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Pathology In Focus Editorial Team

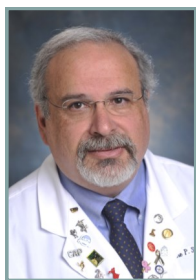
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Message from the Interim Chair:



Seasons

Ask the stereotypical American kid what's his or her favorite season and more often than not Summer will head the list. It's that long anticipated break from school, and whether you're a "nerd" or "jock," it offers the endless possibilities of uninterrupted hours of video games, playing with dolls, baseball, comic book reading and vacations to the beach, mountains or our nation's parks with the folks. Ask an adult the same question and I would guess the sweet spot shifts one season later to the Fall – the break in the hot weather, the kids finally back in school, football, basketball, the World

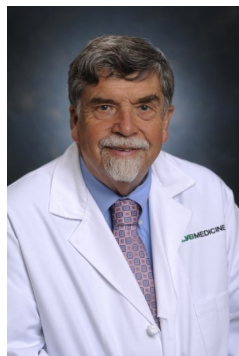
Series and the arrival of the now three month long holiday season. For me the holiday season focuses on seasonal cooking, family reunions and exchanging of gifts. In my world pot roast and potato pancakes come to mind, in yours perhaps it's baked ham and mashed potatoes or lamb, rice and figs.

Fall and its sense of academic rebirth also come to the campus. Our new faculty recruits have begun to arrive and settle in on campus and in the practices we now run in Montgomery and Anniston. It is recruiting season for new residents and clinical fellows along with graduate students and post-docs. We have completed our annual Departmental review with the Dean and are positioned well as we begin in earnest our search for a new permanent Chair. Thanks to the extraordinary work of our cadre of experimentalists we appear to be re-positioned back in the top 10 of NIH funded Pathology Departments and when you recognize many of those ahead of us are dual departments Pathology/Cell Biology or Pathology/Immunology or have tied to them institutional Centers like the University Cancer Center, we're actually closer to the top 5. Our housestaff continue to bring great honor to themselves and us through their research/abstract performance at multiple national meetings and their publications. Our clinical volume continues to swell along with the finances.

In summary, there is much to be thankful for and Birmingham remains a phenomenal place to work and live. Enjoy the cool weather and I promise, just this one last piece of Halloween candy, and I'll stop.

All the best,
Gene P. Siegal, M.D., Ph.D.

Faculty Profile: William E. Grizzle, M.D., Ph.D.



Dr. Grizzle has an AB honors degree (Chemistry and Physics) from Harvard University and Ph.D. (Biophysics) and M.D. degrees from Johns Hopkins University. He is board certified in Anatomic and Clinical Pathology and is Professor of Pathology. Previously, he served as Head of the Autopsy Section at UAB and VA hospitals in Birmingham, 1990-2000, and since 2000, has been Head of the Program in Translational Research in Neoplasia of the Department of Pathology. He has been Director of the Tissue Collection and Banking Facility at UAB since 1983, the principal investigator (P.I.) of the Southern Division of the Cooperative Human Tissue Network (CHTN) since 1987 and the P.I. of the Biorepository of the Pulmonary Hypertension Breakthrough Initiative since 2006. He is a frequent consultant for national and international biorepositories and governmental agencies. He also considers the education of biorepository personnel a key area of his work and he presents national and international workshops on factors affecting and limiting the use of human tissues in research. Together with his colleague, Ms. Katherine Sexton, he presents national and international workshops on the Design and Operations of Biorepositories. He is a founding member of the International Society of Biological and Environmental Repositories (ISBER), and he is a former council member and Past President of ISBER. He received the 2015 ISBER Award, Outstanding Achievement in Biobanking. He has been a trustee of the Biological Stain Commission (BSC) since 1992 and he has requested to become emeritus in 2016. He served as President (2000-2004) and Vice-President (1996-2000) of the BSC. He is currently on the editorial board of the BSC journal, *Biotechnic & Histochemistry*.

He has published approximately 500 peer-reviewed manuscripts and book chapters and is a senior editor of *Clinical Cancer Research*, associate editor of *Cancer Biomarkers* and a member of the editorial boards of *Biopreservation and Biobanking* and other journals.

When he began working in biorepositories in 1982, there were only a few biobanks that stored solid cancers. His approach is based on a prospective tissue collection and distribution model that he developed, proposed, and piloted in 1983; this model was subsequently adopted as the model of the Cooperative Human Tissue Network (CHTN) in 1986. Importantly, this model includes an approach to quality control in which investigators were informed as to the specific characteristics of the actual tissue aliquots provided to them to support their research (e.g., diagnosis, amount of tumor, % necrosis, fibrosis and mucin, % malignant cells). The model also emphasizes the distribution of tissues to investigators to support research rather than just the collection and banking of specimens without an emphasis on use of tissues. In addition, he has disseminated information on the use of human tissues in research via multiple publications and has expanded the knowledge in biorepository sciences by investigating issues which affect the use of human tissues in research. His studies with Dr. Dennis Otali in biorepository sciences have focused on the effects on tissue and on immunorecognition in tissues of fixation, tissue processing to paraffin, and of storage of tissues.

Recently, much of his translational research has returned to prostate cancer (PrCa) including the improvement of diagnosis via more targeted biopsies. These studies in collaboration with Tufts (Dr. S. Gaston) together with collaborations with urology and pathology faculty at UAB (Drs. S. **Rais-Bahrami**, J. Nix, and J. Gordetsky) in the use of magnetic resonance imaging fused with active ultrasound (MRI-US) to direct biopsies to areas suspicious for PrCa and to identify molecular profiles of these suspicious areas, especially epigenetic changes. Also, with the same collaborators plus Drs. P. Kolettis, S. Sudarshan and J. Mobley, molecular markers of lipid processing are being evaluated as well as how these molecules vary with race and affect the aggressiveness of prostate cancer in African Americans. In separate collaborations, he is studying how microRNAs are involved in the development of castration resistant prostate cancer (CRPC) with Dr. R. Chakrabarti at University of South Florida and the importance of the molecule, Kaiso and its signaling pathways in the process of epithelial to mesenchymal transition (EMT) in prostate and breast cancers, how exosomes provide intercellular communication in breast and prostate cancers, and how communication via exomes varies with race (Dr. C. Yates at Tuskegee University).

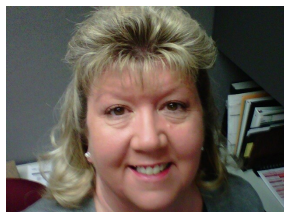
In a new and very novel collaboration (Dr. Lacey McNally, University of Louisville, Dr. Desiree Morgan at UAB and radiology faculty at the University of Arizona) focuses on a new method of molecular imaging using multispectral opticoacoustic tomography (MSOT). This method is applicable even for molecular imaging of features of pancreatic and other deep cancers and is outstanding at identifying areas of hypoxia.

In collaboration with Dr. G. Pizza (University of South Alabama), he is evaluating the effects of novel non-steroid anti-inflammatory drugs (NSAIDs) on pre-invasive cancer and cancer, including alternate methods of action of NSAIDs via autophagy and phosphodiesterase modulation (PDE10) as well as new drugs targeting the Ras pathway.

He continues to collaborate with Dr. Upender Manne in racial differences in colon and breast cancers, with Dr. L. Samant on breast cancer drug resistance secondary to hypoxic effects on hedgehog signaling, Dr. S. Bellis on glycosylation dependent mechanisms controlling ovary, colon and pancreatic cancers, and other collaborations with the faculty of the Pancreatic and Breast SPORES. He also is active in mentoring faculty in translational research.

See: Complete List of published work at: <http://www.ncbi.nlm.nih.gov/sites/myncbi/william.grizzle.1/bibliography/41164804/public/?sort=date&direction=ascending>

Spotlight on Administration: Kathy Cornelius



Kathy Cornelius is an OAll in the Division of Molecular and Cellular Pathology and assists Drs. Xu Feng, Adam Wende, Joseph Messina, and John Shacka. She also manages the MCP Seminar Series and is responsible for coordinating the schedule and organizing external speaker visits.

Before UAB, Kathy was with Southern Research Institute for 18 years, 15 years as the assistant to the Director of Cancer Therapeutics and Immunology and 3 years as assistant to the Vice-President of Corporate Development.

Kathy and her husband, Danny, have been married for 36 years and live in Pleasant Grove. They graduated from Minor High School and were high school sweethearts. They have 2 grown children and 3 grandchildren (ages 13, 6, and 3). Kathy enjoys having her family together for dinner on Sunday afternoon and loves spending time with her grandchildren.

Where Are They Now?

Wayne Orr received his PhD from the Pathology Department at UAB in December 2002, working in the laboratory of Dr. Joanne Murphy-Ullrich. Upon leaving UAB, Dr. Orr accepted a post-doctoral position in the Cardiovascular Research Center at the University of Virginia working with Dr. Martin Schwartz, a leader in the field of mechanotransduction and integrin signaling. With a background in cell-matrix interactions from working with Dr. Murphy-Ullrich, Dr. Orr spent his post-doctoral training examining how changes in vascular matrix composition affect the endothelial cell response to shear stress, a frictional force generated by blood flowing across the surface of the vessel. Dr. Orr received multiple fellowships during his post-doctoral training, including two post-doctoral fellowships from the American Heart Association and a position on the Cardiovascular Training Grant at the University of Virginia headed by the late Dr. Brian Duling. In 2007, Dr. Orr was promoted to Research Assistant Professor in the Department of Microbiology at the University of Virginia and received



his first independent funding, an American Heart Association Scientist Development Grant to study the signaling mechanisms regulating matrix-specific control of endothelial cell function. Dr. Orr was quickly recruited to the Department of Pathology at the LSU Health Sciences Center in Shreveport in December 2007, joining a group containing several UAB alums including Drs. Guillermo Herrera, Kevin McCarthy, and Christopher Kevil. His research group at LSU has continued his work on the regulation of vascular cell biology by the microenvironment, publishing 28 manuscripts since 2008 and receiving funding from the National Institutes of Health, American Heart Association, and American Diabetes Association. Additionally, Dr. Orr takes great pride in mentoring students and trainees, including five residents and fellows, five graduate students, four medical students, and seven undergraduate students to date.

Dr. Orr was promoted to Associate Professor with tenure in 2013 and maintains active involvement in university committees at LSU including the Institutional Research Advisory Committee, the Institutional Animal Care and Use Committee (vice chair/chair from 2011-2015), the Department of Cell Biology and Anatomy Graduate Committee, and the Pathology Education Curriculum Committee, as well as previously serving on the Faculty Senate and Institutional Review Board. He serves on grant review committees for the American Heart Association (chair of Endothelial Biology 3 since 2015) and the American Diabetes Association, and he has served as an ad hoc reviewer for the Atherosclerosis and Inflammation in the Cardiovascular System (AICS) study section at the NIH, the Research Council United Kingdom (RCUK), and the Council for Earth and Life Sciences for the Netherlands Organization for Scientific Research. Dr. Orr serves on the Research College and Advisory Council for Dublin City University, the North American Vascular Biology Organization (NAVBO) Membership Committee, and the Arteriosclerosis, Thrombosis, and Vascular Biology (ATVB) Membership and Communications committee for the American Heart Association.

Dr. Orr currently lives in Bossier City, Louisiana, with his wife Stephanie and their children Charlotte and William. While he doesn't really have a single favorite memory of the Department of Pathology at UAB, his favorite thing about his time at UAB were the people with whom he got the privilege to work and grow as an academic scientist. These include his fellow graduate students, the post-docs and junior faculty who provided advice and direction (including Drs. Christopher Kevil, Rakesh Patel, and Silvia Goicoechea), the senior faculty who scared him into wanting to be better (Drs. Jay McDonald and Victor Darley-Usmar come to mind), and his mentor Dr. Joanne Murphy-Ullrich who always had more faith in him than he had in himself and who made him believe that the past 13 years were possible.

From the Chief Residents: Brandi McCleskey and Jessica Tracht

We have recently begun the new resident recruitment season and are excited to interview all of the highly qualified applicants. We appreciate the faculty, residents, and staff for their assistance in making this an excellent and successful recruitment season.

National Meetings and Publications:

Dr. Tiansheng Shen published "Sinonasal renal cell-like adenocarcinomas: robust carbonic anhydrase expression" in *Human Pathology* with former faculty mentor Dr. Brandwein-Gensler.

Dr. Tiansheng Shen published "Characterization of estrogen receptor-negative/progesterone receptor-positive breast cancer" in *Human Pathology* with faculty mentor Dr. Shi Wei.

Dr. Alston published "Suspicious Cytologic Diagnostic Category in Endoscopic Ultrasound-Guided FNA of the Pancreas: Follow-Up and Outcomes" in *Cancer Cytopathology* with faculty mentor Dr. Eltoum.

Dr. Brandi McCleskey published "GATA3 expression in advanced breast cancer: Prognostic value and organ specific relapse" in *American Journal of Clinical Pathology* with faculty mentor Dr. Shi Wei.

Dr. Vishwas Parekh published "Clinicopathologic and Cytogenetic Characterization of Therapy-related Acute T Lymphoblastic Leukemia in Adult Population" in *Leukemia and Lymphoma* with faculty mentor Dr. Peker.

College of American Pathologists (CAP)

Dr. Ruby Ma presented a poster titled "A Case of Adult Annular Pancreas with Pancreatic Duct Atresia and Subsequent Chronic Pancreatitis" with faculty mentor Dr. Shen and Scott Young.

Dr. Tiansheng Shen presented a poster titled "Histiocytic Sarcoma of the Adrenal Gland" with faculty mentor Dr. Shi Wei.

Dr. Vishwas Parekh presented a poster titled "Therapy-related Acute T Lymphoblastic Leukemia – Report of Two Cases" with faculty mentor Dr. Peker.

Dr. Vishwas Parekh presented a poster titled "Primary Rosai-Dorfman Disease of the Bone." with faculty mentors Drs. Eltoum, Fallon, Siegal, and Wei.

American Society of Cytopathology

Dr. Alston will present a poster titled "What Is the Optimal Management for the Atypical Cytologic Diagnostic Category in EUS-FNA of the Pancreas: an Algorithm Based on Regret Decision Curve Analysis" with faculty mentor Dr. Eltoum.

Dr. Alex Hanna will present a poster titled "Hürthle Cell Lesions of Undetermined Significance and Hürthle Cell Neoplasms Have the Same Implied Risk of Neoplasm/Malignancy as Their Follicular Counterparts" with faculty mentors Dr. Eltoum and Dr. Frost.

Dr. Alex Hanna will present a poster titled "Unsatisfactory/Non-diagnostic Thyroid Fine Needle Aspiration: Rates, Follow-up Methods, and Risk of Neoplasm/Malignancy" with faculty mentors Dr. Eltoum and Dr. Frost.

American Society of Dermatopathology

Dr. Vishwas Parekh presented a poster titled "Primary Signet-ring Cell/Histiocytoid Carcinoma of the Eyelid" with faculty mentors Dr. McKay and Dr. Velosa.

Dr. Vishwas Parekh presented a poster titled "An Unusual Presentation of Tinea Pedis in a Diabetic Patient" with faculty mentor Dr. McKay.

American Society for Clinical Pathology

Dr. Vishwas Parekh presented a poster titled "Adenomatoid Tumor of the Posterior Mediastinum – the First Case Report" with faculty mentors Dr. Winokur and Dr. Stevens.

Society for Hematopathology/European Association for Haematopathology (SH/EAHP) Workshop on Immunodeficiency and Dysregulation

Dr. Vishwas Parekh presented a case titled "Monomorphic B-cell post-transplant lymphoproliferative disorder" with faculty mentor Dr. Peker.

Dr. Vishwas Parekh presented a case titled "EBV-related primary splenic lymphocyte-depleted classical Hodgkin lymphoma" with faculty mentor Dr. Peker.

20th Congress of the European Hematology Association

Dr. Vishwas Parekh presented a poster titled "Therapy-related Acute Myeloid Leukemia in Adults: Is Age Younger age than 40 Clinically Relevant?" with faculty mentors Dr. Rosenblum and Dr. Peker.

From the Chief Residents Cont'd....

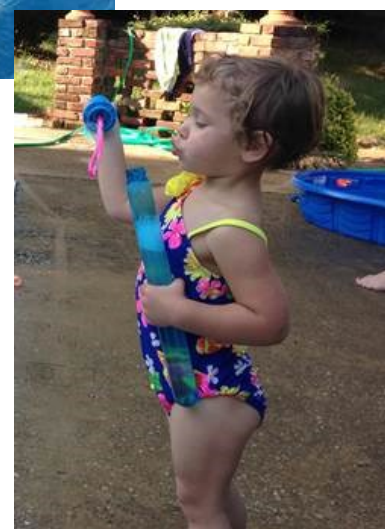
Resident Events

We would like to thank Dr. Vishwas Parekh and his wife, Eun-hee Shim, for hosting a resident pool and pizza party.

We appreciate the department for the continued support of residents' events. It was great to mingle outside of work and send off the great Alabama summer with our friends and families!



Dr. Melissa Dillard's Daughters



Dr. Ruby Ma's Son and Daughter; Dr. Vishwas Parekh's Daughter



Dr. Brandi McCleskey and Son



Dr. Ben Saylor and Daughter



Dr. Liz Staley's Sons

Residency Program Director:
C. Bruce Alexander, M.D.

Residency Program Support:
Karen Lewis
934-4060
kflew@uab.edu

Accolades

Dr. Marisa Marques - Elected as Treasurer to the Society for the Advancement of Blood Management (SABM)

Dr. Rakesh Patel - Dr. Selwyn Vickers, M.D., F.A.C.S., Senior Vice President for Medicine and Dean, School of Medicine, and **Dr. Richard Marchase, Ph.D.**, Vice President for Research and Economic Development, are pleased to announce that **Dr. Rakesh Patel, Ph.D.**, will be the new director of the Center for Free Radical Biology (CFRB) from October 1, 2015, when **Dr. Victor Darley-USmar, Ph.D.** steps down after serving as Director since 2006. Dr. Darley-USmar will be focusing on developing the Translational Bioenergetics Program at UAB. Dr. Patel has been a member of the center since 1996 and served as part of the CFRB leadership team since 2004. He has made important contributions to the teaching and training missions at UAB and is a nationally recognized expert in the metabolism of nitric oxide and its interactions with heme proteins. A member of the Department of Pathology he also holds secondary appointments in the Departments of Anesthesiology and Environmental Health Sciences.

Dr. Rajeev Samant presented an invited talk at CNIO Frontiers Meeting, September 28-30, 2015, Spanish National Cancer Research Centre (CNIO), Madrid, Spain. The conference was titled "Metastasis Initiation: Mechanistic Insights and Therapeutic Opportunities."

Dr. Ralph Sanderson - At the Federation of European Biochemical Societies meeting on "Matrix Pathobiology, Signaling and Molecular Targets" held in Rhodes, Greece on September 24-29, Dr. Ralph Sanderson presented the Honorary Plenary Lecture and received an Honorary Medal Award from the University of Patras in recognition of "significant contributions and scientific achievements in the fields of matrix pathobiology and cell signaling."

Dr. Shi Wei - Appointed to the CAP Publications Committee for 2016

Willayat Wani, Postdoctoral Fellow in Dr. Jianhua Zhang's lab, was one of 30 nationally to receive a Society for Free Radical Biology and Medicine (SFRBM) travel award. He has also been chosen to give an oral presentation, "*Role of O-GlcNAcylation in Autophagy, Protein Homeostasis, and Neuronal Bioenergetics*" at the SFRBM 22nd Annual Meeting in Boston, Massachusetts, held November 18-21, 2015.

Congratulations to **Helen Collins, Postdoctoral Fellow** in Dr. John Chatham's lab for the following:

- Elected to full membership in the Physiological Society of the UK
- Received a Postdoctoral Scholar Award from the Office of Postdoctoral Education
- Received an American Diabetes Association Postdoctoral Fellowship
- Second place poster presentation winner at the 4th annual UAB Comprehensive Cardiovascular Center's Symposium

Matthew Ryan Smith, Graduate Student in Dr. Landar's lab, has been chosen to give an oral presentation, "*Mitochondrial protein thiols control metabolism by modulating activity and levels of key metabolic enzymes*" at the 22nd Annual Meeting of the Society for Free Radical Biology and Medicine in Boston, Massachusetts, held November 18-21, 2015.

Three Department of Pathology teaching faculty were selected as teaching award recipients among the faculty honored by students from the UAB School of Medicine with 2015 Argus Awards.

The Argus Awards, created in 1996 to recognize faculty members, give medical students the chance to honor their mentors, professors, courses and course directors for outstanding service to medical education. Faculty are nominated by course evaluations and students vote to select award winners in each category. Pathology teaching faculty who were winners and nominees for the 2015 Argus Awards include:

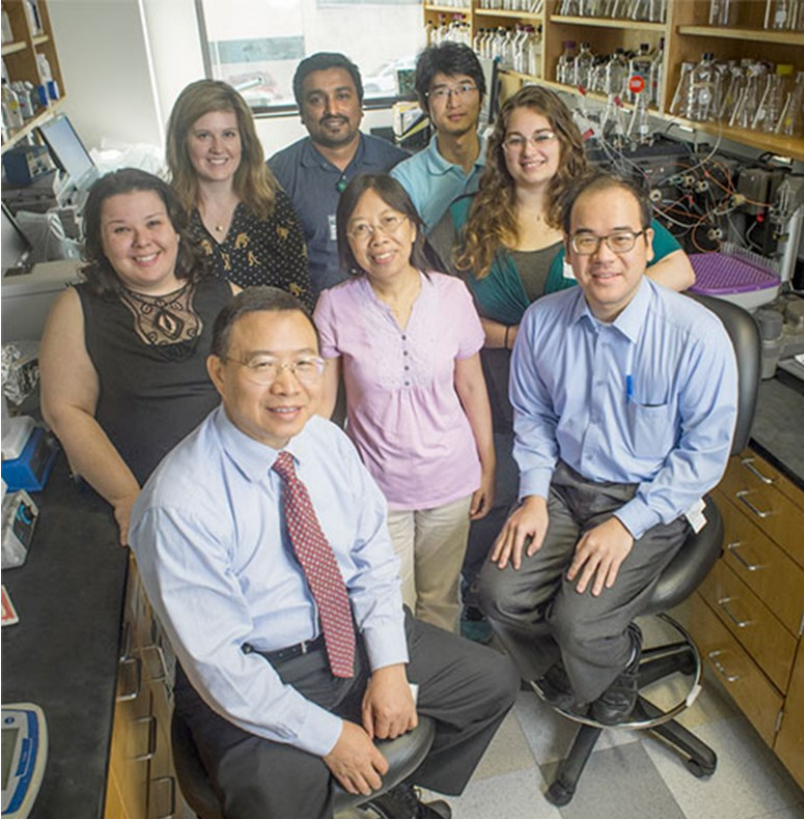
For the fifth year in a row **Ken Waites, M.D. was selected as the Best Educator** in the Fundamentals 2 module. The Cardiovascular Module directed by **Silvio Litovsky, M.D.** received the award for Best MS1 Organ System Module. And **Jennifer Gordetsky, M.D. was lauded as the Best Educator** in the Reproductive Module.

Additional pathology faculty and their courses nominated by the students for award consideration included: **nominee for the Best Introductory Module** was Fundamentals 2 directed by **Peter Anderson, D.V.M, Ph.D.** and **Ken Waites, M.D.** Nominees for the award of Best Organ Module included the Pulmonary Module directed by **C. Bruce Alexander, M.D.**, the **Hematology-Oncology Module** directed by **Vishnu Reddy, M.D.**, and the Reproduction Module directed by **Jennifer Gordetsky, M.D.**

Kudos to all pathology teaching faculty who help to make the pathology undergraduate teaching program a rousing success.

UAB grant will use DNA and RNA sequencing to decipher thrombotic microangiopathy

by Jeff Hanson - UAB Reporter



The lab team of Long Zheng, M.D., Ph.D., the Robert B. Adams Endowed professor and director of the Division of Laboratory Medicine in the Department of Pathology, who is seated, bottom left. Clockwise from Zheng, they are Catherine Zander, Ph.D., Jenny McDaniel, M.D., Vikram Pillai, Ph.D., Liang Zheng, Ph.D., Nicole Kocher, B.S., and Huy Pham, M.D., Ph.D. Standing in the center (pink shirt) is Wendy Cao, M.D., Ph.D.

much smaller portion of hemolytic-uremic syndromes are caused by an innate immune system problem — dysregulation of the complement system, whose normal purpose is to help antibodies and white blood cells clear pathogens from the body.

Lastly, besides these three categories with known causes, there is another group of TMA cases that have no clear cause. The TMA may occur when there is some infection, after a bone marrow transplant, in some cancers, with certain drugs or during pregnancy.

Zheng and his UAB colleagues will look for the factors that cause TMA in patients where the cause is unknown, and they will look for factors that act as triggers in patients with known causes. They plan to get a sample of blood when patients appear in the emergency department, isolate the white blood cells, and do DNA and RNA sequencing. The goal is a total of 30 to 50 patients over five years. Gene expression can then be compared in the same patient when he or she goes into remission.

“We could find something really significant, and the collected data will provide a resource for future study,” Zheng said. One hypothesis is that some TTP patients who already have the ADAMTS13 deficiency will also show complement system activation as well. “They could

[University of Alabama at Birmingham](#) researcher X. Long Zheng, M.D., Ph.D., has received a five-year, \$2.5 million National Institutes of Health grant to study the pathogenesis of thrombotic microangiopathy, or TMA. In simple terms, this means looking for factors that cause or aid the onset of extensive microscopic clots in small blood vessels throughout the body. Though tiny, these spots can damage kidneys, heart and brain, and they can cause death.

“If you look at a tissue sample in the microscope,” said Zheng, the Robert B. Adams Endowed professor and director of the Division of Laboratory Medicine at the UAB [Department of Pathology](#), “and see microthrombi — spots where the tissue is blocked from blood flow and red blood cells are sheared and ripped apart — it is called thrombotic microangiopathy.”

Most of the TMA cases result from three known categories of either internal or external causes. First are the deficiencies of the human enzyme ADAMTS13 that can cause the subset of TMA cases known as thrombotic thrombocytopenic purpura (TTP).

The second and third categories both cause a type of TMA known as hemolytic-uremic syndrome. A majority of these cases are caused by *E. coli* bacterial infection.

“Say you eat a hamburger that is not well-cooked and have diarrhea for a few days, and later have kidney failure,” Zheng said. “That is classic hemolytic-uremic syndrome.”

In hemolytic-uremic syndrome, the red blood cells break as they squeeze past the microscopic clots, and the debris clogs the filtering system of the kidney. A

Zheng and his UAB colleagues will look for the factors that cause TMA in patients where the cause is unknown, and they will look for factors that act as triggers in patients with known causes.

DNA and RNA sequencing to decipher thrombotic microangiopathy ... cont'd...

play a synergistic role,” he said.

At the University of Pennsylvania, Zheng’s co-investigator Wenchao Song, Ph.D., will provide Zheng’s lab a mouse model that has complement dysfunction, which will then be bred with ADAMTS13-deficient mice to create mice with double hits, and see whether anti-complement antibody, eculizumab, is protective. About 80-90 percent of the grant funds will be spent at UAB.

Zheng and his UAB colleagues will also do DNA whole-genome sequencing of about 50 TTP patients. “Over the past 10 years at UAB,” Zheng said, “my colleagues have treated more than 100 patients with TTP, and about 80-90 percent survived. We can look at these patients’ DNA and RNA to learn something new.”

Zheng has assembled a team that includes physicians and nurses in Transfusion Medicine, the Emergency Department, and researchers in the [Divisions of Laboratory Medicine and Informatics](#). It also includes five M.D./Ph.D. researchers in Zheng’s lab, with plans to hire more.

Highlights from Improving Diagnosis in Health Care, the New Report from the National Academy of Medicine - by Virginia Duncan, MD, PGY-3

The 2000 publication of the Institute of Medicine (IOM) report “To Err is Human” and their follow-up 2001 report “Crossing the Quality Chasm” summarized the under-recognized problem of medical error and provided a comprehensive set of recommendations as a blueprint for improvement. But just as importantly, these reports collectively heightened national awareness of patient safety, and catalyzed a movement toward quality improvement in medicine which continues to gain momentum.

However, these early reports focused mainly on treatment-based error (e.g. medication errors, surgical errors and hospital-acquired infections), rather than on *diagnostic* error. A new report from the National Academy of Medicine (formerly the IOM), published in September 2015, seeks to fill this gap.

Importantly for pathologists, also missing from the early IOM reports was a focus on the consultative services, including anatomic pathology and laboratory medicine. This updated 2015 report brings pathology into the spotlight, highlighting the importance of autopsies in defining diagnostic error; the rising prominence of molecular diagnostics; and the importance of maintaining the integration of pathology into medicine as a whole.

At 450 pages, the new report provides a comprehensive literature review of the issues surrounding diagnostic error, and organizes a set of recommendations for current and future directions into 8 overarching goals. As an initial step toward this ambitious objective, the authors sought to distill the varying existing definitions of diagnostic error into one patient-centered definition: diagnostic error is “The failure to (a) establish an accurate and timely explanation of the patient’s health problem(s) or (b) communicate that explanation to the patient.” The goals are as follows:

Diagnostic error is “The failure to (a) establish an accurate and timely explanation of the patient’s health problem (s) or (b) communicate that explanation to the patient.”

- Goal 1: Facilitate more effective teamwork in the diagnostic process among health care professionals, patients and their families.
- Goal 2: Enhance health care professional education and training in the diagnostic process.
- Goal 3: Ensure that health information technologies support patients and health care professionals in the diagnostic process.
- Goal 4: Develop and deploy approaches to identify, learn from, and reduce diagnostic errors and near misses in clinical practice.
- Goal 5: Establish a work system and culture that supports the diagnostic process and improvements in diagnostic performance
- Goal 6: Develop a reporting environment and medical liability system that facilitates improved diagnosis by learning from diagnostic errors and near misses.
- Goal 7: Design a payment and care delivery environment that supports the diagnostic process.
- Goal 8: Provide dedicated funding for research on the diagnostic process and diagnostic errors.

Three broad themes run throughout the publication and are emphasized within every goal. First, a patient-centered approach is necessary for an effective diagnostic process, and requires equal partnership between patients and healthcare professionals at every step. Second, the iterative and inherently uncertain environment of the diagnostic process necessitates a flexible approach as well as continual

Highlights from Improving Diagnosis in Health Care, the New Report from the National Academy of Medicine - by Virginia Duncan, MD, PGY-3... cont'd...

and effective communication. Finally, the authors emphasize that an approach that takes into account the interrelationships among systems, rather than a laser focus on details, is necessary for successful navigation through-and improvement of - the diagnostic process.

For pathologists, this report underscores the importance of continuing our ongoing efforts toward improving diagnosis and patient safety, consideration of how we can bring to bear our unique training in quality control and quality assurance to the challenges of diagnostic error, and the importance of active engagement in the diagnostic process as a whole. Given the explosion of attention garnered by the first IOM reports from over a decade ago, and the resultant sweeping changes, the potential exists for this new report to inform policy and research funding directions at the highest levels.

References

1. Institute of Medicine. *To Err is Human: Building a Safer Health System*. Washington, DC: The National Academies Press; 2000.
2. Institute of Medicine. *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, DC: The National Academies Press; 2001.
3. National Academies of Sciences, Engineering, and Medicine. *Improving Diagnosis in Health Care*. Washington, DC: The National Academies Press, 2015.

The Foundation for Mitochondrial Medicine, UAB and Seahorse Bioscience announce establishment of comprehensive mitochondrial patient care clinical program. [by Jim Bakken](#) September 23, 2015

The Foundation for Mitochondrial Medicine, the [University of Alabama at Birmingham](#) and Seahorse Bioscience today announced the creation of the Foundation for Mitochondrial Medicine Program at UAB — a comprehensive clinical program for the diagnosis of neuromuscular mitochondrial diseases using precision medicine models for monitoring therapeutic interventions.



Victor Darley-Usmar

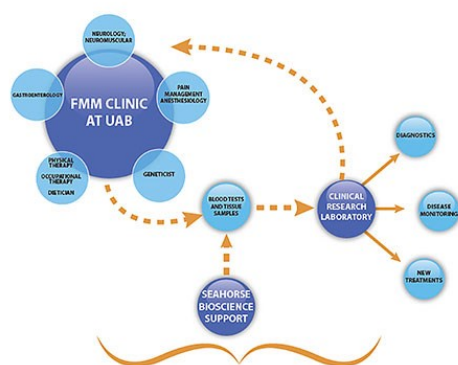
The shared academic, philanthropic and medical mission of the clinic is to revolutionize the treatment and diagnosis of mitochondrial diseases by establishing and integrating state-of-the-art techniques in bioenergetics and therapeutics using a precision medicine approach. The clinic plans to realize this vision by developing two parallel components: 1) a monthly multidisciplinary clinic to evaluate and care for adults and pediatric patients with mitochondrial disease and 2) a reference laboratory for metabolic bioenergetics focused on establishing mitochondrial-targeted clinical, noninvasive laboratory measurements and instruments.

“By establishing the clinic and sharing this vision, we plan to address the unmet clinical, diagnostic and therapeutic needs of the mitochondrial patient community,” said Laura Stanley, Executive Director of FMM. “Clinical needs of the patient community will be coordinated under one roof, and multiple specialists will join together to serve complex patient populations whose symptoms

require the collective knowledge of neurologists, geneticists, gastroenterologists and others. UAB and Seahorse Bioscience have made revolutionary advancements in the field of bioenergetics, and UAB’s established research expertise and longstanding work in neuromuscular diseases make it the ideal location for the program.”

Mitochondrial disease can be caused by genetics and mutations to the mitochondrial or chromosomal DNA or can be acquired due to metabolic, aging or environmental stress. Despite significant advances in recognizing, diagnosing and treating patients over the last 40 years, there are still lacks of effective treatments that are targeted to the specific deficit in a patient. The precision instrumentation developed by Seahorse Bioscience and the bioenergetics testing from UAB will allow advances in metabolic and genetic analysis to be applied to the diagnosis and treatment of patients with mitochondrial disorders. Mitochondrial dysfunction is an underlying cause of many neurodegenerative diseases, cancer and cardiometabolic syndromes. From Parkinson’s to Alzheimer’s, diabetes and beyond, an understanding of mitochondrial stresses can lead to better treatments and quality of life for many.

UAB has a tradition of excellence in research and participation in clinical trials. UAB is also uniquely placed to advance the field of diagnostics, biomanufacturing systems and consumable labware products for biological research. Scientific expertise in mitochondrial medicine is longstanding at UAB and is available through a network of departments and the centers, especially the Center for Free Radical Biology. The UAB Mitochondrial Medicine Laboratory was established in 2011 in the Department of Pathology in the School of Medicine, and has been pioneering translational tests to assess mitochondrial function through noninvasive tests in human subjects.



“The most serious diseases that affect developed nations, such as atherosclerosis, neurodegeneration and diabetes, are known to involve changes in bioenergetic health,” said Victor Darley-USmar, Ph.D., endowed professor of mitochondrial medicine and pathology, vice-chair for research in the UAB Department of Pathology, and scientific director of the program. “The challenge is to translate the findings in basic research in mitochondrial function and the pathology of disease to the clinic, and this program will be a major step toward achieving that aim. For the first time, we will apply new means of measuring bioenergetic health to the management and care of patients with mitochondrial diseases.”

Seahorse Bioscience developed the enabling technology upon which bioenergetics measurements, for the first time, can provide the necessary precision and reliability required to establish Clinical Laboratory Improvement Amendments (CLIA) tests for mitochondrial pathologies. Seahorse is the industry leader in metabolic analyzers

and assay kits for measuring cell metabolism in live cells, in real time. XF Technology and stress test kits render the understanding and diagnosis of mitochondrial disease into a simple, efficient and user-friendly process, enabling researchers to understand better how bioenergetics regulates cellular function. Utilizing XF Technology and a bioenergetics stress test, researchers will measure and analyze respiratory complex activities and mitochondrial DNA damage in white blood cells and platelets from blood samples. This information will then form the basis of a Bioenergetic Health Index (BHI). The test is much easier to administer than a diagnostic muscle biopsy, and can effectively monitor the progression and response of patients to treatment. An important objective for the first three years of the UAB Program and Clinic will be to validate and provide CLIA certification for these tests using the XF platform.

“One of the keys to the resurgence in mitochondrial research and treatment has been our ability to redefine metabolism in the context of the complete cellular architecture of a living cell,” stated David Ferrick, chief scientific officer of Seahorse Bioscience. “Making this complexity addressable allows researchers and physicians to ask and answer questions that were out of reach, and thus limited them to theory and speculation. The combination of compelling patient advocacy by the FMM, basic and clinical expertise of UAB, and enabling technology from Seahorse will be the perfect storm for mitochondrial diseases.”

--article reprinted from the [UAB Media](#) page.

Pathology Publications:

Kimberly J. Dunham-Snary and Scott W. Ballinger. *Mitochondrial-nuclear DNA mismatch matters* [Science](#) 25 September 2015: 349 (6255), 1449-1450. [PMID: 26404813](#)

Rajeev Samant, Ph.D. - Collaborative work from Dr. Samant's laboratory was published: Yu VZ, ... **Samant R.S.**, et. al. (2015) *Nuclear Localization of DNAJB6 is Associated with Survival of Patients with Esophageal Cancer and Reduces AKT Signaling and Proliferation of Cancer Cells.* [Gastroenterology](#), 5085(15),01193-2. [PMID: 26302489](#)

William E. Grizzle, Ph.D. - Recently, a “Notice of Proposed Rule-Making” (NPRM) was published with the goal of modernizing, strengthening, and making more effective the Federal Policy for the Protection of Human Subjects that was promulgated as a Common Rule in 1991 (1). Specifically, this NPRM proposes future changes, after a compliance date, to the Common Rule requiring consent for nearly all research on biospecimens, even when the specimens are de-identified or anonymized. Currently, most translational research using archival collections is performed without problems based on a waiver of consent by the local IRBs. If this were no longer permitted except in very rare circumstances, translational research would be crippled and many advances in medical care would be delayed. This proposal would also reduce research studies focused on minorities, increase racial disparities, and introduce biases into research because only selected patients will be studied. Excerpt reprinted by permission from the American Association for Cancer Research.

Grizzle WE. *Missed opportunities and lost lives: consequences of some proposed changes to regulations on research with human tissues.* Clin Can Res. 2015 Oct 19. [Epub ahead of print]. doi:10.1158/1078-0432.CCR-15-2513. [PMID: 26482038](#)

Pathology Grants Awarded...

YABING CHEN

VA

VA-IPA "Yong Sun"

\$113,456 4/1/15—3/31/17

VICTOR DARLEY-USMAR

NIH

Comparative Energetics and Aging - Core D

P30 AG050886

\$114,758 07/15/15 - 06/30/20

NIH/Emory University

"Diverse Roles of Reactive Oxygen Species and Inflammation in Vascular Disease"

T437148

\$7,000 08/01/15 - 04/30/16

UAB/SOM (AMC21)

"Integrating Energetics with Personalized Medicine"

\$100,000 09/01/15 - 08/31/16

XU FENG

NIH/Cedar Sinai Medical Center

Prostate Cancer Bone Metastasis Biology and Targeting

P01CA98912 PO 0001131984

\$61,425 03/03/15 - 02/29/20

JENNIFER GORDETSKY

SOM Dean Research Award

"Tumor Board Case Development and Virtual Microscopy for Medical Students"

\$4,000 09/01/15 - 08/31/16

ZDENEK HEL

NIH / Univ of Cape Town, South Africa

"Combination Treatment for Protection Against HIV-1"

R01HD083026

\$787,500 03/23/15 - 02/29/20

NIH

"The Guts of HIV: Innate Immune Dysregulation as a Central Mechanism of Gastrointestinal and Liver Disease in HIV-1-infected Individuals"

R01 DK108353

\$1,624,995 09/24/15 - 08/31/20

JOSEPH MESSINA

VA

VA-IPA

"Trauma and Hemorrhage-Induced Skeletal Muscle Insulin Resistance" John Franklin

\$144,274 04/01/15 - 03/31/17

VA

VA-IPA

"Trauma and Hemorrhage-Induced Skeletal Muscle Insulin Resistance" Tatyana Gavrikova

\$119,744 04/01/15 - 03/31/17

MOON NAHM

NIH

"Acquired Deficiency of Innate Immunity (ficolin-2) Among Elderly Adults"

R01 AG050607

\$1,580,250 08/15/15 - 04/30/20

RAKESH PATEL

NIH

Nitrite Dependent Protection Against C12 Gas Toxicity Role of Chlorinated Lipids

U01 ES023759 Admin Supplement

\$99,995 08/15/15 - 06/30/18

New Health Sciences

Research Agreement with New Health Sciences and UABNEW

HLTH SCIENCE

\$67,473 09/11/15 - 09/10/16

Selvarangan Ponnazhagan

DOD

Osteoimmune Mechanisms of Segmental Bone Fracture Healing and Therapy

W81XWH-15-1-0314

\$294,000 08/18/15 - 02/28/17

Ed Postlethwait

NIH

Apical Trans-Membrane Electron Transport Drives ELF Reducing Capacity - R21 ES024203

\$404,250 09/30/15 - 08/31/17

Rajeev Samant

UAB/CCTS/ADDA

Development of a High Throughput Screen for Inhibitors of EMT

\$50,000 08/01/15 - 07/31/16

Ken Waites

Nabriva Therapeutics AG

Comparative In Vitro Activities of Nabriva Lefamulin (BC-3781) and Other Antimicrobial Agents Against Human Mycoplasma

NABRIVA

\$21,750 07/31/15 - 06/30/16

Casey Weaver

UAB/SOM (AMC21)

Integrating Energetics with Personalized Medicine

\$100,000 09/01/15 - 08/31/16

NIH

Gene Regulatory Networks Controlling Effector and Regulatory T Cell Balance in IBD

R56 DK106343

\$299,640 09/15/15 - 08/31/16

Majd Zayzafoon

NIH/Cedar Sinai Medical Center

Prostate Cancer and Bone Metastasis: Biology and Targeting

PO-01CA098912-11

\$824,670 03/03/15 - 02/29/20

ACLPS 2016—A Must Attend Event!!

ACLPS SCIENTIFIC PROGRAM HIGHLIGHTS

Thursday, June 2, 2016 - Afternoon Opening Session

Opening remarks: Marisa B. Marques, MD and Jay McDonald, MD, PhD

New treatments for Thrombotic Thrombocytopenic Purpura - Long Zheng, MD, PhD

Promising future for patients with sickle cell disease - Tim Townes, PhD

Considerations for labs offering "Precision Oncology" - Neal Lindeman, MD

Good Terminology Practices for Laboratory Medicine - James Cimino, MD

Diabetes, past, present and future - David Sacks, MD, PhD

Friday, June 3, 2016 – Morning Break-Out Sessions

Young Investigators sessions

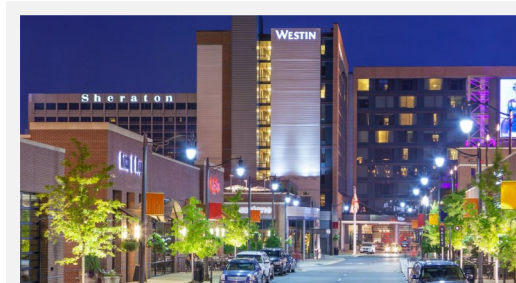
Friday, June 3, 2016 – Afternoon Plenary Session

Cotlove Award lecture: 35 years of HIV epidemic - Michael Saag, MD

Laboratory role in anticoagulation monitoring in 2016 - Mark Crowther, MD, PhD

Institute of Medicine (IOM) report "Improving Diagnosis in Health Care" - Michael Laposata, MD, PhD

Direct-to-consumers laboratory tests: Point and Counterpoint - Robin Lorenz, MD, PhD, Robert Hardy, PhD, and Alexis Carter, MD, moderated by Bruce Alexander, MD



Saturday, June 4, 2016 – Morning Session

Ellis Benson Award lecture - TBA

Laboratory Medicine: The Next 50 Years

Patient Blood Management (PBM) - Marisa B. Marques, MD

How to prepare your lab for patients with Ebola - Scott Koepsell, M.D., Ph.D.

What is new with troponin measurements - Fred Apple, MD, PhD

Regulatory issues with laboratory-developed tests (LDTs) - Jonathan Genzen, MD, PhD

Molecular methods in Microbiology - Audrey N. Schuetz, MD, MPH, D(ABMM)

2016 ASFA Apheresis guidelines - Joseph Schwartz, MD, MPH

Wei Zhao, MD, PhD Remembered

Former Pathology resident and fellow Wei Zhao, MD, PhD (1999-2003) passed away last November after a year long battle with cancer. People from the Brown Cancer Center at the University of Louisville collected donations to honor Dr. Zhao's legacy with an engraved brick and a dedicated tree in front of the Cancer Center "Garden of Hope" - According to her husband Wolfgang Zacharias "It clearly reflects how much Wei was appreciated and loved as a co-worker and friend to many."



Dear UAB Department of Pathology Friends and Colleagues:

The UAB Department of Pathology is recognized nationally for excellence in biomedical research, undergraduate and graduate medical education, and diagnostic pathology. This rise to prominence has been accomplished through the hard work and dedication of numerous Department of Pathology faculty and trainees who have made UAB a phenomenal environment for pathology education and clinical practice. Several decades ago, the former Departments of Anatomic Pathology and Clinical Pathology of the University of Alabama School of Medicine merged into a single Department of Pathology of the UAB Health System. More than 250 residents have received their graduate training in Pathology at UAB and have gone on to populate the state, region and the nation. In fact, the vast majority of Pathologists in the state of Alabama have received some or all of their training here at UAB. This program of excellence in graduate medical education has been appropriately balanced by a world-class graduate program that has similarly trained generations of scientists who fill academia, industry and government service. Our department has been bolstered in recent years by an ever increasing number of post-doctoral fellows, clinical fellows and junior faculty members who have achieved academic, research, and/or clinical excellence, and ascended to leadership positions at UAB or other institutions.

Please consider making a gift to the Department of Pathology at UAB to support our missions of clinical practice, teaching, research and service. Any amount would be most gratefully received and would be fully deductible*. One could direct it to a particular area of need, to fund current and future endowed professorships or create new awards, prizes or similar recognition opportunities to honor yourself, a family member, a favorite professor, etc.

We would be pleased to assist you and your professional advisors in including the UAB Department of Pathology in your estate plan or in exploring other giving strategies. A simple tear off sheet is found below.

* One should always check with their tax advisor.

Thank you for your serious consideration of this request.

Please fill out each of the 3 Sections:

If anyone has any news items, accolades, etc. to be put in the quarterly newsletter, please send it to the Path In Focus e-mail address at: pathinfofocus@uab.edu.

Thank you.

Kathy Coleman

A1—Enclosed, please find my contribution to the UAB Department of Pathology in the amount of:

___ \$50
___ \$100
___ \$500
___ \$1000
___ Other: _____

Please make all checks payable to the UAB Department of Pathology and return them to Ms. Lynne Roden, Departmental Administrator, 500 22nd Street South; Suite JNWB 404, Birmingham, AL 35294-0500.

Cont'd...

A2—Please contact me to discuss further:

Name: _____

Address: _____

Telephone Number: _____

E-mail Address: _____

*Please indicate your preferred means of communication.

B—I wish to direct this gift to the Department towards:

___ Where the need is the greatest

___ Teaching

___ Research

___ Named Chairs or Professorships

___ Awards for teaching/research/clinical excellence

___ Naming opportunities (Rooms, collections, equipment, etc.)

C—Person(s) and complete address to be acknowledged for tax purposes:

Do you want this gift to be anonymous? Yes ___ No ___

Do you want to honor a particular person or event?

Specifics: _____

D—If you prefer to donate via credit card, please call the UAB Development office at (205) 975-5659.