# WIRGINIA HEALTH SYSTEM UVA Department of Pathology

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# A Message from the Chairman

NIVERSITY

"Publish or perish" has long been an aphorism in academia but one wonders about the health of traditional outlets of medical literature in the current age of the internet and digital media. The plight of declining subscriptions to newspapers and magazines is well known, with some survivors successfully navigating the transition to online content, but with many others indeed perishing in the digital age. One may wonder how medical journals are faring and what changes have been seen in this arena over the past few decades. It turns out that the Department of Pathology at The University of Virginia is a good place to make queries about the health and changes in medical and scientific literature. Over the past 10 years, eight faculty have served as editor or associate editor of the following journals, representing some of the top journals in our field:

*Clinical Chemistry* (Jim Boyd, David Bruns) *Diagnostic Molecular Pathology* (Mark Stoler) *Intl. Journal of Gynecological Pathology* (Mark Stoler) *Journal of Immunology* (Tim Bullock, Jim Gorham) *Journal of Immunotherapy for Cancer* (Tim Bullock) *Journal of Neuropathology and Experimental Pathology* (James Mandell)

Laboratory Investigation (Jim Gorham) Practical Reviews in Pathology (Stacey Mills) The American Journal of Clinical Pathology (Mark Wick) The American Journal of Surgical Pathology (Stacey Mills)

In general, the basic tenets of traditional medical and scientific publications haven't changed much – journals are still seen as the primary venue in which to vet and report advances and findings in the field, and the process of rigorous peer review remains intact. However, the business side of publication and how practitioners consume this information has changed, parallel to the changes that have been seen in the lay press.

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We have asked Stacey Mills, MD (Editor-in-Chief, *The American Journal of Surgical Pathology*, 2000-present) and David Bruns, MD (Editor-in-Chief, *Clinical Chemistry*, 1990-2007), to describe some of the changes they have seen in our "In Focus" section of this year's newsletter.

In other news about our Department, you will see that we are busy adding to the literature as well as guiding its publication. The learners in our Department and their faculty mentors have contributed over 115 publications in the last year. Our research portfolio includes 12 new grants and contracts awarded to our

faculty in the last year, worth over 12 million dollars in total support. This complements 18 other active grants and contracts, which provided over 5 million dollars in research funding in 2016. Please turn the page to learn about prominent editors' views on Pathology progress over the years, meet the newest members of our academic family, and see what else we have been up to in the past year.

Christopher Moskaluk, M.D., Ph.D.



### **UVA** Path Report

## In Focus: Editors Eye Pathology Progress

#### Laboratory Medicine, by David Bruns, M.D.

In this issue of *UVA Path Report*, Chris Moskaluk has reflected on "the health of traditional outlets of medical literature in the current age of the internet and digital media". He invited me to write about the changes that I saw as editor of *Clinical Chemistry*, from 1990 to 2007. On reflection, the thing I find most interesting is that, despite upheavals in publishing during those years, *Clinical Chemistry* flourished financially and by every measure of scientific impact, and did so without levying submission fees, page charges or open access fees. This outcome was the result of many factors; below are some that I suspect were important. Although I didn't realize it at the time, the environment of the Department of Pathology made several of them possible.

In 1990, the Journal's impact factor was falling as was the number of subscriptions. The Journal's print advertising, a key source of revenue, was decreasing; a plot of the number of ad pages per year versus calendar year showed a straight line downward. Extrapolation of the line suggested that ad pages would reach zero a few years hence. A colleague suggested that we should take the high ground and announce one year before the inevitable that the Journal would no longer accept ads. The clinical chemistry association, AACC, which publishes the Journal, was not enthralled with that idea.

Fortunately, the AACC leadership judged the success of the Journal based not on financial performance, but on scientific impact, and they gave the editor a free hand. I was able to subject all submitted papers to stricter peer-review, and had papers reviewed by 2-3 experts on clinical aspects, analytical aspects and the biomarker or gene being measured. Experts in specialty areas such as lipids and toxicology agreed to serve as Associate Editors. Notably Jim Boyd of our department became Deputy Editor and reviewed the statistics in countless papers. I pursued getting the Journal online very early. Stanford University Library's "HighWire Press" agreed to host the Journal online, thus linking us with major pioneering journals including NEJM and Science. And we worked with Stanford and two other journals to develop an online manuscript submission and tracking system, "Bench>Press", now used by scores of Journals including Clinical Chemistry.



Importantly we signaled that we viewed the field of clinical chemistry very broadly, encompassing all endeavors in which chemistry (including biochemistry) was used to address clinical problems. The Table of Contents was divided into sections so that we could advertise our interest in receiving papers in nontraditional areas such as "Molecular Diagnostics" and "Proteomics".

The move, in 1990, to view Molecular Diagnostics as part of clinical chemistry, although controversial at the time, seemed a natural decision for a person who grew up in the pathology department at UVA. As a few readers may recall, my wife, Liz, and I did research here in the 1970s and 1980s on control of gene expression by vitamin D. Reading the relevant scientific literature, and watching which grants the NIH was funding, anyone could see that breakthroughs in genetics were coming. We knew that scientific breakthroughs that affect medicine often have their first clinical impact in diagnostics. In the early 1980s, while most clinical chemists elsewhere were working on classical areas of the field (enzymes, toxicology, electrolytes etc.), John Savory, Mark Lovell, Ted Mifflin, Liz and I, and several others were meeting periodically to learn about nucleic acid techniques and how we might use them diagnostically. Our colleagues in Jordan Hall were generous in meeting with us, just as they had been in helping Liz and me in our first forays into nucleic-acid techniques earlier. John found ways to quietly move some clinical chemistry resources into molecular diagnostic testing. Diagnostic opportunities appeared quickly (although not ways to get paid for the testing), and we were poised to move rapidly when new techniques appeared. So for me it seemed natural in 1990 for the journal Clinical Chemistry to move into molecular diagnostics.

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## In Focus: Editors Eye Pathology Progress

#### Surgical Pathology, by Stacey Mills, M.D.

The American Journal of Surgical Pathology (AJSP) began its "career" at the same time that I began mine, in 1977. These were the days of simple case series. You collected a group of cases representing an entity, documented the histologic and clinical features, and wrote them up for publication. The histologic features were predominantly based on H&E stains. Immunohistochemistry didn't exist. Neither did HIPAA or IRB regulations. Patient's names, of course, were not disclosed and identifiable images were not published without permission, but otherwise there was no consent form or IRB approval required.

The life of a manuscript in the '70s began as a handwritten document, written and rewritten until you had a cogent handwritten draft. This was taken by a departmental secretary (now administrative assistant), and converted to a more legible typed form, double or quadruple spaced so that you could make additional changes on that draft. References? There was no End Note or Reference Manager software. References were written out by hand, manually organized, numbered, and the numbers handwritten in the text at the appropriate points.

For illustrations, black and white print photography was the only form journals would accept. The premier camera lived in the department of biomedical communications and was supervised by an extremely good photographer. You set the field and magnification and the photographer did the rest, adjusting the condenser, light and focus, and capturing your image on a large format 4"x5" negative. You took the subsequent prints (3 copies), trimmed them carefully on a paper cutter, labeled them on the back in pencil and packaged them up into three "figure packets". The figure packets and three copies of the manuscript were mailed (snail, not e-) to the journal office, along with a cover letter. Then you waited. There was no acknowledgement of receipt, so you hoped it got there.

When I first began editing *Modern Pathology* in 1995, we were still receiving manuscripts as hard copies by snail mail. These arrived daily, the copies got sorted; one came to me for reviewer assignment and, after that, they were mailed out to two selected reviewers with the third copy staying in the office. With about 750 manuscripts a year, each going out to



two reviewers, then back to the authors for either revision or rejection, the files took up a lot of space and the yearly postage charges were in the thousands of dollars.

When I switched to editing AJSP in 2000, we were still receiving hard copy manuscripts but within about a year we switched to online submissions using the Editorial Manager system. Digital versions of the text and illustrations replaced physical copies. I was initially not at all comfortable with this change and had visions of server crashes, delays, lost manuscripts, etc. None of this ever came to be and the change has been a vast improvement for both authors and editors, saving time, space, and postage and providing much better author feedback.

Just as the manner of submitting and handling manuscripts has changed dramatically in the last decades, their content has changed as well. Pure H&E morphologic studies, once the bread and butter of surgical pathology literature have been largely replaced by submissions dealing, at least in part, with newer molecular technologies. Although newer techniques have brought tremendous advancements, there is still (and always will be) room for careful morphologic observations. It is always disappointing when a manuscript devotes only a few lines to what the lesion actually looked like on an H&E section and then devotes many pages to ancillary studies of variable diagnostic value. The ability to write a careful morphologic description, moving methodically from low to higher magnification is a skill that should not be allowed to atrophy. As an example hunt up the article on nasopharyngeal angiofibroma by Steve Sternberg, published in Cancer in the 1950s. This is an absolutely exquisite description of the microscopic appearance and variations of this lesion. There's really nothing else to say on the topic, and almost no one else has tried.

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## In Focus: Editors Eye Pathology Progress

#### Laboratory Medicine Continued.

A desire to get papers in a new area is not a guarantee of good papers. Fate was on our side when we looked for Associate Editors for *Molecular Diagnostics*. I was lucky to meet and recruit two leading scientists as Associate Editors: One was Dennis Lo, who pioneered diagnostic applications of cell-free nucleic acids in plasma, including applications in the prenatal diagnosis of trisomies by characterizing fetal DNA in maternal plasma. The second was Carl Wittwer, a pathologist who developed rapid-cycle PCR (usually just called "PCR" these days), real-time PCR, melting curve analysis, film array analysis and the analyzers called LightCycler and BioFire, among others. Lo and Wittwer raised the standards for publication of molecular diagnostics papers in *Clinical Chemistry*.

As with molecular diagnostics, the move to proteomics followed naturally from events in the Department of Pathology. In the mid-1980s, John Savory obtained an NIH grant to bring triple-quadrupole mass spectrometry to our department. Dave Herold, when he was a resident and later an Assistant Professor, used that instrument to study prostaglandins and organized a course for us on mass spectrometry. At about the same time, Liz and I had the great good fortune to provide our favorite protein (calbindin-D9k, later called S-100G) to Don Hunt, in the Departments of Chemistry and Pathology, for amino-acid sequencing; this adventure showed us up close the power of mass spectrometry for protein analysis. While many clinical chemists continued to think of mass spectrometry as a technique for small molecules, the pioneers like Don Hunt showed that proteins, too, were fair game. So, the Table of Contents got a heading of "Proteomics" and the Journal became the highest-impact journal actively publishing in that field.

These and various other efforts to stay ahead of the field paid off. The impact factor of the Journal increased steadily over a decade, rising from 1.6-something to over 7.7, moving it ahead of competing journals in laboratory medicine, analytical chemistry, endocrinology, and pathology. With steady growth in the number of times that the Journal was cited each year, librarians held onto their subscriptions. The online presence increased the Journal's reach and revenues. Despite the virtual absence of ads in its print or online editions, the Journal was even profitable.

It appears in retrospect that the key to survival and, really, to success of the Journal, was to look to a future that could be surmised from trends in science, medicine and publishing. These trends included not only the growth of molecular diagnostics and proteomics, but also the rise of digital communication, the increasing demand for transparency in reporting of clinical studies and the increasing scrutiny of the quality (and value) of peer review. The faculty and trainees in the Department of Pathology saw important trends in pathology and laboratory medicine and thus set the stage for the success of *Clinical Chemistry*, which continues today.



A recent Letter to the Editor of *Clinical Chemistry* written by Dr. Bruns and colleagues Dr. Garrett Mullins and Dr. James Harrison describes a novel use of smartphones in monitoring blood sample transport through hospital pneumatic tube systems.

A video demonstration of their findings can be found at: https://news.virginia.edu/content/watch-smartphones-wildride-through-hospitals-pneumatic-tube-system

## In Focus: Editors Eye Pathology Progress

#### Surgical Pathology Continued.

Electron microscopy (EM) serves as a cautionary tale about the rise and fall of technology. Authors such as Hector Battifora and Jerry Taxy wrote numerous articles describing the electron microscopic appearance of a wide variety of tumors. The more enthusiastic in the field postulated that electron microscopy would ultimately allow the distinction of malignant from benign cells! Today EM remains a valuable tool for renal pathology and still has value for a limited number of other diagnoses (e.g. mesothelioma), but many labs no longer have this technology due to insufficient use to justify its existence. Whereas pathology board exams used to have electron micrographs of classic structures and tumors such as hairy cell leukemia, there are now no electron micrographs on the general AP pathology boards.

Just as EM was peaking as a diagnostic tool, immunohistochemistry (IM) arrived on the scene in the 1980s as the next great diagnostic aid. I was dispatched to the NIH for a one-day course in how to do IM. Initial IM stains weren't very good to say the least. They were done by hand using poorly characterized polyclonal antibodies. Nonetheless, the technique was a major advance and journals began to be flooded with manuscripts utilizing each new antibody. First reports of each new antibody were often based on small series and were overly enthusiastic with regard to its sensitivity and specificity, only to be followed by larger series variably deflating the initial enthusiasm. Eventually, however, most antibodies found their proper place in the diagnostic armamentarium.

It seems unlikely that IM will ever suffer the diagnostic fate of EM due to its established clinical utility, relative simplicity, and growing catalog of diagnostic and prognostic stains. Nonetheless, its glamour has faded to 'routine' status and been replaced by a host of molecular techniques in the morphologic world. These techniques have revolutionized pathology, often validating and occasionally overturning our morphologic taxonomy and ushering in the beginnings of personalized medicine. Here again history has repeated itself with over enthusiastic initial stains used for disease classification pronouncements. In particular, early use of polymerase chain reaction (PCR) in surgical pathology led to problems due to its exquisite sensitivity and lack of morphologic correlation. Early studies, for example purported to show that all sorts



of tumors were related to Epstein Barr virus (EBV) by PCR when in reality, the scattered EBV-containing normal lymphocytes which most of us harbor were being amplified, rather than the neoplasm. Similar mistakes have occurred with regard to human papillomavirus and PCR.

It is not surprising that we hear current pronouncements about the death of traditional histopathology in the face of ever-expanding genomic technologies. We have heard this tale before (see above). There is no doubt that ancillary immunohistochemical and molecular techniques will continue to advance our understanding of disease and in collaboration with the venerable H&E-stained section, advance our appreciation of morphology. These differing techniques should not be viewed as rivals with winners and losers but as complementary tools in the pathologist's armamentarium.

While the role of journals to provide updated, peer-reviewed content to its readers and an archived source of knowledge for future generations is likely to remain indefinitely, the manner in which this content is presented and accessed is clearly undergoing rapid changes. Print subscriptions are decreasing for all journals in all fields as more and more end users get their content electronically. Libraries, always pressed for space, are happy to substitute online multi-journal subscription services like Ovid for paper journals. Publishers are learning to cope with this shift in content presentation, while trying to maintain peer-reviewed guality and a revenue stream to support their endeavors. Though my generation felt comfort in holding a paper copy, younger pathologists are not so inclined and are happy to deal with electronic subscriptions, often through their medical library with no perceived need for a paper copy or personal subscription. For my own part, I've learned to embrace the online journal world, mainly for the ease of searching and storage of content. In the end, how the information is delivered is of little or no importance as long as it gets to the end user. No doubt the future holds even more changes.

## **Research Spotlight**

The Bullock Lab research focuses on understanding the basis of why T cells lose their function in the tumor microenvironment and how to re-functionalize them. Recent studies from Lelisa Gemta have indicated that part of the dysfunctional state may be attributable to the loss of glycolytic activity as a result of aberrant enolase function. He's expanding his studies to look at human tumor infiltrating lymphocytes. Aaron Stevens has been working on elucidating how transcriptional changes in tumor infiltrating lymphocytes regulate their activity, with a particular focus on the transcriptional repressor, BLIMP1. Aaron has also discerned that vaccinating against tumor antigens sustains T cell function in the tumor and substantially enhances their ability to control tumor outgrowth. As our ability to identify new antigens in tumors that arise due to their mutagenesis improves, these vaccination approaches could become very useful. Melissa Gonzalez has been studying how mitochondrial function influences T cell activity and whether regulating fission and fusion can increase T cell function in tumors. She has also been establishing the function of the TNF superfamily member, CD70, on T cells. The lab has an expanding collaboration with the Focused Ultrasound group in Biomedical Engineering in which we will try to understand how this novel technology can be leveraged to augment T cell infiltration and function within the tumor microenvironment. Finally, we have been collaborating with members of the Cancer Center to understand whether standard of care chemotherapies can be integrated with immunotherapy, or whether we can define other chemotherapies that act more synergistically.

The Felder Laboratory is dedicated to discovering the etiology of hypertension and salt sensitivity of blood pressure, the world's most prevalent and costly diseases. Using a multidisciplinary and translational approach, we have deciphered some of the biochemical mechanisms behind these diseases. Furthermore, we have studied their impact on human health through the development of novel biosensor technologies, developed novel diagnostic devices and assays to identify their presence, and developed novel technologies to reduce their economic impact on individuals and society. The work in the Felder Lab has led to over 300 publications, 22 patents, three edited textbooks, \$35M in NIH grant funding, and 9 companies spun out of UVA.

The Goldfarb Lab has made some exciting advances in the realms of megakaryocyte and red cell development. We have found a key factor in normal human megakaryocytes that dictates whether they develop in the manner of fetal/neonatal or adult megakaryocytes. This developmental difference is important as it underlies the clinical problems of thrombocytopenia in neonates and delayed platelet recovery on cord blood stem cell transplant patients. Identification of this fetal masterswitch has enabled design of small molecule inhibitors that can convert fetal-type megakaryocytes into adult-type cells. In the realm of red cell development, we have identified a novel nutrient deprivation pathway in which iron availability dictates erythropoietin responsiveness of erythroid progenitors. Specifically, a protein complex has been identified which couples iron levels both inside and outside the cell with surface delivery of the erythropoietin receptor and with the signaling properties of this receptor. This pathway is relevant to the pathogenesis of anemias associated with chronic inflammation and underlies the development of treatment resistance in anemic patients treated with erythropoietin. These findings also shed new light on the therapeutic mechanism of action of our new anemia therapy, isocitrate.

The Li Lab – A gene is defined as the molecular unit of hereditary information. Genes and their products (RNA and protein) are believed not to intermingle except in cancer. However, we have found isolated examples of chimeric fusion RNAs in the past. This year, we performed, curated, and analyzed nearly 300 RNA-Seq libraries covering 30 different non-neoplastic human tissues and cells as well as 15 mouse tissues. A large number of fusion transcripts were found. Most are tissue unique, while a subset is ubiquitously expressed. We proved function for two examples *Continued on next page*.

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(L to R) Marissa Gonzales, Lelisa Gemta, Dr. Tim Bullock, Aaron Stevens, and Zachary Wallace



(L to R, front row) Dr. Mahabuba Akhter, Dr. John Gildea, Katherine Shiermeyer, Monica Mae Majillo, Dr. Rana Abdel-Fattah, Dr. Peng Xu, and Dr. Robin Felder (back row) Dr. Robert M. Carey





Top, Lorrie Delahanty Bottom (L to R) Katie Freeman, Peter Balagh, Dr. Kamal Alagib, and Dr. Adam Goldfarb (Shadi Khalil not pictured)

## UVA Path Report

## Research Spotlight

(NAR, Babiceanu et al., 2016). Even though we have proven that fusion RNAs as a phenomenon are not unique to cancer, cancer does have different profiles of fusion transcriptomes. In one study, we developed a bioinformatic pipeline to identify prostate cancer specific fusion. One such fusion was found recurrently in prostate cancer, silencing of which resulted in reduced prostate cancer cell proliferation. It likely functions as a long non-coding RNA (Cancer Letters, Oin et al., 2016). While over 30 fusion RNA mining software tools have been developed, they behave differently. We compared the 12 most frequently used tools using simulated data as well as real experimental data. Their performance in terms of sensitivity, positive prediction value, computation time and memory were compared and ranked (Scientific Reports, Kumar et al., 2016).

The Luckey Lab – Many patients are exposed to foreign red blood cells (RBC) via either transfusion or pregnancy. Though only a subset of patients respond by making anti-RBC alloantibodies, RBC alloimmunization represents a significant cause of morbidity and mortality worldwide. For chronically transfused patients who are unfortunate enough to generate multiple alloantibodies, provision of compatible antigen negative RBCs can be both time and resource intensive. In some cases, this can result in an inability to locate an otherwise life-saving therapy. Our research is focused on understanding the molecular drivers of anti-RBC alloantibody production. Specifically, we investigate how cytokines induced by transfusion become translated into the genetic programs required for anti-RBC antibody production and maintenance. Our initial work in mouse models has identified a key role for the cytokine IL-6 in controlling both anti-RBC r cell responses and subsequent alloantibody production. We are now investigating the role of IL-6 and related cytokines in the regulation of patient responses to RBC transfusion. The goal of our research is to better understand the molecular controllers of this pathogenic process in high risk patients such as those with sickle cell disease, and in so doing provide diagnostic and therapeutic targets for further clinical development.

The Mahadevan Lab is focused on understanding RNA toxicity and its role in the pathogenesis of myotonic dystrophy (DM1), the most common inherited muscular dystrophy in adults. The lab also has a strong translational focus on identification of pathways and targets that may be amenable to pre-clinical evaluation. To that end, we have developed the first inducible/reversible mouse model of RNA toxicity and have used it to identify novel pathways such as the TWEAK/ Fn14 signaling pathway and provided a proof of concept for the utility of a therapy that targets this pathway. We continue to have active collaborations with multiple pharmaceutical companies to evaluate novel therapeutic strategies to treat RNA toxicity in DM1. The collaborations are founded by our work and studies aimed at finding and understanding the molecular mechanisms of RNA toxicity especially in skeletal muscle and the heart.

The Mandell Lab – Inclusion body myositis (IBM) is one of the idiopathic inflammatory myopathies that together affect greater than 75,000 Americans. Recent work has suggested that some aspects of IBM pathogenesis may be related to aberrant RNA metabolism. An explosion of basic research, including work done in the lab of our collaborator on this project, Dr. Anindya Dutta, has identified key regulatory RNAs, including microRNAs that have essential roles in muscle differentiation and regeneration. These RNAs are released into the extracellular space, reaching the bloodstream and other body fluids in very stable forms, due to both membrane encapsulation and protein binding. Because muscle makes up nearly half of the total body mass, its RNAs and their metabolic products contribute a large component to body fluids, including blood and urine. Our work over the past year has revealed that a small group of microRNAs, many of which are derived from a cluster on chromosome 14g32, is highly and selectively upregulated in IBM muscle biopsies, and derive from the diseased myocytes, and not the associated inflammatory cell infiltrates. We and others have demonstrated that muscle-specific microRNAs can be detected in human blood plasma. The goal for ongoing work is to profile 30-50 patient blood samples to identify a small panel of plasma miRNAs that will serve as a sensitive, specific and noninvasive blood test for the diagnosis and monitoring of IBM.



Li Lab at a summer party, 2016



(L to R) Dr. Jelena Medved, Dr. Abhinav Arneja, Juan Salazar, and Dr. John Luckey



(L to R) Dr. Mani Mahadevan, Dr. Ramesh Yadava, Qing Yu, and Mahua Mandal



(L to R) Michael Kidd and Dr. Jim Mandell

## Research Spotlight

The Moskaluk Lab has been focused on understanding the role of cofactors that interact with the MYB transcriptional control protein in adenoid cystic carcinoma (ACC). The majority of ACC tumors have translocation mutation of the MYB gene, up-regulating the transcription of this gene and in some instances deleting negative regulatory domains. We have done a survey of known MYB-interacting genes in ACC samples and found that most of them are present in the tumors. We have focused on the CBP/p300 co-regulatory proteins, and have shown by co-immunoprecipitation and proximity ligation assays that MYB-CBP/p300 interactions can be demonstrated in tissue samples of ACC xenograft tumors. In allied efforts we have successfully grown several short term cell lines of ACC tumor cells derived from our ACC xenograft models. We are using these cell lines as model systems to demonstrate the effect of MYB loss and disruption of MYB-CBP/p300 interactions. Our early attempts at RNAi-mediated knockdown of MYB in these cell lines indicate that when MYB gene products are nearly eliminated, the effects on ACC tumor cells is a decreased transition through the G2/M phase of the cell cycle, and an increased rate of apoptotic cell death.

The Tung Lab has published one paper in the *Journal of Immunology*: a second paper is under review: and a third project is under active pursuit. We first documented that autoimmune gastritis (AIG) associated with H+K+ATPase and intrinsic factor autoantibodies occurs in normal mice after Treg depletion. Their strongly Th2-biased effector T cells develop resistance to Treg cell-mediated suppression. We then documented that male meiotic germ cell antigens (MGCA) are neither completely sequestered nor consistently immunogenic. Some egress and maintain Treg cell-dependent tolerance; others are sequestered and are non-tolerogenic. Significantly, sequestered MGCA are targeted in vasectomy, whereas non-sequestered MGCA are targeted in spontaneous infertility. Both MGCA are also expressed as cancer testis antigens and may influence tumor immunity. We presently study the effect of age on autoimmune ovarian disease (AOD) and AIG that develop in the same mice. Adult DEREG mice develop Th2-dominant eosinophilic AOD with Th2 response that targets ZP3, whereas juvenile mice develop severe Th1-dominant and NK/NKT cell-dependent granulomatous AOD, targeting different ovarian antigens. These striking ontogenetic differences are not replicated in the concurrent Th2dependent AIG. Thus two distinct immune mechanisms can be operating in the same juvenile mice against different target organs.

The Vande Pol Lab – Papillomaviruses are the most prevalent sexually transmitted disease and leading infectious cause of cancer in the US, with a yearly economic impact of about \$2.9 Billion (1). Despite a vaccine, lethal clinical disease will be a significant problem for many decades to come, especially in developing nations. The virus expresses two oncoproteins, E6 and E7, whose continuous expression is required to maintain the cancer. Our most recent studies are confirming that the contacts between E6 and p53 are in fact what is important in living cells, and determining if there are additional E6 functions beyond the degradation of p53 that are required for the viral life cycle. A graduate student in the lab, Camille Lewis, is mapping additional features in the cellular enzyme UBE3A that associates with E6, to determine how E6 interactions with UBE3A trigger ubiquitin ligase activity. This may open new therapeutic opportunities. While the cancer associated HPV E6 proteins target the degradation of p53 that is not how most human and animal E6 proteins work. Their E6 oncoproteins inhibit a tumor suppressor pathway called NOTCH. We were the first to report this mechanism of E6 action, and we are extending this observation to explore how E6 proteins in diverse vertebrate species work. Finally, another recently graduated student, Sydney Strickland, discovered a new mechanism of E7 oncoprotein action. She found that E7 manipulates cellular signaling to alter the global translation of cellular proteins in a way that induces the expression of the cellular protein c-myc. We hypothesize that the induction of c-myc by E7 is important in papillomavirus E7 cancer phenotypes and we will be testing this hypothesis in the coming year.



(L to R) Dr. Chris Moskaluk, Craig Rumpel, Dr. Hao Fan, and Dr. Jyoti Thaikoottathil



(L to R) Agata Litwinowicz, Dominik Lenart, Dr. Ken Tung Hui Oiao and Dr. Jessica Harakal



A figure of p53 (purple) bound to the LXXLL peptide motif in the target cellular protein (orange) and E6 (green, yellow, and blue)













**UVA** Path Report

# **First Residents**

Joseph (Joe) Coppock, M.D., Ph.D., was born and raised in Sioux Falls, South Dakota. He grew up working in a family owned shoe business and went on to attend Augustana University in Sioux Falls, earning his B.A. in both Chemistry (ACS Certified) and Biology with a minor in Mathematics. Early immersion in research as an undergraduate led to him to pursue the combined MD/PhD program at the University of South Dakota, where his research focused on modulating the metabolism of HPV-related head and neck cancer cells as a means of enhancing the anti-tumor immune response. As an MD/PhD student, Joe published five research articles, was elected into the Alpha Omega Alpha Honor Medical Society, and was a founding member of SCOPE (Student Club for Ongoing Pathology Education), the USD Sanford School of Medicine pathology interest group. His wife, Sara, works as a nurse in the thoracic-cardiovascular intensive care unit (TCV-ICU) at UVA. Outside of medicine, Joe enjoys reading, biking, hiking and birding, dabbling in photography, exploring new places, and watching professional basketball and tennis.

Jacob Curley, D.O., received his medical training at Oklahoma State University's College of Osteopathic Medicine in Tulsa, Oklahoma. His undergraduate background was in mathematics at Northeastern State University in Tahlequah, Oklahoma. Although Jacob spent the last 8 years in Oklahoma, he is originally from Monroe, Michigan, which he still considers his home state. He is interested in dermatopathology, but also finds the field of bioinformatics highly intriguing. In his free time he loves trail running. He also enjoys participating (as a very mediocre amateur) in the sport of trail ultrarunning. While he'll be very busy this year, he hopes to run another 100-mile race sometime this winter/spring.





Jennifer Ju. M.D., grew up in northern Virginia and briefly left the state to do her undergrad at Brown University where she double majored in Neuroscience and Art History. She returned to Virginia for medical school at UVA where she is excited to continue her training as a Pathology resident. Outside of the hospital, she enjoys exploring what Charlottesville has to offer, from concerts to local festivals to dining out. She looks forward to getting to know everyone better.

Ashley Volaric, M.D., is officially a "triple Hoo" and very happy to be! She went to UVA for her undergraduate education and majored in chemistry with a specialization in biochemistry. During her undergraduate years, she spent every summer conducting research in a membrane protein lab looking at the structures of pathogenic proteins, while spending her free time hiking, running, and exploring Charlottesville with her then-boyfriend (now-husband). After graduating, she spent a year in Alexandria, VA, and worked at a small science consulting company. She enjoyed discovering Washington DC and playing soccer with her friends, but she came running back (guite eagerly!) to Charlottesville the moment she was accepted to UVA School of Medicine. During her time in medical school, she helped lead a pilot project in South Africa training Community Health Workers in diabetes and hypertension management. She returned to South Africa her fourth year to continue the project with additional training in Motivational Interviewing. Her time abroad in the community health setting allowed her to gain a true appreciation for public health efforts, which she hopes to carry over to the pathology realm. She is so thankful and excited to spend another four years at UVA for residency and looks forward to continuing to do what she loves as well - running, hot yoga, walking her dog (or just watching him run with other dogs at the dog park!), hiking and camping, and just spending lazy afternoons on her back patio reading and watching her tomato plants grow. She truly considers Charlottesville her home - a place where she has found her family, both personally and professionally.

## First Year Trainees



### **First Year Fellows**

Ashton Brock, Ph.D., is from Columbia, South Carolina. She received her B.S. in Chemistry from Winthrop University and her Ph.D. in Chemistry from the University of Virginia. Her Ph.D. thesis was completed in the biophysics and biochemistry lab of Dr. Linda Columbus, investigating detergent micelles and lipid-detergent bicelles as membrane mimics for membrane protein characterization. Ashton enjoys painting, trying new foods, listening to music, and travelling with family and friends. She is currently a Clinical Chemistry fellow at UVA.



Hongyan Dai, M.D., Ph.D., was born and raised in China. After receiving her medical degree and M.S. in Pathophysiology from Hebei Medical University, she came to the U.S. to pursue her interest in basic medical research. She studied the role of preconditioning in alleviating ischemia and reperfusion injury at the University of Missouri and graduated with a Ph.D. degree in Physiology. She then completed a residency in Anatomic and Clinical Pathology and a fellowship in Surgical Pathology at the University of Kansas. She is now working on a fellowship in Dermatopathology at UVA. She and her husband have three young boys. In her spare time, she enjoys cooking, travelling and spending time with her children.



**Chris Heitz, M.D.,** was born in Harrisonburg, VA. He received his B.S. in chemical engineering from Virginia Tech and completed his medical degree at Virginia Commonwealth University. He completed a residency in Anatomic and Clinical Pathology at UVA in 2016, where he was Chief Resident in his final year. He is now completing a fellowship in Hematopathology at UVA. He and his wife have a wonderful 3 year-old daughter, Claire. His outside interests include sports, Hokie sports, fitness, guitar, music, and spending time with family.



Jessica Kwock, M.D., is originally from Boston, Massachusetts. She received her undergraduate degree from McGill University in Montreal and her medical degree from Georgetown University School of Medicine. She recently completed residency in Dermatology at UVA and is delighted to have the opportunity to stay at UVA as a Dermatopathology fellow. She enjoys hiking, cooking, painting, and spending time with friends and family.

Edward (Kelly) Mrachek, M.D., grew up on a family farm in westem North Dakota. He went to undergrad at Concordia College, Moorhead, MN, where he graduated cum laude with honors in biology in 2008. He went to medical school at Creighton University School of Medicine, Omaha, NE, graduating in 2012. He then pursued pathology residency at Penrose Hospital, Colorado Springs, CO, and is board certified in Anatomic and Clinical Pathology. He is currently a Neuropathology fellow at UVA. Kelly and his wife, Becky, have one young daughter, Sophia. When not spending time with family and friends. Kelly enjoys the outdoors with hunting, fishing, reading and watching science fiction, and keeping up with the family farm.

### UVA Path Report

## First Year Trainees



### **First Year Fellows**

Sydney Webb Strickland, Ph.D., received a B.S. degree in Biochemistry from Roanoke College and a Ph.D. degree in Experimental Pathology from UVA. Her Ph.D. research was focused on the altered cell signaling induced by HPV E7. She is now looking to broaden her interests as she begins a Clinical Chemistry fellowship at UVA. Her outside interests include playing on several city league volleyball teams and beach volleyball whenever she gets a chance. She also loves watching UVA men's basketball (Wahoowa!) and reading murder mystery novels.



Lindsey (Verduin) Serkes, M.D., was born in South Florida but much prefers the mountains of Virginia. She received a B.S. degree, M.S. degree in Forensic Science, and M.D. degree from the University of South Florida. She then completed a residency in Anatomic and Clinical Pathology at UVA in 2016, where she was Chief Resident in her final year. She is now completing a Cytopathology fellowship at UVA. She and her husband enjoy hiking and mountain climbing, especially in Germany, and share their home with a beloved Weimaraner named Kobalt.



Patrick Voorhees, M.D., was born in Indiana. He attended university at Loyola University in Chicago. He received a M.S. degree in Oceanography at the University of Maine. He worked as an editor in Bethesda, Maryland for seven years before going back to medical school at the Uniformed Services University in Bethesda Maryland where he was commissioned as an officer in the United States Army. He completed his residency in Anatomic and Clinical Pathology at Walter Reed Army Medical Center and has since served as a staff pathologist at Tripler Army Medical Center in Honolulu, HI and at Fort Belvoir Community Hospital in northern Virginia. He is thrilled to have the opportunity to train at UVA as a Dermatopathology fellow. He enjoys playing baseball and spending time with his family.



**Brian Willis, M.D.,** grew up in the small town of Mt. Shasta in Northern California. He attended UC Davis and Pacific Union College in California for undergraduate studies and graduated with a Bachelors of Science in Biology. After taking a year to work as a lab tech for Hess Collection Winery in Napa he headed back to school to complete his M.D. at Loma Linda University. Along the way, he completed a one year AP only Post Sophomore Fellowship at the Loma Linda Department of Pathology. He then headed to Atlanta where he completed his AP/CP residency at Emory University, with a particular focus on soft tissue pathology under Dr. Sharon Weiss. He is currently the Gynecologic Pathology Fellow at UVA.



## First Year Trainees



### **Entering Graduate Students**

John "Robbie" Cornelison hails from Lynchburg, Virginia and did his undergraduate degree in Biology at George Mason University followed by a Master's in Biotechnology at Johns Hopkins. After a stint in industry doing some esoteric RNA techniques, he was hired to help complete the development of the tissue microarray technology at NHGRI/NIH back in the late 90's, and was also involved in developing the RNAi live cell microarray. He continued at NCI for 12 years in breast cancer lead target discovery and investigating viral etiologies in pediatric glioblastoma and other neural malignancies. He joined Dr. Chip Landen's group in early 2015, and is investigating chemoresistance in epithelial ovarian cancer and novel compounds to circumvent it. Robbie also loves hiking, classical guitar, cooking and cats.

Pedro Costa-Pinheiro was born in Porto, Portugal and received a B.S. in Biology and M.Sc. in Molecular

Oncology from the University of Porto. During his undergraduate and master programs he worked in the

Cancer Biology & Epigenetics Group at Research Center of Portuguese Oncology Institute-Porto. For 5





Marissa Gonzales received her undergraduate degrees from Virginia Tech in 2015 in Chemical Engineering (B.S.), Biochemistry (B.S.) and Chemistry (B.A.). During her undergraduate time, she performed tissue engineering research with Estee Lauder in NY, which sparked her interest in biology/ biochemistry. Marissa then worked with Marathon Petroleum in KY on her senior project in process and plant design. Her graduate studies will be focused on mitochondrial and metabolic defects in tumor infiltrating lymphocytes (TIL) in Tim Bullock's lab; she is supported by the Immunology Training Grant. Outside of the lab, Marissa enjoys watching sports – particularly football, reading, playing with her dog Maci, and baking.



**Riley Hannan** is from Atlanta, Georgia, and received his B.S. in Biology from Georgia Tech in 2014. As an undergraduate, he spent three years studying synthetic platelet-like particles and the dysfunctional clotting cascade of newborns. He is pursuing his thesis research with Dr. Thomas Barker and Dr. Shayn Peirce-Cottler. Riley hopes to better our understanding of how chemo-mechanical cues drive the cellular and tissue level balance between regeneration and fibrosis. His future after defending is uncertain, but the draw of scientific discovery means he won't end up far from a lab bench. When able, Riley enjoys cooking, reading, hiking, haircare, and scrapping electronics for spare parts.



Md. Jashim Uddin was born in Bangladesh and received B.S. and M.S. degrees in Biochemistry and Molecular Biology from University of Dhaka, Bangladesh. Before coming to UVA, he worked at International Centre for Diarrhoeal Disease Research Bangladesh (ICDDRB) for a few years. While there he worked to define the biological basis for the under performance of oral polio and rotavirus vaccines in Bangladesh. He also worked to determine the major pathogens responsible for childhood diarrhea in Bangladesh. At UVA, he will be working with Dr. William A. Petri's group in the fields of infectious disease and immunology. He is a great fan of cricket and played cricket almost every day during his high school years. He still loves to watch cricket on TV and would like to be able to make a cricket team here. He enjoys cooking as well!

## Alumni News

Felicia Allard, M.D., completed a cytopathology fellowship at UVA in 2016 and is currently an Assistant Professor in the Dept. of Pathology at the University of Oklahoma Health Sciences Center in Oklahoma City.

Audrey Bennett, M.D., completed her AP/CP residency and hematopathology fellowship at UVA and has been a pathologist at Licking Memorial Hospital in Newark, Ohio for the last 8 years, "seeing a fair amount of hemepath and cytology". She lives in Columbus, OH with her fiancée (to whom she is "permanently engaged"), along with their dog and cat.

Rahat Bhatti, M.D., completed his AP/CP residency in 2015 and hematopathology fellowship in 2016 at UVA. He is currently in community practice at Henrico Doctors' Hospital in Richmond, VA.

Ben Cho, M.D., completed his AP/CP residency at UVA in 2014 and a hematopathology fellowship at Stanford in 2015 before accepting his current position at CORPath in Columbus, OH.

Miriam Conces, M.D., completed her AP/CP residency at UVA in 2015, and a Pediatric Pathology fellowship at Nationwide Children's Hospital in Columbus, OH in 2016. She is currently a Pediatric and Perinatal Pathologist in the Dept. of Pathology and Laboratory Medicine at Nationwide Children's Hospital in OH.

Peter Cummings, M.Sc., M.D., completed his AP residency and Neuropathology fellowship at UVA in 2008. He is currently board certified by the American Board of Pathology in anatomic pathology, neuropathology, and forensic pathology. After leaving UVA he completed his forensic pathology fellowship in Boston, MA in 2009. He has been featured in People Magazine (A Cold Case Comes to Life, April 13, 2009) and appeared on two episodes of NOVA 'Can Science Stop Crime?' (Oct 17, 2012) and 'Cold Case: JFK' (Nov 19, 2013). As part of his work on the NOVA JFK episode, he was granted permission by the Kennedy family to review the original autopsy material in the National Archives. He is the only private, non-government appointed forensic pathologist in history to review the original JFK autopsy material. He has also authored two textbooks, in conjunction with UVA Path alumnus Dr. Darin Trelka, 'Atlas of Forensic Histopathology' (Cambridge University Press, 2010) and 'Forensic Pathology: Pearls and Pitfalls of Infant and Child Death Investigation' (Cambridge University Press, Sept 2016). He is currently an assistant professor of anatomy and neurobiology at Boston University School of Medicine and the CEO of a non-profit forensic medicine consulting group focusing on post conviction cases, social justice issues, and forensic pathology policy and law. He lives outside of Boston with his wife, Sarah, and son Fionn, who is now 10--- believe it or not.

William E. Field II, M.D., completed his AP/CP residency at UVA in 1996 and then went on to a fellowship in Surgical Pathology at the University of Pittsburgh Medical Center. He is currently Chairman & Medical Director at the Saratoga Hospital Department of Pathology & Laboratory Medicine as well as President of Saratoga Springs Pathology, PC.



Faculty members Kristen Atkins, Anne Mills, and Mark Stoler celebrate with graduating cytopathology fellows Tatjana Terzic (center) and Felicia Allard (far right)

Garth Fraga, M.D., completed his Dermatopathology fellowship at UVA in 2000 and is currently an Associate Professor of Pathology and Dermatology at the University of Kansas in Kansas City. His three kids Hannah (15), Charlie (13) and Sydney (10) "keep us busy with their swim meets, fencing, and love of performing arts (nary a day goes by without someone busting out a song from the musical Hamilton)".

Sheryl Johnson, M.D., completed her AP/CP residency at UVA in 2016 and is currently a Pediatric Pathology fellow at Cincinnati Children's Hospital in Ohio.

Kristin La Fortune, M.D., completed her AP/CP residency at UVA in 2015 and a cytopathology fellowship at Indiana University in 2016. She is currently a pathologist with Ohio Valley Pathologists, as well as an Assistant Professor at Indiana University School of Medicine in Evansville, IN.

**Stephen Long, M.D.**, completed his AP/CP residency in 2013 and a hematopathology fellowship in 2014 at UVA. He is currently a pathologist at UC-San Francisco.

Yunchuan Delores Mo, M.D., completed her AP/CP residency in 2015 and fellowship in Blood Banking and Transfusion Medicine in 2016 at UVA, before accepting her current position at Children's National Health System in Washington, DC.

Karyn Prenshaw, M.D., completed her dermatopathology fellowship at UVA in 2016 and is currently a cytopathology fellow at UVA.

Akeesha Shaw, M.D., completed her AP/CP residency in 2014 and cytopathology fellowship in 2015 at UVA, followed by a fellowship in ENT Pathology at University of Pittsburgh. She is currently Associate Staff at the Cleveland Clinic in Ohio.

**Scott Wendroth, M.D.,** completed his AP/CP residency at UVA in 2016 and is currently a hematopathology fellow at Stanford University.

Zimin Zhao, M.D., completed her AP/CP residency at UVA in 2016 and is now completing a Cytopathology fellowship at UCLA.

## Philanthropy



Margaret Moore and Lisa Friedman, Pathology Summer Enrichment Program participants

#### Sponsor a Pathology Summer Fellowship

With the retirement of long-time physician educator Don Innes, M.D. from our department in 2015, we received significant donations in his honor for use in supporting 2nd year medical students interested in exploring Pathology as a career option. Margaret Moore and Lisa Friedman recently concluded their participation in the 8-week Summer Enrichment Program in Pathology, and describe the experience in their own words below.

"In underaraduate medical education, it is sometimes difficult to gain experience in pathology until the fourth year. This delays students' exploration of the field. The Patholoav Summer Enrichment Program provides rising second year students with a unique blend of clinical skills, education, and research opportunities. We feel honored to have been the first students to participate in this internship. The program exposed us to many of the varied domains of both clinical and anatomic pathology. We were able to work directly with residents and faculty, attend tumor boards and lectures, and start research projects. We participated in activities as diverse as blood bank rounds, autopsy reviews, brain cuttings, and cytogenetics analysis. In reviewing our summer activities, we participated in over 30 unique educational experiences in different areas of pathology. Over the summer, our knowledge of pathophysiology deepened, and we became increasingly competent and confident in reviewing cases. Though we may not be able to diagnose all the cases that come through surgical pathology, we nonetheless feel like we have improved our clinical thinking and gained a great appreciation for the specialty. This was a wonderful experience, and we look forward to helping shape the program for future students."

### Engender a Culture of Investigative Learning

Every trainee in the UVA Pathology Training Programs is expected to participate in research projects that illuminate disease mechanism, advance diagnostic procedures or improve the quality of Pathology/Laboratory Medicine clinical services. We also strongly encourage the trainees to present their work for peer review at national meetings. While the cost of these projects and travel expenses vary widely, the Department currently provides \$2000 annually to each clinical trainee to help support these activities. With tightening budgets, such allocation is becoming increasingly difficult to maintain. Please consider sponsoring one project that will offer an invaluable learning opportunity for a trainee and support an advance in the fields of diagnostic pathology and laboratory medicine.

#### Honor a Faculty Mentor

Our clinical faculty members have international reputations for their diagnostic expertise, solidified by authorship and editorship of major medical texts and journals. All our faculty carry out research that spans the spectrum of biomedical inquiry: basic research into biological and disease mechanisms, translational research that brings advances in experimental science to clinical utility in diagnostics and therapeutics, and clinical research that refines and advances current medical practice. Thank your faculty mentor by making a gift to the Department of Pathology in his or her honor.



Donations can be made online by clicking on the "Make a Gift" button on the UVA Pathology website: https://med.virginia.edu/pathology/

OR, donations can be made by check or credit card using the enclosed self-addressed return envelope.

## Grants and Contracts

### New Grants and Contracts

PI: David Bruns. MD

Thermo Fisher Scientific, Inc Contract Validation of New Biomarker Assay 06/22/16-6/21/18 Total Budget: \$37,250 Abbott Labs Contract Validation of New Prognostic Test 09/18/15-09/17/16 Total Budget: \$84,700

#### PI: Timothy Bullock, PhD Focused Ultrasound Foundation Contract

Microbubble Cavitation for Immunity to GBM 10/01/15-4/30/17 Total Budget: \$52,463 Calithera, Inc Contract Arginase-1 inhibition in NSCLC 09/01/16-08/31/17

Total Budget: \$19,750 Theraclion, S.A. Contract Dev Mouse Model Focused Ultrasound 05/09/16-05/09/17 Total Budget: \$20,540

Cancer Research Institute Grant Development of SAS1B based immunotherapeutics 08/01/15-09/01/17 Total Budget: \$12,950

#### PI: Helen Cathro, MD

Luna Innovations, Inc. Contract Low-Cost Sprayable Barrier for the Prevention of Surgical Adhesions 12/01/15-08/18/17 Total Budget: \$32,460

#### PI: Robin Felder, PhD National Heart, Lung and Blood Institute Grant Molecular Mechanisms in Salt Sensitivity of Blood

Pressure 06/01/16-05/31/21 Total Budget: \$11,130,903

George Washington Univ. Contract Renal Dopamine 09/15/15-04/30/16 Total Budget: \$78,098

PI: Adam Goldfarb, MD National Institute of Diabetes & Digestive & Kidney Diseases Grant Validation of Aconitase-Isocitrate Pathway as a Target for Anemia Treatment 04/01/16-03/31/19 Total Budget \$711,000

PI: James Gorham, MD, PhD Bloodworks Northwest Contract Genetics of Red Cell Storage 05/01/16-04/30/21 Total Budget: \$154,825

PI: Alejandro Gru, MD Seatle Genetics, Inc. Contract Title: Analysis of CD30 06/06/16-06/05/17 Total Budget: \$28,350

## Other Active Grants and Contracts

PI: Thomas Braciale, MD, PhD National Institute of Allergy and Infectious Diseases Grant CTL Response to Influenza Virus 09/01/91-11/30/17 Annual Budget: \$395,000

PI: Timothy Bullock, PhD Melanoma Research Alliance Grant Title: Enhancing Immune Therapy for Brain Metastases with Focused Ultrasound 12/01/15-11/30/18 Annual Budget: \$125.000

National Cancer Institute Grant Immunotherapeutic Nanoparticle Delivery to Melanoma with MR-guided FUS 06/01/15-5/31/20 Annual Budget: \$159,578

Celldex Therapeutics, Inc. Contract Immune Correlate Study of Varilimumab and Ipilimumab 05/26/15-05/31/22

Annual Budget: \$14,529 National Cancer Institute Grant BLIMP-1 Mediated Regulation of CD8+ TIL 01/01/13-12/31/17 2016 Budget: \$737,291

#### PI: Adam Goldfarb, MD

National Heart, Lung, and Blood Institute Grant Controlling an Ontogenic Masterswitch to Maximize Thrombopoiesis 09/10/15-05/31/19 2016 Budget: \$445,926

National Institute of Diabetes & Digestive & Kidney Diseases Grant Dissection and Manipulation of the Cellular Response to Iron Restriction 02/01/08-06/30/18 2016 Budget: 5343,650

#### PI: James Gorham, MD, PhD

Emory University Contract Adverse Effects of RBC Transfusions: A Unifying Hypothesis 09/01/14-07/31/18 Annual Budget: \$49,387

**UVA** Path Report

PI: Dede Haverstick, PhD Blue Ridge Medical Center Contract In-Office Consultations 02/26/15-12/31/16 2016 Budget: \$5000

PI: Hui Li, PhD American Cancer Society Grant Functional Study of Chimeric RNA SLC45A3-ELK4 in Prostate Cancer 07/01/14-06/30/18

Annual Budget: \$198,000 **St. Baldrick's Foundation Grant** Gene Fusions in Rhabdomyosarcoma

07/01/14-06/30/17 Annual Budget: \$110,000 National Cancer Institute Grant

CIS-Splicing of Adjacent Genes in Prostate Cancer 09/22/14-08/30/19 2016 Budget: \$327,850

#### PI: Mani Mahadevan, MD

National Institute of Arthritis & Musculoskeletal & Skin Disease Grant Role of FN14 in RNA Toxicity 09/15/11-07/31/17 2016 Budget: \$346,500

PI: James Mandell, MD, PhD National Institute of Arthritis & Musculoskeletal & Skin Disease Grant Circulating Non-coding RNA's as Biomarkers of Inclusion Body Myositis

05/12/15-04/30/17 2016 Budget: \$173,800

### PI: Chris Moskaluk, MD, PhD

DOD-Army-Medical Command Grant Lung Cancer Biospecimen Resource Network 07/01/15-09/19/17 2016 Budget: \$395,000

National Cancer Institute Grant Biospecimen Procurement & Tissue Microarray

Manufacture for the CHTN 04/24/14-03/31/19 2016 Budget: \$597,282

#### PI: Kenneth Tung, MD National Institute of Allergy & Infectious Diseases Grant Zona Pellucida: Immunopathologic Study 09/01/93-10/31/17 2016 Budget: \$395,000

PI: Scott Vande Pol, MD, PhD National Cancer Institute Grant Papillomavirus E6 Structural Consortium 07/01/15-06/30/20 2016 Budget: \$443,504

## Publications and Awards

### Selected Faculty Publications

#### Journal Editors

Bullock TN: Associate Editor, Journal of Immunotherapy for Cancer

Bullock, TN: Associate Editor, Journal of Immunology

Gorham, JD: Associate Editor, Journal of Immunology

Gorham, JD: Associate Editor, Laboratory Investigation

Mandell JW: Associate Editor, Journal of Neuropathology and Experimental Neurology

Mills SE: Editor-in-Chief, The American Journal of Surgical Pathology

Mills SE: Editor, Practical Reviews in Pathology (a monthly audio review series)

**Stoler MH:** Editor-in-Chief, International Journal of Gynecological Pathology

#### Journal Articles

Aguilera NS, Auerbach A. Extranodal-adrenal myelolipoma presenting in the spleen: A report of two cases. Human Pathol: Case Reports 2016; 6: 8-12.

Bhatti R, Aguilera NS. Reverse variant of follicular lymphoma: uncommon morphology in a common lymphoma. Blood (accepted) DOI 10.1182/blood-2016-01-694521

Campbell ST, Santen RJ, **Bruns DE**. Undetectable Urine Calcium in a Gastric Bypass Patient. Clin Chem. 2016; 62(8): 1161

Mullins GR, Harrison JH, **Bruns DE**. Smartphone monitoring of pneumatic tube system-induced hemolysis. Clin Chim Acta, 2016 (in press)

Mullins GR, Harrison JH, **Bruns DE**. Smartphones can monitor medical center pneumatic tube systems. Clin Chem 2016; 62:891-3. Mullins GR, Caldwell SH, **Bruns DE**. Undetectable alanine aminotransferase during hospitalization. Clin Chem 2016; 62:535.

Kelting SM, Kimpel, DL, **Bruns DE**. Persistence of infliximab in circulations for 7 years? Clin Chem 2015; 61:1420-1.

Dong H, Franklin NA, Ritchea SB, Yagita H, Glennie MJ, **Bullock TN**. CD70 and IFN-1 selectively induce eomesodermin or T-bet and synergize to promote CD8+ T-cell responses. Eur J Immunol. 2015; 45(12): 3289-301.

Jose PA, Yang Z, Zeng C, **Felder RA**. The importance of the gastrorenal axis in the control of body sodium homeostasis. Exp Physiol. 2016; 101(4): 465-70

Gildea JJ, Xu P, Carlson JM, Gaglione RT, Bigler Wang D, Kemp BA, Reyes CM, McGrath HE, Carey RM, Jose PA, **Felder RA**. The sodiumbicarbonate cotransporter NBCe2 (slc4a5) expressed in human renal proximal tubules shows increased apical expression under highsalt conditions. Am J Physiol Regul Integr Comp Physiol. 2015; 309(11): R1447-59.

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Gorham J, Gleeson M. Cirrhosis and dysbiosis: New insights from next- generation sequencing, Hepatology. 2016; 63(1): 336-8.

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**Gru AA**, Lehman NL, Otero J. A 59-Year-Old Man with History of Renal Transplantation. Brain Pathol. 2015; 25(6): 788-9.

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McLaughlin CT, Kaffenberger BH, **Gru AA**. A hybrid tumor with schwannoma-perineuriomaneurofibroma morphology. J Cutan Pathol. 2015: 42(11): 911–3.

Smith SM, Kiracofe EA, Clark LN, **Gru AA**. Idiopathic Hypereosinophilic Syndrome With Cutaneous Manifestations and Flame Figures: A Spectrum of Eosinophilic Dermatoses Whose Features Overlap With Wells' Syndrome. Am J Dermatopathol. 2015; 37(12): 910-4.

Jia Y, Xie Z, Li H. Intergenically Spliced Chimeric RNAs in Cancer. Trends in Cancer TRECAN 92, 2016 (in press)

Kumar S., Vo AD, Li H. Identification of Fusion RNAs Using Next generation Sequencing. Wiley Interdisciplinary Reviews: 2016 Aug 2. doi: 10.1002/wrna.1382.

Babiceanu M, Qin F, Xie Z, Jia Y, Lopez K, Janus N, Facemire L, Kumar S, Pang Y, Qi Y, Lazar IM, Li H. Recurrent chimeric fusion RNAs in non-cancer tissues and cells. Nucleic Acids Res. 2016; 44(6): 2859-72.

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Kumar S, Vo AD, Qin F, Li H. Comparative assessment of methods for the fusion transcripts detection from RNA-Seq data. Sci Rep. 2016; 6: 21597.

Oin F, Song Z, Chang M, Song Y, **Frierson H**, Li H. Recurrent cis-SAGe Chimeric RNA, D2HGDH- GAL3ST2, in Prostate Cancer. Cancer Letters. 2016; 380: 39–46

## Publications and Awards

### Selected Faculty Publications

#### Journal Articles Continued.

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Mills AM, Paquette C, Terziac T, Castle P, Stoler MH. CK7 Immunohistochemistry as a Predictor of CIN1 Progression: A Retrospective Study of Patients from the Quadrivalent HPV Vaccine Trials. Am J Surg Pathol 2016 (in press)

Sloan EA, **Moskaluk CA**, **Mills AM**. Mucinous Differentiation With Turnor Infiltrating Lymphocytes Is a Feature of Sporadically Methylated Endometrial Carcinomas. Int J Gynecol Pathol. 2016 Aug 10.

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Wick MR. Cutaneous melanoma: A current overview. Semin Diagn Pathol. 2016; 33(4): 225-41.

Delhiwala KS, Vadakkal IP, Mulay K, Khetan V, Wick MR. Retinoblastoma: An update. Semin Diagn Pathol. 2016; 33(3): 133-40.

Mulay K, **Wick MR**. Ophthalmic immunoglobulin G4-related disease IgG4-RD Current concepts. Semin Diagn Pathol. 2016; 33(3): 148-55.

Bush JW, Wick MR. Cutaneous histiocytoid Sweet syndrome and its relationship to hematological diseases. J Cutan Pathol. 2016; 43(4): 394-399.

Larson K, **Wick MR**. Pagetoid Reticulosis: Report of Two Cases and Review of the Literature. Dermatopathology (Basel). 2016; 3(1): 8-12.

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## Publications and Awards

### Selected Faculty **Publications**

#### Journal Articles Continued.

Wick MR, Marchevsky AM. Neuroendocrine neoplasms of the lung: Concepts and terminology. Semin Diagn Pathol. 2015; 32(6): 445-55

Marchevsky AM, Wick MR. Diagnostic difficulties with the diagnosis of small cell carcinoma of the lung. Semin Diagn Pathol. 2015; 32(6): 480-8.

#### **Book Editors**

Burtis CA. Bruns DE. eds. Tietz Fundamentals of Clinical Chemistry and Molecular Diagnostics. 7th ed. St. Louis: Saunders/Elsevier, 2015

Mills SE, Greenson JK, Hornick JL, Longacre TA. Reuter VE: Stemberg's Diagnostic Surgical Pathology, 6th ed, Wolters Kluwer Health, 2015

#### **Book Chapters**

Aguilera NS. Multiple chapters (Hairy cell variant, Plasma cell myeloma, T-Prolymphocytic leukemia. Diffuse large B cell lymphoma. Monoclonal gammopathy of uncertain significance, Aggressive NK cell leukemia, Adult T cell leukemia/lymphoma, Histiocytic lymphoma, Chronic lymphoproliferative disorder of NK cells. Overview of lymphoid neoplasms). In: Diagnostic Pathology: Molecular Oncology (Auerbach A, Vasef MA, Eds.) Elsevier, 2016.

Mills AM, Longacre TA. Lynch Syndrome: Female Genital Tract Tumor Diagnosis & Screening. In: Surgical Pathology Clinics on Gynecologic Pathology. (Clarke B, McCluggage G, Eds.) Elsevier, June 2016.

Mills AM, Stoler MH. Cervical Squamous Intraepithelial Lesions. In: Pathology of the Cervix. (Herrington CS, Ed.), Springer, London, In Press

Mills SE: The nose, paranasal sinuses, and nasopharynx. In: Sternberg's Diagnostic Surgical Pathology, 6th ed. (Mills SE, Greenson IK Homick II Longacre T Reuter VE Eds.) Wolters Kluwer Health, Philadelphia, 2015.

Mills SE: The salivary glands. In: Sternberg's Diagnostic Surgical Pathology 6th ed (Mills SE Greenson JK, Hornick JL, Longacre T, Reuter VK, Eds.): Wolters Kluwer Health, Philadelphia,

Williams ES. Silverman LM Molecular Diagnosis of Human Disease. In: Molecular Pathology, 2nd edition (Coleman and Tsongalis, Eds.), In Press.

A more complete picture of faculty/trainee publications can be found on UVA Pathology Department's faculty websites at: https://med. virginia.edu/pathology/contact/pathologyfaculty/

#### Awards

Kristen Atkins received the Alumni Academic Achievement Award from the University of Vermont in June 2016, as well as the American Society of Cytopathology Excellence in Education Award in 2016

David Bruns was profiled in the "Inspiring Minds" Feature in the journal Clinical Chemistry, Clin. Chem 2015 61:573-6. http://clinchem. aaccinls.org/content/clinchem/61/4/573. full.pdf

The London publication "The Pathologist" listed David Bruns among the 100 Most-Influential Pathologists (in position 16) and published a short biography which is available in print and online. https://thepathologist.com/thepower-list-2015/

Graduate student Lelisa Gemta (Bullock Lab) received Travel Scholarships for:

"Metabolic Regulation of Tumor Infiltrating Lymphocytes," Poster presentation, 48th annual Society of Leukocyte Biology meeting (Immunity in Health and Disease). Raleigh, NC. Sept 27-29, 2015.

"Metabolism as a Functional Constraint of Tumor Infiltrating CD8+ T cells." Oral and poster presentation, Keystone symposia on Immunometabolism in Immune Eunction and Inflammatory Disease. Fairmont Banff Springs, Banff, Alberta, Canada, Feb 21-25, 2016.

Clinical Chemistry Fellow Garrett Mullins received the People's Choice Award at the Student Oral Presentation Contest during the 2016 Annual Meeting of the American Association for Clinical Chemistry. His talk won the Second Place prize overall, with a \$500 cash award

Garrett Mullins received the 2016 AACC Capital Section Travel Award and an AACC Student Research Travel Award: and. separately, he was selected to attend the Siemens Medical and Scientific Learning

Mullins, PhD, presented talks for which they recieved Young Investigator Awards at the 51st Annual Meeting of the Academy of Clinical Laboratory Physicians and Scientists. The titles of their talks are listed below:

and Scientists. Birmingham, June 2016. (Paul

Clinical Chemistry Fellow Garrett Mullins (PhD, UVA Pharmacology) won the Department of Pharmacology's prestigious Rall Award at their department retreat in October 2015.

Exchange Program sponsored by Siemens. Two fellows, Min Yu. MD. PhD. and Garrett

Yu M. Bruns DE. Jane JA Jr. Nass RM. Oldfield EH. Vance ML. Thomer MO. Remission of acromegaly predicted by fall of IGF-I measured by LC/MS within 72 hours of pituitary surgery. 2016 Annual Meeting of Academy of Clinical Laboratory Physicians E Strandjord Young Investigator Award) Mullins GR. Harrision JH. Bruns DE. Smartphones can quickly and economically monitor medical center pneumatic tube systems, 2016 Annual Meeting of Academy of Clinical Laboratory Physicians and Scientists, Birmingham, June 2016, (Paul E Strandjord Young Investigator Award)

Bruns DE, Epidemics and duty of care, Athena Society, Seventh International Meeting, Crete, June 16-20, 2015.

**Oral Presentations** 

Bruns DE, Safe Diagnostics: How Good Do Medical Tests Need To Be? Trainee Research Day, Washington University, St. Louis, April 18-19, 2016.

National Presentations

Felder RA. Automation of 3D Cell Culture. Society for Laboratory Automation and Screening, San Deigo, CA, January 2016.

Lopes MB. Practical Diagnosis of Pituitary Adenomas for the Practicing Clinician. The 26th Annual Meeting of the Japanese Society for Hypothalamic and Pituitary Tumors. Fukushima, Japan, February 19-20, 2016.

Lopes MB. Hypophysitis and TTF-1 Expressing Pituitary Tumors. The 26th Annual Meeting of the Japanese Society for Hypothalamic and Pituitary Tumors. Fukushima, Japan, February 19-20, 2016.

Lopes MB. TTF-1 Expressing Pituitary Tumors - case presentation. Neuropathology Specialty Night at the United States & Canadian Academy of Pathology Annual Meeting, Seattle, March 2016.

### **Oral Presentations**

Bruns DE. Epidemics and duty of care. Athena Society, Seventh International Meeting, Crete



Chelsea Gottlieb, M.D., and Anne Mills, M.D., U.S. and Canadian Academy of Pathology meeting, March 2016

Our faculty and trainees have also authored a wide selection of poster presentations, several of which are highlighted here. A more complete listing can be found at: https://med.virginia.edu/ pathology/2016/03/21/uva-uscap-2016-representation/



Sarah Kelting, M.D., U.S. and Canadian Academy of Pathology meeting, March 2016



Jenny Ju, M.D., and Dylan Coss, M.D., U.S. and Canadian Academy of Pathology meeting, March 2016

# **Final Notes**

## 2017 Calendar of Events

### March 4-10, 2017

United States and Canadian Academy of Pathology (USCAP) 106th Annual Meeting Henry B. Gonzalez Convention Center San Antonio, TX

Alumni Dinner at USCAP (Check UVA Pathology website for date/time)

## April 28, 2017

University of Virginia Dept. of Pathology 13th Annual Research Day Jordan Hall Conference Center Charlottesville, VA

## **Faculty Promotions**



Nadine Aguilera, M.D., has been awarded tenure.



Robin LeGallo, M.D., has been awarded tenure.

Congratulations to each of you on achieving this major milestone!

## **Digital Pathology Study**

UVA pathologists Helen Cathro, James Mandell, Anne Mills, Stacey Mills, Mark Wick and Chris Moskaluk (P.I.) partnered with Philips Healthcare on a clinical trial to test the performance of a digital pathology system. The UVA pathologists independently assessed glass slides and their digitized analogs for 500 cases to determine if diagnoses rendered on the digital system matched traditional microscopic methods. The results are currently being used to support an application to the FDA for clinical use of the digital system.



ORIEN members (including Dr. Moskaluk, center) meet with White House officials in January to discuss their role in the Cancer Moonshot initiative to accelerate cancer research.

## **ORIEN Program Update**

The UVA Cancer Center became a member of the Oncology Research Information Exchange Network in 2015 (PI: Chris Moskaluk). In the last 8 months, UVA has enrolled over 700 cancer patients who have consented to donate their tissue and clinical data with the goal of developing more targeted cancer treatments and more quickly matching eligible patients to clinical trials. Please contact Joyce Miller, Ph.D., at jma8m@virginia.edu for more information.



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For more information, please visit www.medicine.virginia.edu/ clinical/departments/pathology

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