Laboratories booth.

M. Qasim Ansari, MD.

Drew Payto.

Dustin Bunch.
News

Dr. Goldblum is co-author of BMA Book Award winner

The updated edition of *Surgical Pathology of the GI Tract, Liver, Biliary Tract and Pancreas* co-authored by John R. Goldblum, MD, and Robert D. Odze, MD, won first place in the pathology category of the British Medical Association's annual Medical Book Awards ceremony in London on Sept. 3. Dr. Goldblum is Chairman of the Department of Anatomic Pathology at Cleveland Clinic and Professor of Pathology at Cleveland Clinic Lerner College of Medicine; Dr. Odze is Associate Professor of Pathology at Harvard Medical School and Director of Gastrointestinal Pathology at Brigham and Women's Hospital.

Published by Elsevier, the book is designed to act as a one-stop medical reference book for the entire gastrointestinal system, providing exhaustive coverage with all of the necessary tools to make a comprehensive diagnostic workup. It includes thousands of high-quality illustrations and eight brand-new chapters to help in the diagnosis and recognition of any pathological slide.

RT-PLMI News

Deepa Patil, MD, joins Ana Bennet, MD, as Co-Director of GI/Hepatobiliary Pathology Fellowship Program.

Ilyssa Gordon, MD, PhD, has been appointed Medical Director for Sustainability in RT-PLMI. While Dr. Gordon has led this cause for several years, she will continue to support the development and implementation of sustainable practices throughout the labs in this official capacity.