Letter from the Deans

Welcome to the seventh 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.

This spring, the BRET Office of Career Development is taking career exploration on the road! We took a small group of graduate students and postdocs to Boston through our ASPIRE on the Road Initiative. They learned first-hand about careers in the biotech and pharmaceutical industries through site visits at four Cambridge-area companies. We reached out to our alumni working in Boston and they were more than happy to help us arrange visits at Amgen, Merck, Pfizer, and Kymera Therapeutics. While there, we had the opportunity to hear about research at each of these companies, meet with scientists working there, and visit their lab space. We also toured LabCentral, a large biotech incubator that helps to launch new startups into the Boston entrepreneurial ecosystem. On the evening of May 3rd, we hosted an alumni happy hour at a local restaurant and saw many familiar faces in attendance. Not only was this a wonderful chance for our current trainees to meet alumni and learn about their career paths, but it was also a great chance for alumni who live in Boston to connect with one another based on their shared ties to Vanderbilt!

We are always eager to engage alumni, family, and industry partners in preparing our graduate students and postdoctoral fellows for their next career steps. Please let us know if you have interest in supporting our mission to train the next generation of scientists.

For more information, please visit our website or feel free to reach out to either of us directly.

Sincerely,

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

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Golgi-Derived Microtubule Formation: Hotspots on the Golgi

By Allyson Mallya, Graduate Student

Microtubules (MTs) are a critical component of the cytoskeleton of a cell, which helps to maintain and define its shape, internal organization, and physiology. Although the majority of MTs originate at a structure called the centrosome, a small subset with unique functions forms at a different structure called the Golgi which is involved in processing, packaging, and shipping proteins throughout the cell. Unlike their radially-directed centrosomal counterparts, most Golgi-derived MTs (GDMTs) point toward the “leading edge” of the cell, which is important for facilitating directional trafficking of proteins and directing cellular movement. Although GDMTs are critical for Golgi integrity and function, how they are formed and organized at the Golgi was – until now – a mystery.

Anneke Sanders, Ph.D., completed her undergraduate and master’s degrees at Utrecht University in her home country of the Netherlands, during which time she participated in two internships that instilled a lasting passion for utilizing microscopy to “see how stuff happens” in biology. She obtained her Ph.D. in genetics from the University College of Dublin, Ireland, studying MT structure in nematodes and joined the lab of Irina Kaverina, Ph.D., Professor of Cell and Developmental Biology, in 2015 as a postdoctoral fellow eager to use advanced microscopy techniques to understand how GDMT networks are established. In a recent report published in Molecular Biology of the Cell, Sanders and colleagues determined that GDMTs are nucleated (formed) in a well-structured process, a hypothesis supported by computational simulations led by William Holmes, Ph.D., Assistant Professor in the Department of Physics and Astronomy, that is dependent on γ-TuRC-mediated nucleation (γ-TuNA).

Using live-cell microscopy, Sanders tracked the growing ends of GDMTs back to their origin and found that MTs assembled on the Golgi in tight hotspots. These sites, however, “are very short lived. Nucleation seems to come in little bursts,” Sanders explained. To probe the mechanisms of hotspot formation, the authors independently inhibited two proteins involved in GDMT nucleation: γ-TuNA and cytoplasmic linker associated proteins (CLASPs). Expression of a nonfunctional γ-TuNA domain (“dead tuna”, as the lab affectionately calls it), but not CLASP depletion, reduced GDMT hotspot formation, suggesting an essential role for γ-TuNA in this organizational process. A remaining question Sanders wants to address is what factors exist on the Golgi that help to form these MTs.

Sculpting the Newborn Gut

By Sanjay Mishra, Graduate Student

Microvilli, 2-3 μm long protrusions on the surface of epithelial cells, are critical for efficient absorption and secretion in the gut. In the newborn gut, microvilli can affect autophagy through a previously unknown, non-canonical pathway. This novel link between microvilli sensors and the transport of fluids indicates that fluid flow may be able to shape the neonatal gut during early development and can protect it from disease.

Kim has come a long way from the days when he devoted more time to kendo, the Japanese martial art of bamboo fencing, than to biology, days that began while pursuing his baccalaureus degree in biotechnology, also at Korea University, and a Ph.D. from the University of Cincinnati, Ohio. Throughout, Kim’s kendo practice has played an important role in his life, helping him to overcome many obstacles and manage the stress that comes with research. Kim continues to practice his kendo skills, and is in fact organizing a club to popularize the sport at Vanderbilt.

Laura Kim, Ph.D., practicing kendo in Nashville.

Graduate Student

Learn More:


Learn More:

Faculty Spotlight: Frederick Peter Guengerich, Ph.D.

By Anne Meyer, Graduate Student

Frederick Peter Guengerich, Ph.D., has been in the Department of Biochemistry at Vanderbilt University for over 40 years. He first arrived as a graduate student in 1970 under the mentorship of Dr. Harry P. Broquist, and completed his Ph.D. in three years. Guengerich moved on to a postdoctoral fellowship at the University of Michigan, but returned to Vanderbilt for good when he became an assistant professor in 1975. During this time, he has served as director for the Center in Molecular Toxicology as well as chair of the Department of Biochemistry. Now, Guengerich has relinquished many of his administrative responsibilities to focus on his research and on the members of his research group. The Guengerich laboratory studies enzymes involved in the activation and processing of xenobiotic chemicals (chemicals that are not normally found in the body, such as drugs and carcinogens). In his free time, Guengerich enjoys photography, fishing, and hiking.

What excites you most about research?

I enjoy discovering new things. Specifically, I have always been very interested in chemistry and in any time we can use chemistry to discover new things. I also get excited about doing things that have an application, for instance, research within the pharmaceutical industry. Another part of research that I am passionate about is training younger scientists and seeing them go on to successful careers.

What advice would you give to new faculty who are just starting their careers?

Work very hard and be prepared to do some sacrifices. This advice is not unique to a career in academic research, but it is important for your career as you are to theirs. Finally, the most important advice is to not lose the excitement and the sight of why you are doing what you are doing.

What is the most important lesson you learned from your mentor?

How to treat and relate to people. For a career in academic research or industry you have to work with others. You have to treat people with respect, help people when it is needed, and learn from the people that you work with.

Where do you think the biggest scientific advances will be in the coming decades?

Every field will have significant advances. There are amazing strides being made in chemistry in terms of materials such as batteries and nanomaterials. There is also a lot of interest in metabolism and the microbiome. It is hard to pinpoint where the biggest advances will be.

Can you share any stories behind the décor in your office?

Over the years I have acquired a collection of orchids; and the oldest is over 25 years old. The background of my computer is photographs I have taken in my free time. I have also framed every hundredth paper from my lab (there are 7), and every time I frame a new paper I take the lab out for a celebratory lunch.

Spying On the Enemy: Uncovering How Cancer Cells Evade Our Efforts to Kill Them

By Bryan Gitschlag, Graduate Student

Just as bacterial infections can become resistant to antibiotics, cancer cells can become resistant to chemotherapy, one of the most effective and widespread cancer treatment methods. Understanding how this happens is a crucial step in the ongoing arms race against one of the most pernicious killers of the 21st century.

A recent study published in Molecular Cell, spearheaded by Huzefa Dungrawala, Ph.D., and Karn Bhat, Ph.D. (who recently accepted a postdoctoral position at Stanford), sheds light on this complex problem. Dungrawala works in the laboratory of David Cortez, Ph.D., Professor of Biochemistry at Vanderbilt University, and studies the proteins present at sites of DNA replication. A postdoctoral fellow native to India, he enjoys watching his favorite football team, Liverpool, in action and exploring different cuisines, especially from Southeast Asia. In lab, however, he has been probing the function of RADX and clarifying its interaction with two DNA repair proteins, RAD51 and BRCA2. Introducing DNA damage through chemotherapy is a common method for combating cancer, so identifying the ways in which cancer cells repair damaged DNA can give us insight into how cancers become resistant to chemotherapy.

Dungrawala and coauthors found that RADX negatively regulates the important DNA binding protein RAD51, which is essential for the error-free repair of damaged DNA. RAD51 function is also regulated by the tumor suppressor BRCA2, which impedes the development of cancer by recruiting RAD51 to sites of DNA damage. Many cancers often have mutations in BRCA2, however, which compromises the ability of the cells to repair DNA damage and results in genomic rearrangements. In this study, Dungrawala and colleagues found that the removal of RADX from cells lacking BRCA2 can cause resistance to chemotherapeutic drugs.

This key breakthrough identifies a novel strategy for how cancer cells can become resistant to chemotherapy: loss of RADX. Since chemotherapeutic drugs often function by introducing DNA damage, and since the damage repair protein RAD51 is compromised in cells with dysfunctional BRCA2, removal of RADX could potentially restore RAD51 function and thus restore the ability of cancer cells to repair their DNA.

"Many patients lacking proper BRCA2 function stop responding to chemotherapy after the first round of treatment," said Dungrawala. "Could restoring RADX function restore cancer sensitivity to chemotherapy? Time will tell."

Moving forward, the Cortez group is seeking further insight into the biochemistry of RADX and RAD51 by purifying and studying them in a test tube. After five years with the lab, Dungrawala is currently pursuing a faculty position of his own, where he hopes to continue his work defining pathways involved in damage repair during DNA replication. As to whether or not he will fulfill his dream of seeing Liverpool play a home game at Anfield Stadium, well, that’s a whole ‘nother ball game.

Learn More:
Dungrawala, H.*, Bhat, K.*, et al., RADX Promotes Genome Stability and Modulates Chemoresponsivity by Regulating RAD51 at Replication Forks (Molecular Cell)
Opportunity Begets Opportunity: Leveraging Connections to Gain Invaluable Career Experiences

By Heather McCartney, Graduate Student

As the stress of preparing for (and passing) my qualifying exam started to dissipate, I began to wonder what type of career I could have after I finally earned my doctorate. Aiming to get exposure to as many different career paths as possible, I started attending BRET Office of Career Development Ph.D. Career Connections – a monthly webinar series highlighting the diversity of career paths available to biomedical scientists as experienced by the invited speakers, many of whom are Vanderbilt alumni.

I became HRA’s first intern and was tasked with helping to coordinate the annual members’ meeting in Chicago in September of 2017. Although I had attended several scientific conferences prior to the internship, I had no real understanding of the extent of the work that goes into planning any type of large meeting. Thankfully, I worked in collaboration with an experienced Program Committee – a group comprised of 22 leaders from various nonprofit organizations. HRA’s Executive Director, Maryrose Franko, Ph.D., and Executive Assistant, Annette Huetter – to develop the sessions, from conceiving of ideas, to inviting speakers, to addressing logistical considerations. Developing the agendas and coordinating the conference calls for weekly Program Committee meetings allowed me to establish familiarity with top thought leaders from a variety of nonprofit biomedical research-funding organizations, such as Alzheimer’s Association, American Cancer Society, Burroughs Wellcome Fund, and many more.

The culmination of my internship was attending the September Members’ Meeting in Chicago, about 6 months after I had started. I was finally able to meet the individuals with whom I had been interacting for months in what proved to be an amazing learning experience and the best networking I could have imagined. The HRA membership is an impressive group of brilliant individuals from unique scientific backgrounds who are committed to collaborating, both at the Members’ Meetings and beyond, to finding solutions to the myriad problems nonprofit organizations face in their goal of reducing disease burden.

My experience was so positive – both for me personally and for the HRA – that I was invited to participate in a second project. This time, I took on the challenge of generating robust data sharing policies in grant agreements, an issue that was brought up at the September Members’ Meeting. Although every HRA member organization funds biomedical research, they all approach the topic of data sharing requirements differently. I am currently working to generate a dynamic data sharing language resource that member organizations can use to build their own robust data sharing policy based on the best practice of other organizations.

So far, this specific project has been eye-opening for me. Although as a scientist I am very aware of the importance of data sharing and understand that data availability makes research advances possible, I had never considered this as a challenge that nonprofit research funders have to address. Updating donors, patient advocates, and other stakeholders on project progression is a critical part of making sure the funded projects are efficiently designed to understand disease etiology and to develop treatments. My project aims to resolve the key issue of generating grant language that maximizes the utility of data derived from the use of each nonprofit’s grant dollars.

I have now been involved with the HRA for over a year and have attended two members’ meetings. On average, I have spent 3-5 hours a week working on projects related to my internship role. This experience has helped me to focus my time to be more efficient, both in achieving my internship project goals and in moving my dissertation research forward.

As a senior graduate student preparing for the next step of my career, I am incredibly appreciative of the opportunities the BRET Office of Career Development and the ASPIRE program have provided to me. I am now forever connected to the largest organization of nonprofit scientific research organizations and the amazing people who run each of them. Although at the moment I don’t know exactly where I will be headed once I defend, I will certainly be able to leverage this experience to open many doors and help me succeed no matter what the future holds.
Cell Membrane Dynamics Offer Critical Insight into Pulmonary Arterial Hypertension

By Natalya Ortolano, Graduate Student

A recent article published by Vanderbilt University graduate Courtney Copeland, Ph.D., explores the role mutant caveolin-1 (CAV1) plays in the incurable pulmonary arterial hypertension (PAH). PAH is a disease that permanently constricts the smallest arteries in the lungs, causing the heart to work harder to send blood to the lungs, resulting in high blood pressure and, in some cases, heart failure. Recently, CAV1 mutations have been linked to PAH, but the exact mechanisms remained elusive until Copeland’s work, published in Molecular Biology of the Cell with co-first author Bing Han, Ph.D., a postdoctoral fellow, shed new light on CAV1 function.

Upon completing her B.S. in biology from the University of Tennessee at Knoxville, Copeland found that her degree was insufficient qualification for entry-level research positions, so she took a job in clothing retail. There, she happened to meet a graduate student venting about recent experimental failures. Copeland, undeterred, asked for her contact information and landed a volunteer position in the virology-focused lab of Tim Sparrow, Ph.D., at the University of Tennessee at Knoxville. Sparrow recognized her potential and encouraged her to apply to graduate school.

Copeland entered the IGR/IMSD program at Vanderbilt in 2011, and from amongst her rotations, chose the lab of Anne Kenworthy, Ph.D., Professor of Molecular Physiology and Biophysics and Cell and Developmental Biology, who studies the role of the cell membrane in the transport of cargo such as bacterial toxins, as her thesis lab. Copeland veered away from toxins and became keen on understanding how membrane dynamics go awry, causing aberrant transport and ultimately leading to disease.

“The cell membrane is composed of unique microdomains like caveolae, which play a critical role in cellular signaling and in protecting the cell membrane from environmental stresses like mechanical stretch. CAV1, which is generated in the endoplasmic reticulum (ER), is a required component of caveolae. Copeland’s studies determined that a CAV1 mutant associated with PAH contained an ER retention signal which trapped it in the ER and promoted its destruction. Decreased incorporation of CAV1 into caveolae caused cells to have fewer caveolae, weaker cell membranes, and increased susceptibility to osmotic stress. These results help explain why cells of the pulmonary arteries in PAH patients are particularly susceptible to mechanical stress.

Studying the role of cellular stress on the CAV1 phenotype during her graduate studies piqued Copeland’s interest in cellular stressors and their relationship to disease. Copeland began a postdoctoral fellowship at Brigham and Women’s Hospital and Harvard Medical School in December. She will continue studying PAH with a focus on the metabolic derangements that occur in cells of diseased vessels.

“During a conference he attended as a graduate student, he met Colleen Niswender, Ph.D., Research Professor of Pharmacology at Vanderbilt University, and they discussed a possible Rett syndrome project. After graduation, Gogliotti took a postdoctoral position with Niswender and P. Jeffrey Conn, Ph.D., Professor of Pharmacology, to work on that project, leading to a series of publications, including one published in Science Translational Medicine last August.

In the article, Gogliotti and colleagues investigated the connection between metabolotropic glutamate receptor 7 (mGlu7) – a neurotransmitter (NT) release regulator – and Rett syndrome. As mGlu7 is found in many brain regions affected by the disease, using human autopsy samples, the authors observed that mGlu7 levels are decreased in the brains of Rett syndrome patients, a finding that was also observed in mouse models of the disease.

Gogliotti has always been dedicated to research in the life sciences. He began his science career with a student internship at Pfizer while he was in college at Eastern Michigan University. After graduation, he took a research associate position at Children’s Memorial Hospital in Chicago, studying neuromuscular diseases under the supervision of Christine DiDonato, Ph.D. Gogliotti eventually completed a doctorate at Northwestern University in the DiDonato lab, where he solidified his passion for studying pediatric diseases of the nervous system through his interactions with patients and their families.

“Rett syndrome is a devastating disorder that primarily affects girls and causes seizures, developmental regression, cognitive impairment, and loss of language and motor skills. A recent study headed by Rocco Gogliotti, Ph.D., suggests a new therapeutic approach to treating and monitoring the disease. Gogliotti and coauthors also discovered a potential clinical outcome that can be measured objectively: suspensions in breathing (apneas) significantly decreased following the administration of an mGlu7 PAM in the mouse model. Overall, the study suggests that mGlu7 modulation may be a therapeutic approach to treating the cognitive, social, and respiratory symptoms in Rett syndrome.

Gogliotti emphasized that his lab’s involvement with the Vanderbilt Center for Neuroscience Drug Discovery (VCNDD) was invaluable to the success of the project. Currently, he is continuing his work in the VCNDD as a Research Assistant Professor, and hopes to transition into a tenure-track position within the next few years with the help of a prestigious National Institutes of Health K01 award he received last year.

Learn More:
Future Directions: Miranda Hallett, Ph.D.

By Leslie Sedgeman, Graduate Student

Miranda Hallett, Ph.D., always had a passion for science and law, but wasn’t sure how to combine them. She completed her Ph.D. in Cancer and Developmental Biology at the University of Tennessee Health Science Center in Memphis, TN, before coming to Vanderbilt University to complete a postdoctoral fellowship in the laboratory of Barbara Pfeilner, Ph.D., Associate Professor of Pharmacology and Medicine. Through the BRET Office of Career Development, Hallett helped plan events and invite guests to speak about intellectual property and patent law, which allowed her to meet like-minded individuals and helped her demonstrate her commitment to patent law to potential employers. Hallett moved to Maryland in 2015 to take a position as a patent law clerk, and now works as an agent at Arnold & Porter in Washington, DC. Although her days as a patent agent are vastly different from her days as a postdoctoral fellow, she still spends a substantial amount of her time reading scientific papers, which helps her become knowledgeable on topics relevant to her clients’ work and helps her determine whether an invention is novel and obvious. I spent some time with Hallett getting a glimpse of a day in her life.

6:00am
Wakes up and checks for urgent emails.

80% of the day in front of a computer researching and reading patent applications and USPTO official correspondence.

20% spent in meetings with clients or patent attorneys and other agents.

7:30am
Takes daughter to daycare and commutes to DC by train or car. Reads if she takes the train.

7:00am
Arrives at work and gets a cup of coffee. Checks the docket for any top priority or critical cases that require immediate attention.

5:00pm
Leaves work.

10:00pm
Checks email for any urgent cases before going to sleep.

EVENINGS:
Works 3 extra hours 1-2 times per week. At-home work includes: 

Free Time
Biking, runs to the playground, trips to Pennsylvania, New Jersey, and South Carolina to visit family, and home improvement projects.

December
Busiest month, clients want their patents submitted before the end of the year.

Our Journey into Business and Management Consulting

By Siwei He and Aparna Shekar, Graduate Students

Working toward a Ph.D. in the biomedical sciences not only instills a wide repertoire of personal and professional qualities in trainees, but also opens many doors in a wide gamut of career paths. Management consulting is one of these paths, and it might be the perfect choice for you if you’d like to solve complex problems in a wide variety of industries, enjoy working in teams, and show high adaptability in a fast-paced, ever-changing work environment.

About a year ago, we started researching careers that would be suited to our strengths and preferences and arrived at consulting for the reasons we mentioned above. We were surprised and excited to learn that individuals with a Ph.D. or an M.D., even without any business experience, are heavily recruited at consulting firms for their scientific and technical expertise, as well as their organizational, analytical and problem-solving skills. Participating in the Management and Business Principles for Scientists and Technology Commercialization (ASPIRE) modules offered by the BRET Office of Career Development was especially helpful to us in deciding on a career path at the intersection of science and business.

In 2017, we applied separately for summer consulting workshops: McKinsey’s Insight Program (Siwei) and BCG’s Bridge to BCG (Anupama). The application process was competitive and involved a resume/cover letter screening and a Skype interview. Thanks to the ASPIRE modules and other resources offered by the BRET Office, we possessed a basic understanding of business management as well as well-honed interviewing skills going into the interview process at each program. This combination of factors helped us both land a coveted spot in the workshops.

The McKinsey Insight and Bridge to BCG programs were excellent opportunities for us to learn more about management consulting careers, as well as about the work and culture at each firm. Both workshops are structured similarly, and each summer, 30 to 40 students from all over North America are accepted into each of the 3-day programs. The McKinsey Insight program is located in Chicago, and the Bridge to BCG takes place in one of four locations depending on the participants’ geographical location (Anupama participated in the Dallas program). We each worked hand-in-hand with consultants, senior partners, and managers to solve a multi-business case by working in teams, brainstorming, conducting interviews with industry experts, data mining, and analyzing, all of which truly resonated with our consulting experiences.

Participating in these summer programs might give you an edge later on when seeking internship offers for full-time positions. Not only have you experienced the culture of the firm, practiced with case studies, and met people who work there, but at insight, for example, you are also supported with resources such as interview coaching and additional networking opportunities. We are both currently in the 90-day internship programs, and the experience has been 100% eye-opening for us to explore job offers at other consulting and venture capital firms as well.

For doctoral candidates and postdoctoral fellows in STEM and healthcare-related disciplines who are interested in exploring the business world, we highly recommend applying to McKinsey Insight, Bridge to BCG, and other management consulting immersion programs (like those at Bain, CBN, or PwC). Not only do we have unforgettable experiences with like-minded individuals and experienced consultants, but participation in these programs also helps us secure heavily sought-after, early full-time internship opportunities at these companies. The deadlines for these programs are usually in late March to early April, so if you don’t have a chance to apply this year, work on enhancing your resume and cover letter and be ready to apply next year. Good luck!
Recent Events

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Congratulations to Our Recent Graduates!

November 2017-March 2018

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- Cassie Retzlaff
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