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📾 UVA Health

# UVA PATH REPORT

News from the UVA Department of Pathology

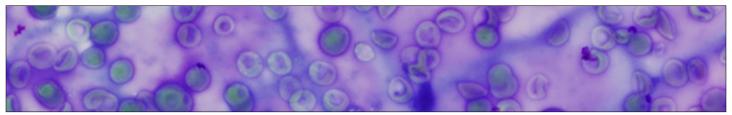


### **INSIDE THIS ISSUE**

Message from the Chairman

In Focus: COVID Response Jim Zimring, MD, PhD Amy Mathers, MD Pat Pramoonjago, PhD Anne Mills, MD Faculty: Moving On Faculty: Moving In Faculty: Moving Up First-Year Trainees Grants and Contracts Publications and Awards UVA Pathology in the News National Presentations Philanthropy

# A Message from the Chairman



Well, this has been a challenging year to say the least. I am sure all of our readers know that UVA Medical Laboratories and UVA Department of Pathology were suddenly the focus of attention as testing (or lack thereof) for SARS-CoV-2 became topic #1 during the early stages of the pandemic. I am proud to say that UVA has performed well, especially given the shortages in equipment and reagents hampering all labs nationwide, and was an asset to the Commonwealth of Virginia and beyond. UVA was the first health system in our state to bring up COVID-19 PCR testing (on March 18!) with equipment and reagents borrowed from basic research labs, and from the first day we had this up and running, we were helping hospitals across the state test critically ill patients with turnaround times (TAT) of a day when commercial labs TAT were measured in weeks. With the addition of more equipment, we then became a lynchpin in our state health department's testing resources for control of outbreaks across the state. Most of the credit for these notable accomplishments belong to two key faculty in our Department: Mendy Poulter, PhD, the Director of Clinical Microbiology and Amy Mathers, MD, the Associate Director of Clinical Microbiology. Easily working 80+ hour weeks for weeks on end, these two heroes, along with the flawless teamwork from administrators, technologists and IT specialists in the medical lab, achieved an increase of over an order of magnitude in our viral PCR testing capacity (up to 1500 assays a day) and a quadrupling of our staff in molecular microbiology laboratory in order to run assays 24/7 on the weekdays and on weekends. When UVA decided on a mass screening protocol for its students, Mendy's expertise was lent to set up a separate CLIA testing lab that is soon to be able to assay over a thousand saliva samples a day to support this program. This program was jump started by a pathology basic science faculty member, Hui Li, PhD, who lent not only his expertise in designing PCR assays, but his own laboratory equipment and technician. Amy Mathers single handedly set up a program of waste water testing of the dormitories to help manage the early phase of the students returning to Grounds. Amy also worked with colleagues in the engineering department to create our own nasopharyngeal swabs, then set up industrial collaborations so that now 65,000 UVA-designed swabs are made a week, with 50,000 being transferred to the state for distribution statewide, freeing us from the international supply chain (and its difficulties) for this one key testing resource. Working with another basic science faculty member, we are making our own viral transport media in a GMP facility in the UVA School of Medicine, again freeing us from the nationwide shortages of this necessary part of COVID-19 testing kits. We have greatly benefitted from the resources of a great academic medical center, from the immediate translation of basic science expertise and equipment to clinical practice, to the resourcefulness, creativity and drive of academic physicians, to provide UVA and the entire Commonwealth of Virginia with COVID-19 testing to help with the management of this pandemic.

Of course, everyone, and all phases of life have been impacted by COVID-19. Again, UVA Pathology faculty have risen to the occasion, not only providing exemplary clinical diagnostic services while adapting to COVID-19 mitigation strategies, but also creating new educational resources and spearheading new avenues of research in response to the pandemic. While absolutely all faculty have pitched in in these endeavors, I would like to highlight two faculty in particular. Robin LeGallo, MD, has worked even more hours than she usually does in creating new online content and creating safe learning venues for our medical school pathology training program. Anne Mills, MD, has, in my opinion, created a nationleading virtual training program and resident recruitment resources that we hope have not only maintained the educational experience for our current residents but will recruit another class of stellar young physicians to UVA.

Of special note, while all of this chaos was going on, our research faculty, through their track records of accomplishments and creativity in proposing new avenues of investigation, were awarded over \$18 million in federal grant funding, a new record for the department. While it is easy to be preoccupied with the problems of the present, it is good to know that our department continues to grow in its capacity to add to the fund of human knowledge to support advances in the future.

Perhaps unsurprisingly, this year's newsletter has focused on the response of the UVA Department of Pathology to the COVID-19 epidemic. We've included vignettes from all of our missions, clinical, research and education.



Tera Moskaluk

Christopher A. Moskaluk, MD, PhD Walter Reed Professor and Chair, UVA Department of Pathology

# In Focus: Coronavirus Response

### Improved Serological Diagnostics for SARS-CoV-2 Infection

By Jim Zimring, MD, PhD



While the treatment, therapy, and potential development of a vaccine remain the primary goals to address the SARS-CoV-2 pandemic, diagnostics remains an essential tool in monitoring and managing COVID-19. In addition to detecting virus by antigen assays or PCR, monitoring the immune response of the recipients is of high importance. This will remain the case even after a vaccine is developed, and, arguably, may be even more important then, as populations are likely to have a wide range of response to a vaccine and for different

durations. Although it remains unclear if antibodies are themselves protective, the generation of antibodies nevertheless indicates an immune response, some component of which was presumably effective if the patient convalesced.

# Specificity of Serological Assays in a World of Different Coronaviruses

Manufacturers and diagnostic labs have stated that the antibody tests are highly specific, with limited cross reactivity with antibodies against common corona- viral species that are endemic to our society. However, there are two major concerns with such a claim. First, there remains a group of people who present with COVID-19 like disease, and are negative by RT-PCR but have high antibody titers. It is unclear if these are people who have been infected and are actually immune or if one is detecting cross reacting antibodies. Second, no one has ever analyzed samples during the cold and flu season, which is just starting. In other words, a cross-reactivity "matrix effect" may be coming due to a change in the nature of the background antibodies. Thus, testing strategies that can remove background noise from serological responses to common coronaviruses may be important. To address this issue, we have developed a cocktail of N proteins from each of the common endemic coronaviruses. This cocktail can be used to block antibodies against other coronaviruses without affecting SARS-CoV-2 specific antibodies. In addition, we have engineered and expressed a variant of the SARS-CoV-2 N protein that lacks three regions that are highly conserved amongst coronaviruses. This can serve as a target with higher specificity than the full SARS-CoV-2 N protein.

#### Sensitivity of Serological Assays in Diverse Patient Populations

A second problem of potential concern is one of biological diversity among the patient population. We now understand that there are greater than 30 natural variants of the IgG constant region amongst humans, and this is just the tip of the iceberg. As we sequence more and more humans, more and more variants are identified. The reason this is a diagnostic issue is that variants in the IgG constant region can alter epitopes recognized by anti-IgG that is present in almost all serological assays. This is not just a theoretical problem; we have reported that one of the major blood analyzers used in the U.S. has an anti-IgG reagent with a blind spot to IgG variants found in Eastern Africa. This risks missing an alloantibody and subsequent transfusion of an incompatible RBC unit. We do not necessarily remedy by using polyclonal anti-IgG. Surprisingly, polyclonal anti-IgG can still have blind spots. To address this problem, we are generating a panel of "switch variant" antibodies against the SARS-CoV-2 spike protein. Antibodies of every IgG variant are being expressed. We can then use such a panel to validate the existing serological assays, and to identify if there are either hypo-reactivities or "blind spots" to. Likewise, standard curves can be generated with each variant to allow more accurate titer determination. This is being carried out in the theme of personalized and precision medicine, recognizing the diversity of our patient population and the necessity of tailoring our diagnostic assays the to patient.



Using Building Wastewater as a SARS-CoV-2 Surveillance Tool of Congregate Living for the University

By Amy Mathers, MD



#### Background and Progress

One of the hardest hit areas of SARS-CoV-2 transmission has been individuals who live in congregate settings. Unfortunately, by the time a small number of unique symptomatic patients are discovered in the same setting, triggering the need for testing everyone, the virus transmission may already be widespread in the facility. The main approach to manage, control, and reduce in congregate settings has been aggressive entry screening of building

occupants (*i.e.*, wellness attestations, admission testing, no movement in and out and temperature checks). As the University reopened to students, one of the highest risk situations was communal living settings such as dormitories. There are specific challenges in the dormitories that make them uniquely high risk for transmission: 1) students obviously need to have free movement in and out of the dorm, 2) it is not realistic that people can wear masks all the time where they live, 3) groups of students want to

### In Focus: Coronavirus Response cont.



congregate with the individuals who live close to them, 4) some students live in double rooms and sharing bathroom space, 5) there may be a higher rate of asymptomatic carriage and transmission in this relatively young population.

Ideally, everyone who lived in the same environment in a congregate setting could be tested every day for early presymptomatic or asymptomatic shedding and spread, but this is currently not logistically possible. An alternative approach to testing a group of people who live together daily would be to test all of them in a pooled way and, if positive, then this would trigger further investigation. We have been monitoring wastewater coming from resident halls on grounds for SARS-CoV-2 RNA. SARS-CoV-2 RNA is known to be shed at high rates early in infection from the nasopharynx, oropharynx and GI tract. This observation has stimulated strong interest in use of wastewater surveillance to track the spread of SARS-CoV-2 in communities as an early warning system in high risk congregate setting.

#### **Pilot Summer Study**

Through an existing Engineering in Medicine collaboration around wastewater, Amy Mathers, MD, of the UVA School of Medicine and Lisa Colosi-Peterson of the UVA School of Engineering decided to attempt to establish methods for pooled wastewater SARS-CoV-2 surveillance. The overarching objective of a summer pilot study was to demonstrate that building-level wastewater surveillance for SARS-CoV-2 is useful for tracking disease transmission in congregate living settings. The focus of the pilot study this summer was collecting and analyzing wastewater samples from the hospital, the wastewater treatment plant, and several occupied university dormitories where occupants were tested frequently. We established a safe, reproducible strategy for wastewater sample collection from occupied congregate living settings was established. In addition, we compared molecular concentration and extraction methods and optimized for the most sensitive and cost-effective method. We based results on external validation data of tested occupants.

#### **Current State**

Once students returned to Grounds, we deployed the refined methods. This has successfully acted as an early warning system for the detection of silent shedding of SARS-CoV-2 in pooled wastewater. We used an autosampler that collects a 24-hour composite sample from the waste stream of a building in a timed fashion. We spun down a portion of this sample with an ultracentrifuge to concentrate the viral RNA. We then extracted the RNA from the pellet and undergoes a SARS-CoV-2 PCR in the clinical laboratory. Through the pilot and accumulating data, we demonstrated a very sensitive yet not quantitative method for detecting COVID-19 infected individuals in a building.

Thus far this semester, we have successfully detected SARS-CoV-2 RNA in pooled wastewater, which triggered testing of all building occupants and found positive individuals. Once identified, individual positive students are then moved to isolation rooms and their close contacts are moved to a quarantine space, thus preventing further transmission in a congregate setting. We reviewed the wastewater data daily and used in conjunction of other student testing to monitor for increases in cases among students in the residents halls.

### UVA COVID-19 Biobank

By Pat Pramoonjago, PhD



In response to the COVID-19 (SARS-CoV-2) pandemic, the University of Virginia School of Medicine created a COVID-19 biobank to provide biospecimens that may be used to elucidate the pathophysiology, diagnoses, and, ultimately, treatments for COVID-19 for UVA investigators. Following the initial discussion on April 8, regarding the process of COVID-19 biobank development, the UVA Institutional Review Board approved the protocol for COVID-19 biobank (HSR 200110). This protocol allows the UVA

COVID-19 research registry and the specimen bank to collect specimens from patients who have tested positive for or are suspected of having the virus. Dr. William Petri leads logistical support for this biobanking protocol as the PI with the COVID-19 biospecimen subcommittee, a new workgroup within UVA School of Medicine that is tasked to provide logistics for collecting specimens, generating standard operating procedures for specimen processing, and sample management. The Biorepository and Tissue Research Facility (BTRF) is assigned to process, store, and distribute samples.

#### **Specimen Collection**

Biospecimens are collected from 1) subjects that have had samples submitted for COVID-19 testing with either positive or negative results for COVID-19; 2) subjects under investigation (PUI) for COVID-19; or 3) subjects who have symptoms of COVID-19 and have been admitted to a COVID unit, ICU COVID unit or have had a COVID-19 antibody test completed. Specimens are collected both retrospectively and prospectively. These samples will include a limited data set that includes patient ID codes on admission, medications, laboratory data, and outcomes.

Retrospective collections are from any discarded samples of clinically indicated procedures for outpatients or inpatients. We collected the samples from all individuals, including every day of hospitalization started at diagnosis or 24 hours prior. We also collected blood specimens from outpatients who are having a COVID-19 antibody test completed and from follow-up outpatients. We also collected and banked additional discarded samples from procedures performed for clinical indications, including urine, bronchoalveolar lavage, stool, and placenta.

### In Focus: Coronavirus Response cont.



We obtain prospective collections after the subject has been consented or the LAR/surrogate has consented for the subject. We collected blood samples on the initial hospital day for COVID-19 subjects, approximately 24 hours and 7 days after the first blood draw, and on the day of discharge. We also collected and banked additional discarded samples from procedures performed for clinical indications, including urine collection, bronchoalveolar lavage, thoracentesis, and paracentesis. Prospective collections also include discarded/leftover samples from any COVID-19 treatment trials.

#### Specimen Processing and Storage

Setting up a COVID-19 biorepository is a delicate and complex task that requires maximum biosafety measures and the best quality of biospecimens. The BTRF has followed guidelines from the CDC and the WHO for COVID-19 specimen handling as follows:

- Interim guidelines for collecting, handling, and testing clinical specimens from patients under investigation (PUIs) for coronavirus disease 2019 (COVID-19) (CDC)
- Interim laboratory biosafety guidelines for handling and processing specimens associated with coronavirus disease 2019 (COVID-19) (CDC)
- <u>Novel coronavirus (2019-nCoV) technical guidance: laboratory</u> testing for 2019-nCoV in humans (WHO)
- <u>Laboratory biosafety guidance related to the novel</u> <u>coronavirus (2019-nCoV) (WHO)</u>

The BTRF first performed a site-specific and activity-specific assessment to identify and mitigate risks, including procedures performed, hazards involved in the processing procedures, competency level of lab personnel, laboratory equipment and other resources available. We then generated our standard operating procedures (SOPs) for general and specific biosafety guidelines for handling COVID-19 specimens. We followed standard procedures for handling clinical specimens, and for routine laboratory practices, including decontamination of work surfaces and management of laboratory waste. We also followed standard procedures for infectious particles generated from aerosols or droplets using a certified Class II Biological Safety Cabinet (BSC) and additional precautions to provide a barrier between the specimen and personnel. Examples of these additional precautions include personal protective equipment (PPE), such as surgical masks, face shields, and splash shields, including centrifuge safety cups, and sealed centrifuge rotors.

We generated the SOPs for lab processing procedures with the COVID-19 biospecimen subcommittee guidance. Below is the information on samples obtained and product types.

Sample	Collection Container	Products
Blood	Red top Lavender top P 100 tube PaxGene DNA PaxGene RNA Urine	Serum Fixed whole blood with Smart reagent, plasma, PBMC Plasma Whole blood for DNA isolation Whole blood for RNA isolation Whole urine and cell-free urine
BAL and other fluids	Special container	Supernatant fluid and cell pellet

#### Sample Distribution

The COVID-19 biospecimen subcommittee has been tasked to review requests for biospecimens from COVID-19 subjects. With a limited number of COVID-19 samples available, each request is evaluated based on the following criteria: (1) type and amount of specimen requested; (2) application of sample sparing methods; and (3) potential for data sharing with other investigators to maximize research efforts while mitigating duplication of results.

The principal investigator is required to get an IRB approval and notify the Institutional Biosafety Committee (IBC) of the nature and location of the work with COVID-19 samples. Once the request is approved by the committee, the investigator will contact BTRF for obtaining the samples. Fees for this service cover all costs involved with collecting, retrieving, and processing/preparing the biospecimen for short or long-term storage or pick-up. The fees vary per type of biospecimen. Please refer to iLab for COVID-19 fee structures that currently are subsidized by iTHRIV for 25% (https:// uva.corefacilities.org).



# In Focus: Coronavirus Response cont.

#### Conclusion

Setting-up a COVID-19 biorepository requires patient advocacy, transdisciplinary collaboration, and creative solutions due to unique challenges<sup>1,2</sup>. The development of a biobank has the same requirements as the development of a research laboratory. However, by obtaining the necessary accreditations and following stringent SOPs, biobanks have the potential to offer the public unique clinical and research-based services. Biospecimens are the critical fuel needed for human disease-oriented research. This biorepository is unique in its comprehensive sample collection; it serves as an important resource for research into the impact of COVID-19 and provides lessons for future biorepository efforts.

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### **Education**

#### By Anne Mills, MD



The COVID-19 pandemic has presented major challenges for pathology education, requiring constant adaptation and innovation. When the virus first hit, medical students were pulled from elective rotations by the School of Medicine and a subset of pathology residents were stationed to work remotely from home. The majority of our trainees, however, continued to remain onsite, providing invaluable hands-on diagnostic services to the many patients who continued to need

our services.

By late spring, all of our residents and fellows resumed working on Grounds, and by the end of the summer, rotating medical students were once again able to join our department in person. UVA Pathology has been able to do this safely by following careful protective measures, including universal masking, social distancing, and use of Plexiglas shields at multiheaded microscopes. Individual services have also been creative, nimble, and proactive about protecting our trainees and staff. For instance, the autopsy service enlisted nasal swab-based COVID testing prior to performing dissection on decedents with histories concerning for the virus. On surgical pathology, we adapted fixation practices for high-risk specimens, requiring prolonged formalin exposure time for tissue types that have been shown to carry high viral loads, such as lung and small bowel. Our cytopathology team validated and deployed a rapid fixation technique for rapid onsite fine needle aspirates to minimize potential exposures. The blood



bank and transfusion service developed creative ways to round on patients remotely while maximized social distancing without compromising patient care.

We have also worked hard to ensure that our trainees' wellness is prioritized during these uncertain times. For the first several months of the pandemic, we held weekly check-ins to keep the residents and fellows abreast of ever-changing risks and recommendations and to keep a pulse on their stress levels. We also hosted faculty from the Department of Psychiatry and Neurobehavioral Sciences' Division of Behavior Medicine, who ran interactive sessions for the trainees on coping strategies for healthcare providers working through the pandemic. Finally, an anonymous faculty benefactor keeps graciously buying them single-serving lunches to counteract the hospital's more limited food offerings; we have been sworn to secrecy but her name starts with a "B" and ends in "Lopes."

The biggest shift in our education and training practice, however, has been the transition to virtual conferences, lectures, and slide sessions. This transition has been largely seamless, and we are proud to say that there was only a single week when teaching conferences were canceled due to COVID-19! While teaching via Zoom can feel impersonal and awkward at times, it has been made considerably easier by the fact that all trainees were provided with webcams and microphones to facilitate face-to-face interaction over the screens. Moreover, there have been unexpected benefits: the ability to easily record lectures has made it easier for residents to review material, and the usual logistical challenges to hosting outside expert speakers are virtually nonexistent (pun intended!). Perhaps the biggest success story of virtual learning has been the two-week rotation that we offered for prospective applicants in August. During these "Path Camp" weeks, more than twenty visitors applying for the upcoming pathology match joined our department for four hours of virtual content each day. These sessions were spearheaded by residents, laboratory medicine faculty, and anatomic pathology faculty and ranged from chemistry and genomics lectures to surgical pathology slide sessions to informal chats about our program, living in Charlottesville, and our department's efforts to promote diversity, equity, and inclusion. This program is just one example of how our UVA Pathology has truly made the best of adverse circumstances.

While COVID-19 has surely presented challenges to teaching and learning pathology, our faculty and trainees have risen to the occasion beautifully, and the fundamentals of our practice have remained largely unchanged. We are confident that we will emerge from this pandemic an even stronger and more cohesive training program.

# **Faculty: Moving On**



#### Stacey Mills, MD

It has been almost a year since Dr. Stacey "Chuck" Mills retired from UVA, but his presence still resonates strongly. His oft-quoted phrases and witticisms resurface regularly, and his name retains its place of prominence on the copies of Sternberg's Diagnostic Surgical Pathology (soon to be Mills & Sternberg's Diagnostic Surgical Pathology) and issues of AJSP that line our shelves. We are reminded of him whenever we see the faculty South Park characters that hang on many of our doors (yes, they're still up!) and by the playfully Socratic manner with which Dr. Stelow moderates the weekly unknown slide session, which will forever be known as "Mills Conference". And every time someone mentions a tumor's "cell-of-origin," he suddenly disapparates from his bucolic retirement life to shake us into reason and strike the term from our lexicon. Indeed, his mark on our department and our field was so indelible, we happily anticipate that his professional legacy will be permanently baked into UVA Pathology's institutional culture and collective wisdom.



When one has such a long and impactful career, it is

easy to imagine that the transition to retirement might be jarring. I am happy to report that in his case, it has been joyful and seamless thanks both to tremendous good fortune and to the virtue of hobbies. Chuck Mills has always been a man of many interests, of which pathology was only one. Since leaving our department, he has thrown himself wholeheartedly into his astronomy work, building not one but two observatories on his Louisa County property and capturing breathtaking images of distant galaxies (including the NGC7331 galaxy pictured here: this galaxy is located 47 million light-years away, measures 130,000 light years in width, and is composed of roughly 300 billion suns). He and Linda are also enjoying socially distanced visits and Zoom calls with their two sets of grandchildren and are relishing training their new puppy, Maxwell (named after physicist James C. Maxwell). Chuck reports that he misses seeing us all every day... but not that much.



#### Mark H. Stoler, MD

The other day I received a text from Mark Stoler. It was a picture from 14 years ago - ten anatomic pathology faculty, all with less gray hair than we have today, three who are about to retire.

"Who ARE those people?" I texted back.

"People with history," he responded.

Mark should know. His career is filled with historical moments. Read any landmark study on HPV and cervical dysplasia and Mark Stoler is an author. Review the registration books from anatomic pathology national meetings and international HPV meetings from the last three decades and MH Stoler is there. Whether as president of the ASCP, as a panelist at the ASC, or as the keynote speaker, he continually educated pathologists around the world about the biology of human

papillomavirus and its detection, vaccines, and best managerial practices. With all his national and international activities, you would think he had little energy left for UVA. But that's really how I know him, my office neighbor who kept me entertained with his boisterous voice and enthusiasm.

During a recent lunch, I asked Mark what makes him proud as he looks back over his career. "The fellows," he says. "The gyn and cytology fellows who are practicing from coast to coast and making a huge impact in the literature, who provide exceptional patient care, and who feel like extended family."



### Faculty: Moving On cont.

#### Mark H. Stoler, MD cont.

Over the last 15 years I have seen firsthand how residents and fellows benefited from his direct and benevolent coaching about good patient care. Fourteen gynecologic pathology fellows and many cytology fellows have spent many an afternoon pouring over research slides or challenging cases with him. You can see the pride in his face at the UVA dinners at national meetings. He loves this legacy.

I was not a resident or fellow under Mark. I met him as a colleague. There is still a moment that resonates with me. I had been at UVA for a year and, in that time, had my first child. I was quietly struggling with the reduced time and mental capacity I had for work. Mark and I were chatting and I unexpectedly said, "I feel like I am not giving UVA my best." Without missing a beat, Mark said, "Sure you are. You are just giving UVA your new best… and it's more than enough." It was the response of someone with history and perspective. It was a response that recalibrated what enough meant.

The faculty in that picture celebrate our shared history. We all watched as Paula's and his girls grew up and married, we cringed at the X-ray of his tib fib fracture during his beach vacation, we were (every one of us) schooled on the latest technology, and we walked with him though life's inevitable ups and downs, and saw the thousands of images of his grandchildren on his screensaver. And, recently, we watched him completely support Paula through her cancer ordeal.

We all know that he gave us his best... and it definitely was enough.



**Thomas Tillack, MD,** retired this year after a 44-year career in the UVA Department of Pathology, functioning as an educator, researcher, and pathologist; he was chairman for 25 years. Dr. Tillack received his MD degree from Yale University School of Medicine in 1963 and completed his training in anatomic and experimental pathology at Washington University School of Medicine and Barnes Hospital in St. Louis, Missouri, from 1963-1966. He then moved to the Laboratory of Experimental Pathology at the National Institutes of Health, NIAMD, as a staff associate and fellow to complete his experimental pathology training. In 1971, Dr. Tillack began his academic career as an assistant professor and then associate professor in the Department of Pathology at the Washington University School of Medicine and Barnes Hospital.

In 1976, he was recruited to UVA as the Walter Reed Professor and Chairman of the Department of Pathology and Pathologist-in-Chief of the University of Virginia Medical Center. At the time of his arrival at UVA, the Department of Pathology was relatively small and included Drs. Ben Sturgill, Shannon Allen, Kuldeep Teja, and Ms. Jamie Covell in the Division of Anatomic Pathology, and Drs. David Normansell and John Schwartzman in the Division of Clinical Pathology. Under Dr. Tillack's leadership an expansion of the faculty of both the anatomic and clinical pathology divisions occurred. In the following 3-4 years of his leadership, Dr. Tillack recruited Drs. Robert Fechner, Phil Feldman, Phil Cooper and Lucien Rubinstein, who were critical for the progression and modernization of the surgical pathology, cytopathology, dermatopathology and neuropathology areas, respectively. In clinical pathology, the faculty was greatly augmented by Dr. Tillack's recruitment of Drs. Michael Willis, John Savory, Dieter Gröschel, David Bruns, James Boyd and Paul Mintz. The addition of the new faculty in the department aided in the education and retention of several trainees including, Drs. Stacey Mills, Don Innes, Scott VandenBerg, Henry Frierson and Pamela Clark, who helped strengthen the department to become one of the finest in the nation.

In addition to being chairman of the department, Dr. Tillack had a research career funded by an NIH R01 grant from 1979 to 1996 in collaboration with Dr. Thomas E. Thompson in the UVA Department of Biochemistry; his research focus was to study the structural and functional properties of biological membranes. As an experimental pathologist, Dr. Tillack also greatly expanded UVA's Division of Experimental Pathology, making research a fundamental mission of the department. He expanded the faculty in that area with recruitment of both PhD-scientists and physician-scientists, including Drs. Steve Gonias, Dede Haverstick, Elizabeth Bruns, and Kenneth Tung, among others. Firmly believing in the expanded role of research in the department, Dr. Tillack concentrated on finding improved facilities for the research mission, culminating in the funding of the MR-5 building to accommodate the experimental division of the department.

In 2001, Dr. Tillack left his duties as chairman of the department, and for the next nearly 20 years contributed as an attending in the autopsy service, teaching the new generation of pathologists the basic principles of general pathology and, most significantly, cardiovascular pathology, a special topic of interest.

The generations of pathologists who trained or practiced at UVA thank Dr. Tillack for his long-standing contributions to the department, his collegiality, and his upmost support of his colleagues.

# **Faculty: Moving In**



**Shyam Raghavan, MD,** received his SB in chemical engineering from the Massachusetts Institute of Technology and his MD from Stanford University School of Medicine. After completing medical school, he spent four years as a plastic surgery resident at the University of California San Francisco, including one year as a biodesign fellow developing a novel device to decrease central line associated blood stream infection (CLABSI). In 2016, he transitioned into a pathology residency at his alma mater Stanford University, where he also completed a fellowship in gastrointestinal pathology as well as dermatopathology. His research interests include identifying novel molecular drivers in melanocytic and soft tissue tumors, along with inflammatory disease of the gastrointestinal tract. Outside of the hospital, he enjoys tennis, golf, being a devoted (painfully so) Arizona sports fan, and spending time with his wife, Rachel, a hospitalist at UVA, his kitten, Elsa, and his puppy, Fitz.

# Faculty: Moving Up



**Nadine Aguilera, MD,** was promoted to professor of pathology. Her main areas of interest are lymphoma and splenic pathology. She has published over 60 peer-reviewed articles and over 50 book chapters on spleen and molecular findings in lymphoid neoplasms. She is involved nationally in American Society for Clinical Pathology, Society for Hematopathology and College of American Pathologists. She participates in Graduate Medical Education at the national level, including sitting on the Fellowship In-service Hematopathology Examination (FISHE) committee. Dr. Aguilera is the section head of hematopathology and medical director of the hematology laboratory. She is also the director of the hematopathology fellowship. Aside from pathology, she enjoys painting and gardening and hanging out with her husband.



**Kristen Atkins, MD,** was promoted to chief of the Division of Anatomic Pathology. Her main areas of interest are in women's oncology and cytopathology, in which she has published over 70 peer-reviewed articles and coedited a breast pathology textbook. She is involved nationally in the American Society of Cytopathology and USCAP and has received numerous teaching awards, including the GME Master Educator Award, the Excellence in Education Award from the American Society of Cytopathology, the Mullholland teaching award for UVA medical students, the University of Vermont Academic Achievement Alumni Award, and the ASC Presidential Award. Dr. Atkins is interested in feedback and effective communication. When she is not teaching or diagnosing, she is performing in the Charlottesville Playback Theater group, playing collaborative board games with her husband and two teenage children and trying to obtain mindfulness in her life perspective.



**Helen Cathro, MBChB,** was promoted to professor of pathology with an adjunct appointment in the UVA Department of Internal medicine, Divisions of Nephrology and Rheumatology. Her special areas of interest are medical disease of the kidney, transplant pathology and genitourinary pathology. She is director of the Electron Microscopy Laboratory and heads the renal pathology program at UVA, which continues to grow based in large part on the doubling of kidney transplant numbers over the last two years. Dr. Cathro teaches pathology trainees, but also fellows in adult and pediatric nephrology, cardiology and rheumatology, and she is proud to have mentored a number of residents who have chosen a career in nephropathology. She has published 58 peer-reviewed articles, many in collaboration with colleagues in urology, nephrology, transplant surgery and otolaryngology. She is co-investigator on an NIDDK grant, and study pathologist on three unfunded grants. She coleads the Wellness Committee for the Pathology Residency Program and is chair of the residency Clinical Competency Committee. Her interests include swimming, cycling and gardening.

# Faculty: Moving Up cont.



**Alejandro Gru, MD,** was promoted to tenured associate professor of pathology and dermatology. He's been at UVA since 2015, prior to which he was on the faculty at the Ohio State University. He's currently the section and fellowship program director of dermatopathology. He's co-authored more than 120 peer-reviewed publications, and is the lead editor of two textbooks, *Hematopathology of the Skin* and *Pediatric Dermatopathology and Dermatology*. Dr. Gru's main area of expertise is in the field of skin lymphomas, pediatric dermatopathology, and melanocytic tumors. He's on the editorial board of the *American Journal of Surgical Pathology, BMC Cancer, Journal of Cutaneous Pathology*, and *Seminars in Diagnostic Pathology*. He's the pathology lead for the international PROCLIPI study and USCLC cancer registry and on the advisory board for the Cutaneous Lymphoma Foundation and part of the board of directors for the United States Cutaneous Lymphoma Consortium.



**Anne Mills, MD,** was promoted to associate professor of pathology. She has been on the UVA faculty since 2015 and serves as the AP/CP Residency program director and Gynecologic and Breast Pathology Fellowship director. She has authored more than 60 peer-reviewed research manuscripts and 15 review articles and textbook chapters, including contributions to the most recent edition of the *World Health Organization's Classification of Tumors of the Female Genital Tract* and the upcoming edition of *Mills & Sternberg's Diagnostic Surgical Pathology*. She has mentored over 20 residents and fellows in research, resulting in more than 35 trainee-driven original manuscripts. She serves on the editorial board for *The American Journal of Surgical Pathology, Archives of Pathology and Laboratory Medicine,* and *International Journal of Gynecological Pathology*. Her expertise centers on biomarkers of immunotherapeutic vulnerability, heritable cancer syndromes, and HPV-associated neoplasia, and she speaks nationally and internationally on these subjects. Beyond the microscope, she enjoys trail running, scuba diving, reading, and spending time with her husband and children.



**Eli Williams, PhD,** was promoted to associate professor of pathology. His main area of interest is the effective application of genetic/genomic technology in medicine, a field in which he has published numerous peer-reviewed articles and textbook chapters. Dr. Williams is medical director of Clinical Genomics for the UVA Health. He also serves as the director of the newly established Laboratory Genetics and Genomics Fellowship (first fellow July 2020) and is the thread leader for genomic medicine for the UVA School of Medicine. When he is not working, Dr. Williams enjoys hiking, biking, and camping with his wife and two teenage children.

# **First-Year Trainees**



### **First-Year Residents**

**Brett Kurpiel, MD,** is from the Pittsburgh, Pennsylvania, area and attended Saint Vincent College where he completed his B.A. in cell and molecular biology. Brett went on to the University of Virginia to complete his MD this past May 2020. Brett and his husband, Cameron, are so excited to be spending more time here in Charlottesville for the next few years! Brett's interests in pathology lie in pediatric pathology, perinatal pathology, and medical education. In their free time, Brett and Cameron like to spend time with their dogs, Tally and Hayden, kayak down the Rivanna, and visit the local distilleries and wineries.

# First-Year Trainees cont.



**Ngome Makia, MD,** is originally from Cameroon in Africa. He came to the U.S. in 2006 for school. He went to medical school at the University of Kentucky in Lexington. He likes to play soccer, tennis, run and sight-see.



**Shannon May, MD,** grew up in Palmer, Alaska. She completed a B.S. in medical laboratory science in 2009 and worked in the clinical laboratory at a tertiary care hospital in Anchorage, Alaska, before heading east to UVA for medical school. She is excited to continue training at UVA as an AP/CP resident. Her husband, Alec, is an electrical engineer. They live in the country with their one-year-old son and a colony of wild rabbits of undetermined size. In her free time, she likes to read, hike, crochet, and fend off the weeds growing in her flower beds.



**Elisabeth Miller, MD,** grew up in Great Falls, Montana, and attended Carroll College in Helena where she majored in biology and minored in chemistry. In medical school, she completed her degree through the University of Washington's WWAMI program, visiting the northwest states for clerkships. She enjoys traveling, painting, and baking. She is excited and thankful to start her first year of pathology residency at the University of Virginia!



**Yongsang Park, MD,** grew up in the Hampton Roads area and has attended the University of Virginia for undergrad, medical school, and now residency. He adopted a greyhound-labrador puppy, Mona, from the Charlottesville SPCA along the way, and the two enjoy going on long excursions downtown or on Grounds. His other non-medical related activities include tinkering with electronics and taking long drives down U.S. 29.

### **First-Year Fellows**



**Wesley Mallinger, DO,** grew up in Windermere Florida, a suburb of Orlando, and went to the University of Florida for undergraduate studies. He went to medical school at VCOM in Spartanburg, South Carolina. He did his third and fourth year clinical rotations in Florence, South Carolina, where he met his wife of two years, Caitlin. He completed his AP/CP pathology residency at the University of Arkansas for Medical Sciences in Little Rock, Arkansas. He likes all kinds of outdoor activities, spending time with his wife, and watching college football, Go Gators!

# First-Year Trainees cont.



**Hong Jiang, MD,** is probably the only person who flew over half of the earth to join the dermpath program. She and her family are from China. Besides the beautiful microscopic world, she really enjoys living in Charlottesville, the stunningly beautiful views, hiking places and parks.



**Virginia Miller, DO,** was raised on a farm in rural Ohio, and trained as a cytotechnologist, while completing medical school and working with underserved rural populations. She then pursued an AP/CP residency at the University of Kentucky in Lexington, Kentucky, where she developed a keen interest in soft tissue and dermatopathology. Dr. Miller then went on to complete a cytolopathology fellowship at MUSC before attending UPMC for a bone and soft tissue fellowship, where she subsequently worked as faculty and worked on research related to dedifferentiation within chondrosarcoma. Interests include soft tissue and dermatopathology, particularly expanding the appreciation of pathology to other medical specialties and beyond. She loves being outdoors, creative writing/ reading, and growing nearly anything!



**Lei Wang, PhD,** from China, received her doctoral degree in physiology and integrative biology at Rutgers University in New Jersey. After her postdoctoral training at Baylor College of Medicine and three years at Baylor Genetics Laboratory as a clinical genomic scientist, she is currently a Laboratory Genetics and Genomics fellow at UVA. In her free time, she enjoys gardening, reading, watching movies and sports games.

### **First-Year Graduate Students**



**Karolina Dziewulska** was born and raised in Warsaw, Poland, where she graduated from the University with an MSc in molecular biology and Biotechnology. She came to UVA in 2017 to work in Dr. Michael Brown's lab as part of Fulbright's Visiting Graduate Research Training Program. After a year, Karolina decided to enroll in BIMS full-time and she now works in the lab of Dr. James Zimring. In her free time, she turns into an amateur movie critic and self-taught chef, spoiling both her fiancée and FITC, the dog.



**Niket Yadav** was born and raised in Cincinnati, Ohio. He completed a double major B.S. in biochemistry and neuroscience at the University of Cincinnati in 2018. Currently, he is a first-year BIMS-MD/PhD graduate student who joined the Bullock lab in March 2020. He transitioned to graduate education after completing the first two years of medical school. His research interests include investigating immunotherapy mechanisms to treat brain tumors. He enjoys various forms of athletic training, including weight-lifting and basketball. He also enjoys playing video games.

# **Grants and Contracts**

### **New Grants and Contracts**

#### PI: Timothy Bullock, PhD Department of Defense

Enhanced Melanoma Vaccine against Neoantigens and Shared Antigens by CD40 Activation and TLR Agonists 07/15/2019-07/14/2023 Total Budget: \$422,524 2020 Budget: \$422,524

#### National Cancer Institute

Leveraging MR-guided focused ultrasound to potentiate immunotherapy for GBM 09/19/2019-08/31/2021 Total Budget: \$382,635 2020 Budget: \$173,754

#### PI: Adam Goldfarb, MD National Institute of Diabetes & Digestive & Kidney Diseases

Dissection and Manipulation of the Cellular Response to Iron Restriction 09/09/2019-06/30/2024 Total Budget: \$2,158,693 2020 Budget: \$1,053,459

#### National Heart, Lung and Blood Institute

Targeting Dyrk1a to Promote Donorindependent Platelet Production 02/20/2020-01/31/2024 Total Budget: \$2,812,131 2020 Budget: \$714,564

### PI: Alejandro Gru, MD

Stemline Therapeutics, Inc. Molecular characterization of Blastic Plasmacytoid Dendritic cell Neoplasm (BPDCN) 11/13/2019-11/12/2021 Total Budget: \$59,614 2020 Budget: \$59,614

### PI: Hui Li, PhD

National Cancer Institute Targeting AVIL in Glioblastoma 03/01/2020-02/28/2025 Total Budget: \$2,476,173 2020 Budget: \$489,873

### National Institute of General Medical Science

Genome-wide Investigation of cis-splicing between Adjacent Genes 09/03/2019-07/31/2023 Total Budget: \$1,292,000 2020 Budget: \$323,000

#### National Cancer Institute

Chimeric RNAs and their implication in lymphatic metastasis of bladder cancer 03/01/2020-02/28/2025 Total Budget: \$1,029,565 2020 Budget: \$ 205,913

#### PI: James Zimring, MD, PhD

National Heart, Lung and Blood Institute Immunobiology of Transfusion 09/15/2019-06/30/2022 Total Budget: \$8,276,223 2020 Budget: \$5,784,049

#### National Heart, Lung and Blood Institute

Immunobiology of Alloimmunization by Platelet Transfusion 08/15/2019-06/30/2023 Total Budget: \$2,202,344 2020 Budget: \$1,101,172

#### Regents of the University of Colorado (NHLBI-R01) PIMT1 in Red Blood Cell senescence and aging 08/01/2019-04/30/2024

08/01/2019-04/30/2024 Total Budget: \$1,610,735 2020 Budget: \$682,798

### The Trustees of Columbia University in the

**City of New York (NHLBI-R01)** The Impact of Oxidative Stress on Erythrocyte Biology 09/25/2019-08/31/20 Total Budget: \$1,876,920 2020 Budget: \$469,230

### University Of Colorado (NHLBI-R01)

Interactions between the ADORA2b/Sphk1 axis and the AE1-Hb switch in red blood cell aging in vivo and in vitro 03/15/2020-02/29/2024 Total Budget: \$1,368,152 2020 Budget: \$402,037

### University of California at San Francisco (NHLBI-R01)

Mechanisms of antibody-mediated lung Injury after blood transfusion 07/01/2019-12/31/22 Total Budget: \$649,200 2020 Budget: \$344,798

### Emory University (NHLBI-P01)

Serious Hazards of Transfusion & Cellular Therapies: Mechanisms and Interventions 07/01/2019-04/30/2020 Total Budget: \$335,306 2020 Budget: \$335,306

### Other Active Grants and

Contracts (Federal Funding)

#### PI: Thomas Braciale, MD, PhD National Institute of Allergy and Infectious Diseases

Leukotriene modifying agents in the prevention of excess morbidity and mortality from influenza 08/07/2018-07/31/2021 2020 Budget: \$381,190

### National Institute of Allergy and Infectious Diseases

Control of Influenza Infection by Lipid Mediators and Macrophages 01/10/2018-12/31/2022 2020 Budget: \$549,761

#### PI: Robin Felder, PhD

National Heart, Lung and Blood Institute Molecular Mechanisms in Salt Sensitivity of Blood Pressure 06/01/16-05/31/21 2020 Budget: \$2,236,673

#### National Heart, Lung and Blood Institute

Renal Dopamine-1 Receptor Defect in Hypertension 01/01/2017-12/31/2022 2020 Budget: \$160,209

#### PI: John Luckey, MD, PhD

National Heart, Lung, and Blood Institute Cytokine Control of Red Blood Cell Alloimmunization 12/15/16-11/30/20 2020 Budget: \$519,149

#### National Heart, Lung, and Blood Institute

Immunobiology of Transfusion 07/01/2019-06/30/2022 2020 Budget: \$570,111

#### PI: Mani Mahadevan, MD National Institute of Arthritis & Musculoskeletal & Skin Disease RNA Toxicity and Muscle Regeneration

02/20/17-12/31/21 2020 Budget: \$397,141

### PI: Chris Moskaluk, MD, PhD

National Cancer Institute Biospecimen Procurement & Tissue Microarray Manufacture for the CHTN 04/01/2019-03/31/2024 2020 Budget: \$992,980

# Total Annual Federal Funding: \$18,309,691

Other Active Grants and Contracts (Non-Federal Funding)

### Pls:

Timothy Bullock, PhD Alejandro Gru, MD Hui Li, PhD Chris Moskaluk, MD, PhD Melinda Poulter, PhD Joe Wiencek, PhD Eli Williams, PhD

Total Annual Non-Federal Funding: \$435,781

# **Publications and Awards**

### **Selected Faculty Publications**

### **Journal Articles**

#### Aguilera NS, Auerbach A

T-cell lymphoproliferative processes in the spleen. Semin Diagn Pathol. 2020 Jan;37 (1):47-56. doi: 10.1053/ j.semdp.2019.12.003. Epub 2019 Dec 18. PMID: 31879048

**Bruns DE**, Metzger BE, Sacks DB Diagnosis of Gestational Diabetes Mellitus Will Be Flawed until We Can Measure Glucose. Clin Chem. 2020 Feb 1;66(2):265-267. doi: 10.1093/clinchem/hvz027. PMID: 32040567; PMCID: PMC7055661.

**Courville EL**, Yohe S, Shivers P, Linden MA VS38 Identifies Myeloma Cells With Dim CD38 Expression and Plasma Cells Following Daratumumab Therapy, Which Interferes With CD38 Detection for 4 to 6 Months. Am J Clin Pathol. 2020 Jan 2;153(2):221-228. doi: 10.1093/ajcp/aqz153.PMID: 31679012

Xu P, Gildea JJ, Zhang C, Konkalmatt P, Cuevas S, Bigler Wang D, Tran HT, Jose PA, **Felder RA** 

Stomach gastrin is regulated by sodium via PPAR- $\alpha$  and dopamine D1 receptor. J Mol Endocrinol. 2020 Feb;64(2):53-65. doi: 10.1530/JME-19-0053. PMID: 31794424

Balogh P, Adelman ER, Pluvinage JV, Capaldo BJ, Freeman KC, Singh S, Elagib KE, Nakamura Y, Kurita R, Sashida G, Zunder ER, Li H, Gru AA, Price EA, Schrier SL, Weissman IL, Figueroa ME, Pang WW, Goldfarb AN RUNX3 levels in human hematopoietic progenitors are regulated by aging and dictate erythroid-myeloid balance.. Haematologica. 2020 Apr;105(4):905-913. doi: 10.3324/haematol.2018.208918. Epub 2019 Jun 6.PMID:

Gradecki SE, Slingluff CL Jr, **Gru AA** PRAME Expression in 155 Cases of Metastatic Melanoma.J Cutan Pathol. 2020 Sep 16. doi: 10.1111/cup.13876. Online ahead of print. PMID: 32939793

#### VanDyke S, Cocks M, $\ensuremath{\text{Gru}}\xspace \textbf{AA}$

A 40-Year-Old Woman With Hypopigmented Patches and a New Papular Rash: Challenge.Am J Dermatopathol. 2020 Sep;42 (9):e126-e127. doi: 10.1097/ DAD.00000000001575. PMID: 32833742

#### VanDyke S, Cocks M, Gru AA

A 40-Year-Old Woman With Hypopigmented Patches and a New Papular Rash: Answer.Am J Dermatopathol. 2020 Sep;42(9):712-713. doi: 10.1097/DAD.000000000001574. PMID: 32833740

#### Cruz DS, Plaza JA, Wick MR, Gru AA

Inflammatory lobular hemangioma (ILH): a vascular proliferation with a prominent lymphoid component. Review of a series of 19 cases. J Cutan Pathol. 2020 Aug 10. doi: 10.1111/cup.13844. Online ahead of print. PMID: 32779250

#### Kwock JM, Kurpiel B, Gru AA

T-Cell Lymphoblastic Lymphoma/Leukemia Presenting as a Diffuse Viral Exanthem-like Reaction: A Clinical and Histopathological Challenge. Am J Dermatopathol. 2020 Jul 23. doi: 10.1097/DAD.00000000001766. Online ahead of print. PMID: 32732689

#### Volaric A, Bacchi CE, Gru AA

PD-1 and PD-L1 Immunohistochemistry as a Diagnostic Tool for Classic Hodgkin Lymphoma in Small-volume Biopsies. Am J Surg Pathol. 2020 Oct;44(10):1353-1366. doi: 10.1097/PAS.00000000001524. PMID: 32649320

#### Subtil A, Gru AA

Secondary cutaneous involvement by direct extension in high-grade B-cell lymphomas. J Cutan Pathol. 2020 Jul 8. doi: 10.1111/ cup.13798. Online ahead of print. PMID: 32639608

Teran VA, McHargue CA, **Gru AA** Photodistributed Rash Progressing to Erythroderma: Answer. Am J Dermatopathol. 2020 Jun;42(6):463-465. doi: 10.1097/ DAD.00000000001413.PMID: 32433320

#### Valdes-Rodriguez R, Bryer B, **Gru AA** A story of a pimple: Newly diagnosed chronic lymphocytic leukemia in a basal cell carcinoma biopsy. J Cutan Pathol. 2020 May 16. doi: 10.1111/cup.13745. Online ahead of print. PMID: 32415679

Westover C, Bacchi C, **Gru AA** Clear Cell Sarcoma With Cutaneous

Presentation in a 4-Year-Old Boy. Am J Dermatopathol. 2020 Sep;42(9):e131-e133. doi: 10.1097/

DAD.00000000001658.PMID: 32324602

#### Gradecki SE, Gru AA

An unusual case of sarcomatoid renal cell carcinoma presenting in the skin by direct extension at a laparoscopic port site. J Cutan Pathol. 2020 Jul;47(7):617-620. doi: 10.1111/cup.13657. Epub 2020 Feb 18.PMID: 31998984

Abbas A, Flowers RH, Noland MB, **Gru AA** Pruritic Blistering Eruption: Answer. Am J Dermatopathol. 2020 Feb;42(2):144-145. doi: 10.1097/DAD.00000000001300. PMID: 31990703

Adkins BD, Ramos JC, **Bliss-Moreau M**, **Gru AA** Updates in lymph node and skin pathology of

adult T-cell leukemia/lymphoma, biomarkers, and beyond. Semin Diagn Pathol. 2020 Jan;37(1):1-10. doi: 10.1053/ j.semdp.2019.12.006. Epub 2019 Dec 20. PMID: 31889601

### Krishnan R, Ring K, Williams E, Portell C, Jaffe ES, Gru AA

An Enteropathy-like Indolent NK-Cell Proliferation Presenting in the Female Genital Tract. Am J Surg Pathol. 2020 Apr;44(4):561-565. doi: 10.1097/

PAS.00000000001387. PMID: 31609783

#### Cocks M, Gru AA

Quality assurance in dermatopathology: A review of report amendments. J Cutan Pathol. 2020 Aug 1. doi: 10.1111/cup.13827. Online ahead of print. PMID: 32740937

#### Wu S, Subtil A, Gru AA

Epidermotropic Epstein-Barr virus-Positive Diffuse Large B-Cell Lymphoma: A Series of 3 Cases of a Very Unusual High-Grade Lymphoma. .Am J Dermatopathol. 2020 Jul 7. doi: 10.1097/DAD.000000000001718. Online ahead of print. PMID: 32649345 No abstract available.

#### Gru AA

Getting CIC of cutaneous soft tissue sarcomas. J Cutan Pathol. 2020 Jun;47 (6):506-508. doi: 10.1111/ cup.13682.PMID: 32166781 No abstract available.

Xu ML, Gabali A, Hsi ED, Fedoriw Y, Vij K, Salama ME, Ramchandren R, O'Malley D, Wick MR, Battistella M, Gru AA Practical Approaches on CD30 Detection and Reporting in Lymphoma Diagnosis. Am J Surg Pathol. 2020 Feb;44(2):e1-e14. doi: 10.1097/PAS.00000000001368. PMID: 3156727

#### Yu M, **Bazydlo LAL, Bruns DE, Harrison JH Jr.** Streamlining Quality Review of Mass Spectrometry Data in the Clinical Laboratory by Use of Machine Learning. Arch Pathol Lab Med. 2019 Aug;143(8):990-998. doi: 10.5858/arpa.2018-0238-0A. Epub 2019 Feb 20. PMID: 30785786.

Xie Z, Janczyk PŁ, Zhang Y, Liu A, Shi X, Singh S, Facemire L, Kubow K, Li Z, Jia Y, Schafer D, **Mandell JW**, Abounader R, **Li H** A cytoskeleton regulator AVIL drives tumorigenesis in glioblastoma. Nat Commun. 2020 Jul 10;11(1):3457. doi: 10.1038/ s41467-020-17279-1.PMID: 32651364

Wu H, Singh S, Xie Z, Li X, **LI H** landscape characterization of chimeric RNAs in colorectal cancer, Cancer Letters 2020, https://doi.org/10.1016/ j.canlet.2020.05.037

# Publications and Awards cont.

#### Elfman J, Pham L, **Li H**

The Relationship Between Chimeric RNAs and Gene Fusions; Potential Implications of Reciprocity in Cancer, Journal of Genetics and Genomics (In press).

#### Shi X, Singh S, Lin E, **Li H**

Chimeric RNAs in Cancer, Advances in Clinical Chemistry, Vol 100 (in press)

Singh S, Qin F, Kumar S, Elfman J, Lin E, Pham L, Yang A, Li H

The landscape of chimeric RNAs in nondiseased tissues and cells, Nucleic Acids Research, 2020, gkz1223, https:// doi.org/10.1093/nar/gkz122

#### Tang Y, Guan F, Li H

Case Study: The Recurrent Fusion RNA DUS4L-BCAP29 in Noncancer Human Tissues and Cells. Methods Mol Biol. 2020;2079:243 -258. doi: 10.1007/978-1-4939-9904-0\_19. PubMed PMID: 31728976.

#### Zhu D, **Li H**

Case Study: Landscape of Chimeric RNAs in Bladder Cancer. Methods Mol Biol. 2020;2079:233-241. doi: 10.1007/978-1-4939-9904-0\_18. PubMed PMID:31728975.

#### Qin F, Shi X, Li H

Separation of Nuclear and Cytoplasmic Fractions for Chimeric RNA Characterization. Methods Mol Biol. 2020;2079:167-175. doi:10.1007/978-1-4939-9904-0\_13. PubMed PMID: 31728970.

#### Wu H, **Li H**

Overexpression of Chimeric RNA by Retroviral Transduction. Methods Mol Biol. 2020;2079:155-166. doi: 10.1007/978-1-4939-9904-0\_12. PubMed PMID:31728969.

#### Qin F, Shi X, Li H

Knockdown of Chimeric RNA by RNAi. Methods Mol Biol. 2020;2079:143-154. doi: 10.1007/978-1-4939-9904-0\_11. PubMed PMID: 31728968.

#### Singh S, Li H

Validation of Chimeric Fusion Peptides Using Proteomics Data. Methods Mol Biol. 2020;2079:117-124. doi: 10.1007/978-1-4939-9904-0\_9. PubMed PMID: 31728966.

Zhao J, Tang J, Elfman J, **Li H** RNase Protection Assay. Methods Mol Biol. 2020;2079:109-116. doi: 10.1007/978-1-4939-9904-0\_8. PubMed PMID: 31728965.

#### Elfman J, Li H

Detection and Measurement of Chimeric RNAs by RT-PCR. Methods Mol Biol. 2020;2079:83-94. doi: 10.1007/978-1-4939-9904-0\_6. PubMed PMID: 31728963.

Singh S, Li H

Prediction, Characterization, and In Silico

Validation of Chimeric RNAs. Methods Mol Biol. 2020;2079:3-12. doi:10.1007/978-1-4939-9904-0\_1. PubMed PMID: 31728958.

Wu H, Singh S, Shi X, Xie Z, Lin E, Li X, **Li H** Functional heritage: the evolution of chimeric RNA into a gene. RNA Biol. 2019 Sep 29:1-10. doi:10.1080/15476286.2019.1670038. [Epub ahead of print] PubMed PMID: 31566065.

#### Wu H, Li X, **Li H**

Gene fusions and chimeric RNAs, and their implications in cancer. Genes & Diseaes. 2019. Dec; 6(4): 385–390., doi: 10.1016/ j.gendis.2019.08.002; PMID: 31832518

#### Lopes MBS

Pathology of prolactinomas: any predictive value? Pituitary. 2020 Feb;23(1):3-8. doi: 10.1007/s11102-019-00997-1. PMID: 31641970 Review.

#### Lopes MBS

World Health Ozganization 2017 Classification of Pituitary Tumors. Endocrinol Metab Clin North Am. 2020 Sep;49(3):375-386. doi: 10.1016/j.ecl.2020.05.001. Epub 2020 Jul 15. PMID: 32741477 Review.

Yadava RS, Yu Q, Mandal M, Rigo F, Bennett CF, Mahadevan MS

Systemic therapy in an RNA toxicity mouse model with an antisense oligonucleotide therapy targeting a non-CUG sequence within the DMPK 3'UTR RNA. Hum Mol Genet. 2020 Jun 3;29(9):1440-1453. doi: 10.1093/hmg/ ddaa060.PMID: 3224221

Park SC, Parikh H, Vegesana K, Stoesser N, Barry KE, Kotay SM, Dudley S, Peto TEA, Crook DW, Walker AS, **Mathers AJ** Risk factors associated with carbapenemaseproducing Enterobacterales (CPE) positivity in the hospital wastewater environment. Appl Environ Microbiol. 2020 Sep 11:AEM.01715-20. doi: 10.1128/AEM.01715-20. Online ahead of print. PMID: 32917755

#### Mathers AJ

The practical challenges of making clinical use of the quantitative value for SARS-CoV-2 viral load across several dynamics.Clin Infect Dis. 2020 Jul 10:ciaa958. doi: 10.1093/cid/ ciaa958. Online ahead of print. PMID: 32645717

Kotay SM, Parikh HI, Barry K, Gweon HS, Guilford W, Carroll J, **Mathers AJ** Nutrients influence the dynamics of Klebsiella pneumoniae carbapenemase producing enterobacterales in transplanted hospital sinks. Water Res. 2020 Jun 1;176:115707. doi: 10.1016/j.watres.2020.115707. Epub 2020 Mar 13.PMID: 32224328 Mathers AJ, Vegesana K, German-Mesner I, Ainsworth J, Pannone A, Crook DW, Sifri CD, Sheppard A, Stoesser N, Peto T, Walker AS, Eyre DW

Risk factors for Klebsiella pneumoniae carbapenemase (KPC) gene acquisition and clinical outcomes across multiple bacterial species. J Hosp Infect. 2020 Apr;104(4):456-468. doi: 10.1016/j.jhin.2020.01.005. Epub 2020 Jan 10. PMID: 31931046

#### Jenkins TM, Mills AM

Putative precancerous lesions of vulvar squamous cell carcinoma. Semin Diagn Pathol. 2020 Sep 6:S0740-2570(20)30082-4. doi: 10.1053/j.semdp.2020.09.006. Online ahead of print. PMID: 32948383

### Dibbern ME, **Bullock TN**, Jenkins TM, Duska LR, **Stoler MH, Mills AM**

Loss of MHC Class I Expression in HPVassociated Cervical and Vulvar Neoplasia: A Potential Mechanism of Resistance to Checkpoint Inhibition. Semin Diagn Pathol. 2020 Sep 6:S0740-2570(20)30082-4. doi: 10.1053/j.semdp.2020.09.006. Online ahead of print. PMID: 32948383

#### Friedman LA, Ring KL, Mills AM

LAG-3 and GAL-3 in Endometrial Carcinoma: Emerging Candidates for Immunotherapy. Int J Gynecol Pathol. 2020 May;39(3):203-212. doi: 10.1097/PGP.0000000000000608. PMID: 32267656

Curley J, Conaway MR, Chinn Z, Duska L, Stoler M, Mills AM

Looking past PD-L1: expression of immune checkpoint TIM-3 and its ligand galectin-9 in cervical and vulvar squamous neoplasia. Mod Pathol. 2020 Jun;33(6):1182-1192. doi: 10.1038/s41379-019-0433-3. Epub 2020 Mar 6. PMID: 32139873

#### Mills AM, Duska LR

Stuck in the middle: diagnostic and clinical management challenges surrounding CIN2. BJOG. 2020 May;127(6):737. doi: 10.1111/1471-0528.16153. Epub 2020 Feb 25. PMID: 32017418

Jenkins TM, Hanley KZ, Schwartz LE, Cantrell LA, **Stoler MH, Mills AM** 

Mismatch Repair Deficiency in Uterine Carcinosarcoma: A Multi-institution Retrospective Review. Am J Surg Pathol. 2020 Jun;44(6):782-792. doi: 10.1097/ PAS.00000000001434. PMID: 31934920

Whitehair R, Peres LC, Mills AM

Expression of the Immune Checkpoints LAG-3 and PD-L1 in High-grade Serous Ovarian Carcinoma: Relationship to Tumor-associated Lymphocytes and Germline BRCA Status. Int J Gynecol Pathol. 2019 Dec 16. doi: 10.1097/ PGP.00000000000657. Online ahead of print. PMID: 31851060

# Publications and Awards cont.

Jenkins TM, Cantrell LA, Stoler MH, Mills AM PD-L1 and mismatch repair status in uterine carcinosarcomas. Int J Gynecol Pathol. In press.

Friedman LA, Bullock TN, Sloan EA, Ring KL, Mills AM.

MHC Class I loss in endometrial carcinoma: A potential mechanism of resistance to checkpoint inhibition. Modern Pathol. In press.

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# Publications and Awards cont.

D'Alessandro A, Hay A, Dzieciatkowska M, Brown B, Morrison EJ, Hansen KC, **Zimring JC.** PIMT1 is Required for in Vivo Control of Oxidative Damage in Red Blood Cells. Haematologica (in press)

### Awards

**Drs. Chuck Mills, Mark Stoler and Kristen Atkins** have been named by their peers to the 2019-2020 Best Doctors in America List. **Dr. Lisa Friedman** won the first place poster in gynecological pathology presented by a trainee within the Stowall Orbison competition at the annual meeting of USCAP with her presentation entitled, "Loss of MHC Class I in Endometrial Carcinoma: a Possible Mechanism of Immunotherapeutic Resistance in Some MMR-Deficient and PDL1 -Positive Tumors." Co-authors: Emily Sloan, University of California San Francisco; Timothy Bullock, Kari Ring, and Anne Mills of the University of Virginia.

**Dr. Megan Dibbern** won the first pace platform in gynecologic pathology presented by a trainee for her presentation entitled, "Expression in HPV-associated Cervical and Vulvar Neoplasia: A Potential Mechanism of Resistance to Checkpoint Inhibition." Coauthors: Timothy Bullock, Taylor Jenkins, Linda Duska, Mark Stoler, and Anne Mills of the University of Virginia.

# **UVA Pathology In the News**

How Federal snafus slowed testing at tip U.S. hospitals By Peter Eisler and Chad Terhune | April 7, 2020 A Reuters Special Report

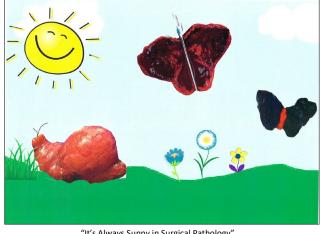
#### 75,000 COVID-19 nasal swab tests from UVA to be distributed across Virginia August 26,2020 WHSV3

Asymptomatic students, faculty, and staff can get a COVID-19 test at UVA By Racel Hrishheimer | August 31, 2020 NBC29

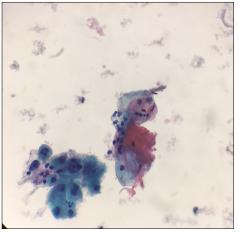
<u>UVA IDs Gene Responsible for Deadly Gioblastoma</u> July 14.2020 UVA Newsroom,



Amy Mathers, MD, shows how COVID-19 nasal testing swabs made at UVA will be used like commercially made tests.



"It's Always Sunny in Surgical Pathology" By: Nicole McGinn



"An Evil Lurks Among Us" By: Jennifer Ju, MD

# **National Presentations**

The University of Virginia's Department of Pathology had another strong showing at the 2020 Annual Meeting of the United States and Canadian Academy of Pathology in Los Angeles, California. Thirteen original research abstracts were presented by UVA medical students, residents, fellows, and faculty. Second-year resident Dr. Megan Dibbern was awarded the International Society of Gynecological Pathology's prestigious W. Dwayne Lawrence Award for her platform presentation "Loss of MHC Class I Expression in PD-L1 -positive HPV-Associated Cervical and Vulvar Neoplasia: A Mechanism of Resistance to Checkpoint Inhibition?", while first-year resident Dr. Lisa Friedman was awarded first place in the gynecologic poster section for her work entitled, "Loss of MHC Class I in Endometrial Carcinoma: A Possible Mechanism of Immunotherapeutic Resistance in Some MMR-Deficient and PD-L1-Positive Tumors." In other meeting highlights, Robin LeGallo, MD, helped lead the organization's first annual session on diversity and inclusion with a talk focused on the healthcare of transgender individuals.



Anne Mills, MD, delivered a talk entitled "PD-L1 immunostaining in Cervical and Vulvar Cancer" to an audience of several hundred at the meeting of the International Society of Gynecological Pathology and a three-hour SAMs/CME course on Biomarkers in Gynecologic Pathology. The most memorable part of the meeting, however, was the fun and fellowship that the UVA folks shared over Mediterranean food at the annual departmental meeting dinner.

#### Oral presentations:

ISGyP Companion Society Meeting,

Presenter: Anne Mills, MD Title: PD-L1 immunostaining in Cervical and Vulvar Cancer

USCAP Focus on Diversity and Inclusion Presenter: Robin LeGallo, MD Title: Healthcare of Transgender Individuals

### Poster Presentations:

#### Presenter: Bre Ana David, MD

**Title:** Mismatch Repair Deficiency and PD-L1 Expression in Sebaceous Carcinomas and Basal Cell Carcinomas with Sebaceous Features.

#### Presenter: Marge Moore, MD

**Title:** The Targetable Immune Checkpoint VISTA is Highly Expressed in a Subset of Endometrial Carcinomas, Particularly Those Exhibiting Mismatch Repair Deficiency and PD-L1 Expression.

#### Presenter: Jacob Curley, MD

Title: Looking Past PD-L1: Expression of Immune Checkpoint TIM-3 and its Ligand Galectin-9 in Cervical and Vulvar Squamous Neoplasia

#### Presenter: Lisa Friedman, MD

**Title:** Loss of MHC Class I in Endometrial Carcinoma: A Possible Mechanism of Immunotherapeutic Resistance in Some MMR-Deficient and PD-L1-Positive Tumors.

#### Presenter: Ed Stelow, MD

**Title**: Low-Grade Tubulo-Acinar Sinonasal Adenocarcinoma: A specific entity with recurrent beta-catenin mutations

#### Presenter: Brian Adkins, MD

**Title:** Characterizing the Lymphocyte Environment in Hospital Autopsy

Short Course

Presenter: Anne Mills, MD Title: Tests, Targets, and Treatments: Emerging Biomarkers in Gynecologic Carcinoma

#### Platform, Gynecologic Pathology Presenter: Megan Dibbern, MD

**Title:** Loss of MHC Class I Expression in PD-L1-positive HPV-Associated Cervical and Vulvar Neoplasia: A Mechanism of Resistance to Checkpoint Inhibition?

#### Presenter: Sarah Gradecki, MD

**Title:** p16 and Rb Expression and High-Risk HPV Status of 18 Sebaceous Carcinomas of the Conjunctiva and Eyelid

#### Presenter: Bea Lopes, MD

**Title:** Liver Metastases from Pituitary Carcinoma Mimicking Visceral Well-Differentiated Neuroendocrine Tumor

#### Presenter: Elisheva Shanes, MD

**Title:** IDO Expression in Uterine Smooth Muscle Tumors: Implications for Immunotherapy

#### Presenter: Marge Moore, MD

Title: HLA-1 Loss is Common in Non-Small Cell Lung Cancer and May Contribute to Failure of Immune Checkpoint Therapy

#### Presenter: Brett Kurpiel, MD

Title: MLH1-Hypermethylation and Mutation Status Among MLH1/ PMS2-Deficient Endometrial Carcinomas: Results from a Universally Screened Population

#### Presenter: Taylor Jenkins, MD

Title: PD-L1 and Mismatch Repair Status in Uterine Carcinosarcomas

# Philanthropy

### **Global Outreach**

We are pleased to announce several global outreach initiatives in pathology. Please consider a generous donation to assist us in providing these pathology outreach opportunities to our faculty and trainees. Professor of pathology Henry Frierson, MD, and pathology residents are spearheading pathology clinical outreach and cervical screening campaigns in Guatemala.

### Cytogenetics and Molecular Genetics Fellowship

A major missing piece to our training programs has been specialized training in molecular diagnostics. Eli Williams, PhD has taken on the task of creating this two-year fellowship program and the department



has decided to self-fund this program without institutional support. We could use your help in supporting this fellowship to enhance UVA's role in shaping the burgeoning fields of molecular diagnostics and clinical genomics.

### Sponsor a Pathology Summer Fellowship

The eight-week summer enrichment program in pathology provides second-year medical students with hands-on experience in disease diagnosis. Each intern rotates through all AP and laboratory medicine services. Please consider supporting our profession by contributing a donation to support a medical student in this program. The cost of hosting each student is \$2,500. With your support, we hope to provide two student stipends in 2020.

### Honor a Faculty Mentor

Thank your favorite 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 at med.virginia.edu/pathology or by check or credit card using the enclosed self-addressed return envelope.

# **WVAHealth**

#### **UVA Health**

Department of Pathology PO Box 800214 | 1215 Lee Street Charlottesville, VA 22908

UVA Path Report is an annual publication of the UVA Department of Pathology at UVA Health

Editors: Ray Selig and Barbara Becker

We would like to acknowledge the assistance of Angela Rogers and Kim Knotts.

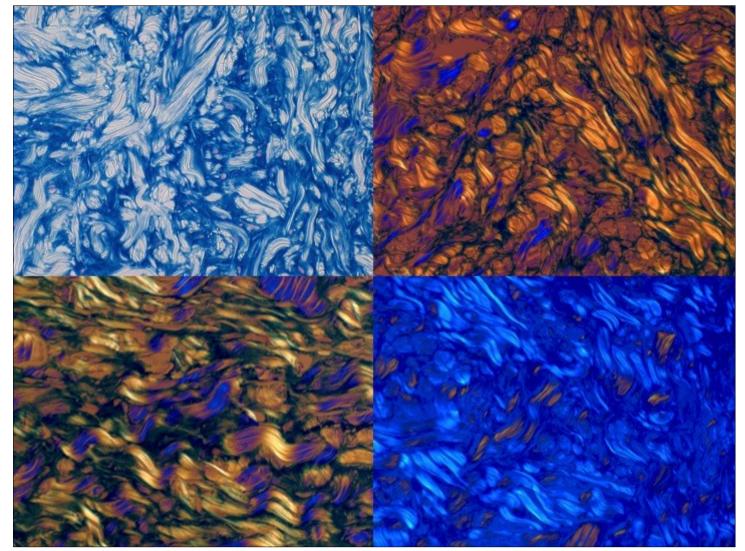
For more information, please visit: medicine.virginia.edu/pathology



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Winning image, titled "Building Blocks," by Margaret Cocks, MD, PhD, one of our dermatopathology fellows for 2018-2019.