

RESULTS & DISCUSSION

BRET Newsletter
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Editor-in-Chief: Alexandria Oviatt

Staff Advisor & Layout: Kate Stuart

Letter from the Deans

Welcome to the ninth issue of *Results and Discussion*, a newsletter sponsored by the Office of Biomedical Research Education and Training (BRET), that is devoted to highlighting the research accomplishments and activities of our Ph.D. graduate students and postdoctoral fellows.

In the increasingly competitive post-Ph.D. job market, hiring managers are demanding more than ever from prospective candidates. New hires must not only be experts in their field of study, but those in pursuit of the next job must demonstrate emotional and cultural intelligence, management and leadership potential, and exemplify professionalism. Transparency, consistency, and reliability embody the perfect candidate.

How is a well-rounded graduate student or postdoctoral fellow going to best prepare themselves for all the demands of the current job market?

Well, the good news is the BRET Office of Career Development has got them covered. Detailed in this edition of our newsletter (now in its ninth issue!) are the many experiential opportunities as well as skill-building sessions our program, ASPIRE, now provides. Professional headshots, etiquette luncheons, and how-to networking sessions fill any gaps in professionalism training required of today's successful job applicant. Internships and employer visits are just what the current trainee needs to arm themselves with the applicable experiences for their next career step.

We are excited to embark on yet another ASPIRE on the Road trip at the end of

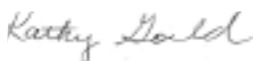
April, this time to San Diego where we will be meeting with alumni and employers in the area to learn more about the dynamics of the city, the rich biotech ecosystem, and why our trainees interested in the industry sector would be a great fit in California. This trip will truly enhance the lives of 12 trainees ready for their next step and if you reside in San Diego, we'd love to see you on our visit.

It's no secret that the Vanderbilt research experience is excellent training for the future scientist. But now the trainee can present themselves as the most well-rounded candidate with enhanced individualized development... an employer won't be able to resist hiring the Vanderbilt grad!

Sincerely,



Roger G. Chalkley, D. Phil.
Sr. Associate Dean for Biomedical
Research Education and Training
roger.g.chalkley@vanderbilt.edu



Kathy L. Gould, Ph.D.
Associate Dean for Biomedical Sciences
kathy.gould@vanderbilt.edu

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Visit us at our website for more information:
<https://medschool.vanderbilt.edu/bret/>

Breaking Norms: How Peripheral Nerve Cell HDAC1 Functions Outside the Nucleus

By Amanda Johnson, Ph.D., Postdoctoral Fellow



Amrita Pathak, Ph.D.

Amrita Pathak, Ph.D., grew up in India where underprivileged children have suffered from relatively high rates of hypothyroidism and intellectual disability due to the scarcity of iodine in the nation's food supply.

"These kids should have a better life," says Pathak, who was recently promoted to a research instructor

position in the lab of Bruce D. Carter, Ph.D., Professor of Biochemistry and Associate Director of the Vanderbilt Brain Institute.

While proper nutrition can prevent such disabilities, there is no treatment for those already disabled. This unfortunate state of affairs motivates Pathak's choice to study neurodevelopment, the process of forming the brain and nervous system.

Neurodevelopment involves a complex interplay of a variety of signals and nerve cells. Signals external to the cell must be transmitted internally to the nucleus, where the cell's genetic material resides and can be employed to execute a cellular response. The distance such signals must travel depends on cell size. For most cell types, this distance is much less than a millimeter. In contrast, nerve cells may be a meter long, and therefore require specialized mechanisms to ensure proper signal transmission.

Pathak has discovered that peripheral nerve cells, a type of nerve cell located in the limbs, break the norms seen in other cell types in order to signal. She was struggling to make headway on her project when she came across a paper showing that histone deacetylase1 (HDAC1) aids signaling in other nerve cell types. To do so, these proteins temporarily act outside the cell nucleus where they normally operate exclusively. These findings

inspired Pathak to look for any presence of extranuclear HDACs in the nerve cells she was studying. To her surprise, she discovered that HDAC1 regularly resides throughout peripheral nerve cells.

"The first time I saw HDAC1 in the axons [nerve cell end furthest from the nucleus] it was unbelievable," says Pathak.

Her work, published recently in *Developmental Cell*, demonstrates that regular HDAC1 activity outside the nucleus ensures signals remain connected to transport proteins so they don't get lost during their long journey over the nerve cell length.

These discoveries were made possible because Pathak's mentor, Carter, gave her the freedom to pursue her (at the time) unconventional idea that an HDAC could be required for nerve cell signaling outside the nucleus. Currently, she is investigating other aspects of long-distance signaling mechanisms involved in neurodevelopment and degeneration. Pathak prizes good mentorship like Carter's and aspires in turn to help train the next generation of scientists as an academic principal investigator running her own neurodevelopmental lab in the future. She also credits these aspirations to her middle school biology teacher, Mr. Vincent Joseph, who taught his students to think about "why" and "how" something is happening. Future breakthroughs depend on it.



Members of the Carter Lab

Learn More:

Pathak, A, et al., [Retrograde Degenerative Signaling Mediated by the p75 Neurotrophin Receptor Requires p150 Glued Deacetylation by Axonal HDAC1](#), *Developmental Cell* (2018) 46(3).

HIV Hijacks the Intracellular Highway

By Nora Foegeding, Graduate Student

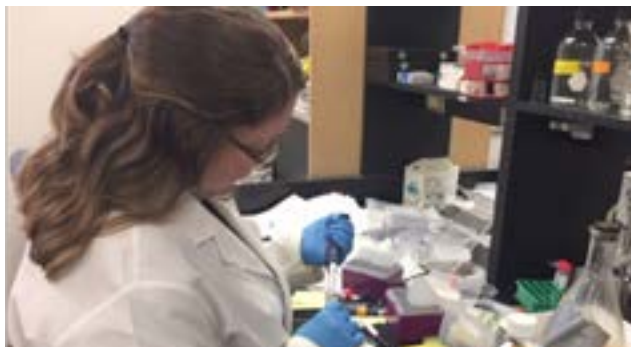
Many viruses must travel to the cell nucleus in order to replicate and successfully establish infection. But the cell is crowded with molecules, vesicles and organelles moving all around. So how does a virus locate the nucleus and then efficiently move toward it? This question frames the research that Stephanie Carnes has pursued as a graduate student.

Indiana University gave Carnes her first scientific research experience. After her high school biology teacher mentioned the summer intensive research program there, Carnes enrolled and completed six weeks of research in the lab of Claire Walczak, Ph.D., Professor of Biochemistry and Molecular Biology, before the start of her freshman year. Carnes was hooked and continued in Walczak's lab for all four years of her undergraduate career before arriving at Vanderbilt University for graduate school.

"I knew I wanted to do some kind of infectious disease research," she says of her start at Vanderbilt.

Carnes joined the laboratory of Christopher Aiken, Ph.D., Professor and Cornelius Vanderbilt Chair of Pathology, Microbiology, and Immunology. It was the perfect fit; Aiken was interested in how HIV traveled inside a cell and Carnes' undergraduate research was on microtubules, the intracellular highway.

When Carnes started her thesis project, researchers in the field were just beginning to understand that HIV could use microtubules, tracks that facilitate the transport of cargo from one part of the cell to another, and dynein, a type of motor protein that moves along



*Top header: Examples of HIV-1 particles infecting cells.
Above: Stephanie Carnes at the bench. Bottom left: the fruit
(or vegetables!) of their labor in her family garden.
Bottom right: Carnes with her new family addition, 2018.*

microtubules, for transport to the cell nucleus. Adaptor proteins tether cargo to dynein, and their binding initiates dynein movement along microtubules. The question then remained whether HIV hijacked a specific dynein adaptor protein for transport to the nucleus.

To begin to test this, Carnes systematically depleted a panel of dynein adaptor proteins from cells to see if their absence inhibited HIV infection. Carnes' research, published in the *Journal of Virology*, revealed that the HIV capsid binds the dynein adaptor protein bicaudal D homolog 2 (BICD2) and that depletion of BICD2 from cells impairs the transport of HIV into the nucleus. These findings suggest that the interaction between BICD2 and the HIV capsid could be a potential target for a new antiviral therapy.

Carnes' forward movement, on the other hand, cannot be slowed down. She is a new mom, confiding

that taking care of her eight-month-old son feels like one large experiment, "except all the variables are constantly changing!" She and her husband also tend to an ever-expanding vegetable garden.

"It's pretty big," she beams, adding, "At one point, we weren't buying any vegetables."

Looking ahead, Carnes aims to direct a clinical microbiology lab, an interest she developed after participating in the Clinical Microbiology Module offered through the BRET Office. In reflecting on how graduate school has prepared her for her future career goals, she says she's thankful for the diverse skillset she acquired. She also appreciates having acquired the ability to say with confidence whenever presented with a new project, "I'll learn whatever I need to learn. I'll figure it out."

Learn More:

Carnes, S.K., et al., [HIV-1 Engages a Dynein-Dynactin-BICD2 Complex for Infection and Transport to the Nucleus](#). *Journal of Virology*. (2018) 92(20).

Faculty Spotlight: Jennifer Pietenpol, Ph.D.

By Lindsay Redman, Graduate Student



Jennifer Pietenpol, Ph.D.

Jennifer Pietenpol, Ph.D., is a Professor of Biochemistry, B.F. Byrd Jr. Professor of Molecular Oncology, Director of the Vanderbilt Ingram Cancer Center, and Executive Vice President for Research at VUMC. She grew up in Minnesota, obtained a B.A. in biology from Carleton College and earned her Ph.D. in cell

biology at Vanderbilt University in the lab of Harold Moses, M.D. Pietenpol continued postgraduate training at Johns Hopkins University with Bert Vogelstein, M.D., before returning to Vanderbilt. She has won numerous awards and worked tirelessly to influence cancer policy, most notably being appointed in 2008 to the National Cancer Advisory Board and in 2017 as Chief Scientific Advisor for Susan G. Komen. Her research for the past 25 years has focused on breast cancer and the p53 family signaling network.

What experience originally sparked your interest in science?

My interest in science started at a young age, nurtured by my grandfather and father whom were outstanding, inventive engineers. My grandfather would ask, "What are you building?" and I always wanted to be building or 'experimenting' so I could give him an answer. I believe my experiences in academics and athletics contributed to my desire to pursue a career in cancer research. As my mother always contends, cancer research was always attractive to me because it allowed me access to an ultimate goal – discovery of a cure for cancer.



Members of the Pietenpol Lab

What do you love most about your job(s)?

Advancing research to patients and the people. My laboratory has studied the p53 tumor suppressor protein and family members, p63 and p73, and become highly engaged in translational research in triple-negative breast cancer (TNBC). I enjoy mentoring students and postdocs, and interacting with a diverse array of scientists and clinicians. The most fulfilling days are those where I watch my graduate students defend their dissertation research and begin their own careers.

What has been your most exciting scientific discovery?

I would highlight two: the molecular subtyping of TNBC that has been translated to clinical trials investigating alignment of patients to targeted therapy and the exciting discovery that p73 is required for formation of multi-ciliated epithelial cells.

What advice would you give to women (and men) who hope to become leaders in science?

My advice is "go for it!" If you love the interplay between science and medicine, a career in biomedical research will keep you engaged for life. If you don't mind competition and working hard, enjoy learning something new every day and have the confidence to persevere when you hit the bumps, this is the life for you. Don't worry that you haven't worked out every step in your life's plan – just do it!

What do you like to do in your free time?

I enjoy spending time with my family – my husband Ian, son Gavin, and stepdaughters Annie and Caroline. Every day I find time to run a 5K and catch up on current events; and, during vacations, I enjoy traveling, hiking, skiing and reading.

Learn More:

Visit the Pietenpol Lab site: www.vumc.org/pietenpol-lab/.

Running on Empty: How Mutations in MYO5B Lead to Extreme Water Loss and Dehydration

By Meagan Postema, Graduate Student

Microvillus inclusion disease (MVID) is a rare intestinal disorder caused by mutations in MYO5B. Patients with this disease are no longer able to absorb nutrients and consequently develop severe, life-threatening diarrhea and dehydration. The symptoms of MVID usually develop a few hours after birth and require lifelong nutritional support or an eventual small bowel transplantation, both of which carry high risks. Even though the general cause of these symptoms is linked to the loss of MYO5B, which helps localize proteins to the intestinal apical domain, the underlying cause of the extreme diarrhea is not known. In a recent article published in *Gastroenterology*, Amy Engevik, Ph.D., determined that misregulation of three intestinal ion transporters leads to decreased water absorption and diarrhea, thus providing potential targets for future therapeutic options for patients with MVID.

Engevik's passion for science began as a graduate student at the University of Cincinnati where she studied gastric repair and helped pioneer the use of gastric organoids as a model system. Organoids are a 3D, in vitro culture system derived from stem cells that recapitulate the complexity of organs and tissues. In 2015, Engevik brought her organoid expertise to Vanderbilt University when she began her career as a postdoctoral fellow in the lab of Jim Goldenring, M.D., Ph.D., Professor of Surgery and Cell and Developmental Biology. Here she continued to work on the gastrointestinal tract, studying intestinal ion transport using organoids to provide a useful in vitro model for MVID.

In her recent paper, Engevik determined that three intestinal ion transporters are misregulated in MVID. She found that two main sodium transporters necessary for sodium uptake, NHE3 and



*Top: Amy Engevik on a recent trip.
Bottom: Engevik (middle) with her sisters, who are in scientific training at different universities.*

SGLT1, are no longer positioned at the apical surface, leading to decreased water absorption and subsequent diarrhea. However, the critical finding of the paper is that a chloride secreting transporter, CFTR, retains its normal position. By remaining at the apical membrane, CFTR allows chloride to be lost in addition to the lack of sodium uptake from the absent NHE3 and SGLT1; this further exacerbates water loss and leads to "ultra" diarrhea and the culmination of MVID symptoms. These results show how critical it is to properly localize ion transporters, and thus the importance of a fully functional MYO5B.

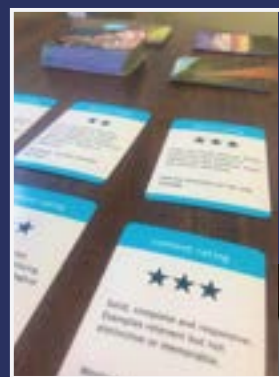
Engevik's future studies in the Goldenring laboratory will be focused on determining therapeutic options for patients with MVID. The ideal treatment would be to use drugs to increase sodium absorption through SGLT1, and use CFTR inhibitors to prevent excess loss of chloride. Engevik is also currently working with organoids from an MVID pig model, which has a gastrointestinal tract more comparable to humans than typical mouse models. From her initial characterization, the pig organoids are validating her current

findings and will hopefully provide a model to successfully determine therapeutic options for children suffering with MVID.

Engevik is currently applying for a K award with the hopes of continuing her studies on the gastrointestinal tract in her own lab one day. Both her passion for science and her love of the gastrointestinal tract are shared by her older sister, a current postdoctoral fellow at Baylor College of Medicine, and her younger sister, a Ph.D. student at the University of Cincinnati. Ultimately, the three sisters hope to connect their different research areas and open a joint lab in the future.

Learn More:

Engevik, A.C., et al., [Loss of MYO5B Leads to Reductions in Na⁺ Absorption With Maintenance of CFTR-Dependent Cl⁻ Secretion in Enterocytes](#). *Gastroenterology* (2018) 155(6).



Above: Practicing professionalism while making interview prep fun with StoryMason© cards. Right: A scene from the annual Lab to Lunch: Business Savvy for Scientists event with speaker Malika Williams.

Look & Act the Part: The Importance of Professionalism in One's Career Development

By Christopher Smith, Ph.D. Former Postdoctoral Fellow, now Postdoctoral Affairs Program Manager, North Carolina State University



module helped her gain the skills and confidence necessary to approach and interact with colleagues. The capstone project "provided a real-world opportunity to network with professionals working in biotech in Tennessee by attending the Life Science Tennessee annual conference in November 2018." Teddy van Opstal, a recent Ph.D. recipient in Biological Sciences, also took part in the networking pacing module and pointed out that many jobs are found by those who expand their networks. "As scientists, we spend a

very small amount of our time communicating with people outside our specific area of interest and don't develop the necessary skills to build lasting networks with people we meet at meetings and conferences. The module trained me to introduce myself and discuss my research in a memorable, engaging way. I also learned to utilize social media platforms such as LinkedIn and Twitter to set up meetings or conversations that connect me with colleagues."

While the BRET Office offers many programs to help trainees act the part, ASPIRE Headshot days help one look the part. A professional headshot is critical for a LinkedIn profile, a necessary web presence for any potential job hunter. Approximately 45 trainees get headshots at each ASPIRE Headshot day and 3 graduate student and 3 postdoctoral fellow headshot sessions will be offered in the 2019-2020 academic year. Roslin Thoppil, a postdoctoral fellow in Cell & Developmental Biology, tells every trainee she knows to take advantage of this opportunity. "Putting up a quality photo helps make the right impression and maximize the number of people who view your profile on LinkedIn. Getting a professional picture taken is usually an expensive affair, but Vanderbilt's headshot day is an amazing opportunity for Vanderbilt postdocs and graduate students to get one for free and the entire process is a breeze."

Key to the success of ASPIRE programming is faculty support. Faculty across the School of Medicine are aware and supportive of the work being done through the BRET Office to prepare trainees, as evidenced in a recent survey across

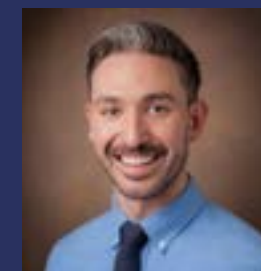
several institutions. "Faculty want to see their trainees rise to their potential and have a productive career after Vanderbilt, regardless of what field (academic, industry) they end up in," according to Gould.

The professionalism offerings are certainly working to help in this regard. Lindsey Morris, a BRET postdoctoral alumna and current director of data science at Axial Healthcare in Nashville, used networking skills learned through ASPIRE programming to get hired early on in the company's lifecycle. Now, Morris routinely interviews candidates for data science positions at Axial. Some points she highlights that set successful job applicants apart are communication skills, emotional intelligence (i.e., eye contact in the interview, not disparaging a past employer), and reputation (being known for your work on a local/national level).

Professionalism and networking are a continual process. Justine Sinnaeve, a Cancer Biology Ph.D. candidate, noted that, "With every experience I learn at least one new way of approaching networking, building confidence in myself and my skills, and tips for maintaining a professional demeanor." The key is to just get started. Morris elaborated on this point, saying, "Volunteer to organize and present at meetups and seminars in topic areas that interest you. By doing so, you will start to be associated with the career area you want to transition into." The BRET Career Development ASPIRE offerings can give you valuable tips and a kickstart. It is up to you, though, to seize the opportunity, do good work, be positive and professional, and distinguish yourself from the pack. Eventually, people (future employers, colleagues, etc...) will notice.



Top: Alumna Lindsey Morris, Ph.D., second from right, speaks to current trainees in the Data Science module at a recent networking event. Above: Speaker Jean-luc Doumont, Ph.D., gives the keynote address at the annual ASPIRE to Connect workshop that focuses on building professional relationships. Left: Networking events are paramount to the BRET Office of Career Development programming opportunities. Below: Headshot Day examples from a recent shoot.



Landing a dream job can be a daunting task for even well-seasoned scientists. However, with underdeveloped soft skills, such as effective communication and emotional intelligence, or an inability to act professionally in a variety of situations, this becomes significantly more difficult. The BRET Office of Career Development ASPIRE Program in the Vanderbilt University School of Medicine offers many useful events, modules, and workshops focused on honing those soft skills that are necessary for career success. Programming ranges from dining etiquette covered in the Lab to Lunch event, ASPIRE Postdoctoral Cafes on job negotiation and the interview process, to modules focused on improving networking skills.

According to Kathy Gould, Ph.D., Associate Dean for Biomedical Sciences, ASPIRE professionalism programming grew out of feedback from trainee exit surveys regarding skills and experiences they wish they had while at Vanderbilt. What became apparent to the BRET staff is that trainees did not have a standardized set of professional experiences, and therefore do not necessarily know what is expected in various professional settings. Once these processes are demystified and trainees know how to interact with people at a networking event, or how to dress for an interview, they become empowered and more confident in their ability to navigate these situations.

Kathryn Trogden, a postdoctoral fellow in Cell & Developmental Biology, found that the networking pacing

Learn More: Visit medschool.vanderbilt.edu/career-development/professionalism-policy/

Now Endowed!

The ASPIRE Scholar Fund

The ASPIRE Scholar Fund provides support for exceptional PhD graduate students and postdoctoral fellows to pursue experiential learning opportunities that furthers their career and professional development. This fund has recently been endowed! Join others who have made this dream a reality and give generously for the next generation of scientists:

<https://medschool.vanderbilt.edu/career-development/giving/>

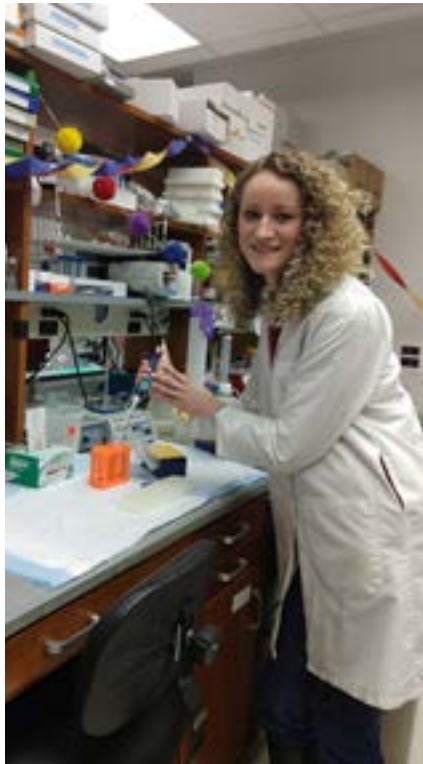
In a 'BID' to Understand Heart Disease: How Bid Protein Upholds Mitochondrial Function and Defends Against Cardiac Dysfunction

By Roslin Thoppil, Ph.D., Postdoctoral Fellow

Mitochondria are specialized double-membraned cellular organelles that convert fuel into chemical energy. A smooth outer membrane encases a folded inner membrane called the 'cristae', which provides the framework for this energy conversion. Mitochondria also play a critical role in apoptosis or 'programmed cell death' wherein the cristae expand to mobilize proteins that will be released to trigger a cascade of enzymes that result in cell death. Apoptosis is regulated by the Bcl-2 family of proteins including mitochondrial protein Bid. However, the purpose for mitochondrial localization of Bid in non-apoptotic cells has been unclear and is the thesis work of graduate student Christi Salisbury-Ruf in the lab of Dr. Sandy Zinkel, Associate Professor of Medicine and Cell and Developmental Biology.

In work published in *eLife*, Salisbury-Ruf and former graduate student Dr. Clint Bertram showed Bid knock-out cardiomyocyte mitochondria utilize less oxygen than wild-type. Cardiomyocytes have a high density of mitochondria, enabling them to quickly produce energy and resist fatigue. A closer look at the mitochondria of cardiomyocytes lacking Bid revealed a defect in cristae structure, causing insufficient energy production. Consequently, mouse hearts lacking Bid displayed decreased performance output and could not respond to increased energy demand. Over time, the stress-induced myocardial dysfunction seen in these mice resulted in fibrosis, or scar formation, within the heart muscle, akin to that observed in patients after a heart-attack.

Salisbury-Ruf, in collaboration with Dr. Eric Gamazon, also investigated the role of Bid in human cardiomyocytes using Vanderbilt's de-identified genetic database, BioVU. This



Christi Salisbury-Ruf

analysis revealed a link between decreased levels of BID and an increased susceptibility to heart attacks. Furthermore, a specific mutation in the BID gene affects Bid's ability to regulate cristae formation. Salisbury-Ruf's work importantly outlines how gene variations, specifically alterations in Bid protein, influence mitochondrial health and heart attack risk.

A native of upstate NY, Salisbury-Ruf is not only pursuing her Ph.D., but she is also a talented musician! A brief laboratory stint during college inspired Salisbury-Ruf to pursue research. Toward the end of her master's degree in cancer immunology at Roswell Park Cancer Center in Buffalo, NY, she knew that she wanted to pursue academic research further.

"Ph.D. training was the right route for me. I wanted to answer questions that could inform what happens in the clinic, and I felt like I ultimately could have a bigger impact on patients that

way. In Sandy's lab, my research work evolved into a new understanding as to how mitochondria maintain their cristae – which definitely has implications for a multitude of diseases."

As she prepares to graduate, Salisbury-Ruf credits several things including family, faith and music for instilling in her the focus and resilience that helped her through graduate school. She confides that she chose the oboe because "the oboe is unique, nobody plays the oboe, and I wanted to be different!" As part of her career goals, Salisbury-Ruf wants to one day run her own lab. For now, she hopes to continue her scientific endeavors as a postdoctoral researcher at the National Institutes of Health in Bethesda, MD, where she would be close to family.

Learn More:

Salisbury-Ruf, C.T. & Bertram, C. et. al., [Bid maintains mitochondrial cristae structure and function and protects against cardiac disease in an integrative genomics study. *eLife* \(2018\) 7.](#)

Future Directions: Dario Gutierrez, Ph.D.

By Shwetha Narasimhan, Graduate Student



The promising field of immunotherapeutics is currently hailed as the new hope in the fight against cancer and Dr. Dario Gutierrez is determined to make this hope a reality. As the Director and Head of the Investigational Biology team at the Merck Exploratory Science Center, he leads a team of expert scientists who study novel immunotherapeutics with a focus on immuno-oncology and infectious diseases.

Gutierrez is fascinated by the intricacy of the immune system and believes that our bodies are equipped with natural immunity against tumors. His interest in the immune system developed during his graduate studies at Vanderbilt University in the lab of Dr. Alyssa Hasty, Professor of Molecular Physiology and Biophysics. Gutierrez continued studying immunology as a postdoctoral fellow at the German Cancer Research

Center (DKFZ) and gradually transitioned into a role at the pharmaceutical giant, Merck. He established the Immuno-Biology team and has since guided the team's scientific strategy towards discovering drugs and vaccines that stimulate the immune system to fight cancer and infectious diseases.

The road to drug discovery is long and arduous, and Gutierrez credits his professional success to methodical perseverance and a continuing joy of scientific discovery that he came to cultivate in graduate school. Though he misses the personal touch of working at the bench, he feels honored to oversee his talented team focused on immunotherapy, infectious disease and microbiome research. He is particularly excited about their foray into gamma-delta-T cell research, which is a promising avenue for cancer treatment. Recently, his scientific passion has extended beyond Merck into the realm of science outreach. With the ultimate goal of inspiring young minds, Gutierrez helped organize a science fair last year in his hometown in Honduras, where he rose from simple beginnings.



Above, Dario Gutierrez, Ph.D. Left, pictures from the Honduras science fair held in Gutierrez's hometown that he helped organize.

Last book he read:

A Cure Within: Scientists Unleashing the Immune System to Kill Cancer by Neil Canavan

Most memorable scientific discovery in grad school:

Finding a novel role for eosinophils (a type of immune cells) in the maintenance of the healthy state of fat tissue.

Favorite things to do in Nashville: Playing soccer, enjoying the vibrant nightlife in the Gulch, and exploring local cuisine.

His advice to graduate students:

Be positive, find your passion, follow it to the end.

Typical number of hours working every week: 60

A Day in the Life

5 AM	Wake up and prepare for the day by answering emails.
6 AM	Exercise
8 AM	Arrive at the office to answer emails and keep up with recent scientific discoveries by reading literature.
9 AM-5 PM	Strategy sessions with multiple drug discovery teams and one-on-one discussions with team members. Internal and external research collaboration meetings. Evaluation of potential academic and industry collaborators. Leadership team and operational meetings.
5 -7 PM	Wrap up work for the day and return home to enjoy time with family.

RIG-I agonist: a Potential Therapeutic Intervention for Aggressive Breast Cancer

By Niyati Vachharajani, Ph.D., Postdoctoral Fellow



David Elion

Breast cancer is the second-most leading cause of cancer-related deaths in women, primarily because this form of cancer is not immunogenic and lacks the tumor infiltrating lymphocytes required to mount an inflammatory response against it. Therefore, there is an urgent need for researchers to develop new treatment strategies which will

enable immune checkpoint molecules to recognize and eliminate tumor antigens.

David Elion, a graduate student, has tackled this issue during his thesis work in the laboratory of Dr. Rebecca Cook, Associate Professor of Cell and Developmental Biology and Biomedical Engineering, and led to the development of a novel therapeutic strategy to treat aggressive breast cancer, work recently published with their collaborators in *Cancer Research*.

In order to accomplish the objective of designing a novel therapy to treat breast cancer, Elion focused on testing an engineered agonist of a viral nuclear sensor, retinoic acid-inducible gene-1 (RIG-I). Binding of RIG-I to its ligand mounts an inflammatory response via activation of pro-inflammatory cytokines. Additionally, RIG-I stimulation results in killing of virus-infected cells through apoptosis. Based on these unique characteristics, RIG-I seemed to be a very promising and attractive candidate for development of a potent synthetic RIG-I agonist in the setting of breast cancer.

“Our study is novel because no other studies in the field of breast cancer have focused on testing the immunotherapeutic effects of the RIG-I agonist,” Elion said.

Elion tested the efficacy of the synthetic RIG-I agonist by delivering it to tumors via nanoparticles. The RIG-I agonist decreased tumor growth and metastasis in a mouse model of breast cancer. Furthermore, the agonist induced apoptosis of tumor cells in addition to mounting a pro-inflammatory cytokine response, thus increasing the immunogenicity of the tumor antigens.

“Our findings suggest that RIG-I activation, via a synthetic agonist, is an extremely feasible and promising novel immunotherapeutic treatment for low immunogenic breast tumors,” Elion concluded when asked about the impact of this research.

Elion plans to defend his thesis next year and, as he is passionate about research and science, he wants to continue in research as a postdoctoral fellow after graduation. Although his work keeps him busy, he finds time to pursue his second passion – music. In his free time, he writes music and plays the violin, a talent he shared at the Vanderbilt Biomed Talent Showcase in December 2018. He double majored in music and biology at Brown University and hopes to continue creating music while pursuing his research career.



David Elion performing at the 2018 Vanderbilt Biomed Talent Showcase.
(Photo by Tolu Omokehinde)

Learn More:

Elion, D.L. et al., Therapeutically Active RIG-I Agonist Induces Immunogenic Tumor Cell Killing in Breast Cancers. *Cancer Research* (2018) 78(21).

Vanderbilt Takes on Capitol Hill

A Look Inside Science Policy for Students and Fellows.

By Colbie Chinowsky, Graduate Student

The BRET Office of Career Development and the Graduate School took to the road in October 2018 to further their combined mission of empowering and preparing Ph.D. and postdoctoral trainees for careers within the biomedical sciences. The trip, hosted by the Vanderbilt University and Vanderbilt University Medical Center Offices of Federal Relations, took 20 Vanderbilt graduate students and postdoctoral fellows to Washington D.C., where they were given the opportunity to explore how policy and science influence one another. The two-day seminar provided insight into how policies are designed and promoted. Furthermore, participants had the opportunity to advance their future careers via networking events.

"I didn't really know what science policy entailed," said fifth-year graduate student Meagan Postema. "This trip helped clarify what a science policy career would look like. It also gave me connections and ideas for what steps I should take post-graduation if I want to continue to pursue a career in policy."

The trip began with a panel discussion from a variety of speakers, including Tobin Smith, Vice President for Policy at the Association of American Universities, who outlined key points in the history of science policy in the U.S., such as how the NSF and NIH came to their current form. He also spoke about the difference between science for policy (science that informs policy decisions) as opposed to policy for science (policy that affects how science is done). After lunch, we engaged in a lively conversation with VU alumnus Sam Feist, CNN Senior Vice President and Washington Bureau Chief. Topics included in our meeting ranged from Election Night coverage at CNN to the accuracy of scientific discovery coverage by news networks.

After a quick walk to the Capitol, the group filed into a Senate committee room to learn first-hand about careers on Capitol Hill. We heard from panelists, including several Vanderbilt alumni, who worked in the legislative offices of various senators and congresspeople. This session was particularly interesting as we got an opportunity to understand how science is communicated to members of Congress by their legislative team and how this communication can influence policy decisions. The first day ended with a networking reception attended by 19 Vanderbilt alumni who now work in a variety of science policy roles. Many of the attendees



Ph.D. Students and Postdoctoral Fellows at the Capitol during their trip to Washington D.C. for the Federal STEM Policy: An Inside the Beltway Look sponsored by the BRET Office of Career Development and the Graduate School.

found the reception both helpful and fun, as it allowed us to connect on a personal level with individuals in a wide range of policy-related jobs, get a sense of their day-to-day life, and see how their career paths developed after graduate school.

The second day kicked off with a budget appropriations case study that allowed participants to experience first-hand how the federal budget for science is determined as they simulated the negotiation and debate that happens within the budget appropriation committees. The day continued with a panel on science and technology policy fellowships, which many trainee participants said they found very helpful as they think about moving forward in their careers. The trip ended in an exercise in advocacy, in which small groups came together to brainstorm ways to convey the importance of basic science funding to the public.

This workshop provided an excellent opportunity for our group to learn exactly what science policy entails. Everyone returned to Vanderbilt having learned a great deal about who influences policy, how science can help, and why we, as scientists, should be involved in science policy advocacy on both a state and federal level. We found that scientists work at all levels of government, from congressional offices to agencies such as the U.S. Geological Survey or the Environmental Protection Agency, where they perform a variety of roles. For those interested in careers involving policy, we learned about fellowships offered through AAAS and many professional organizations, such as the American Astronomical Society or the American Chemical Society. As we reflected on this trip, we found that this experience gave each of us valuable new knowledge, connections in a new arena, and furthered our interest in the world of science policy.

Congratulations to our Recent Graduates!

September 2018-February 2019

Matthew Albertolle

Caleigh Azumaya

Stephen Bailey

Shawn Barton

Thomas Bass

Brian Bender

Ankita Burman

Victoria Cavener

Merrida Childress

Jacob Choby

Ryan Doster

Aidan Fenix

Tracy Fetterly

Jessica Finn

Siwei He

Marilyn Holt

Lorena Infante Lara

Nergis Kara

Michael Kim

Krystian Kozek

Heather McCartney

Stephanie Moore

Jean-Paul Noel

Leshana Saint-Jean

Gabriela Santos Guasch

Carl Sedgeman

Leslie Roteta Sedgeman

Alexander Sevy

Aparna Shekar

Lina Sulieman

Mehmet Takar

Carrie Wiese

Christopher Wilson

David Wooten

Edward van Opstal

RESULTS & DISCUSSION

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