

RESULTS & DISCUSSION

BRET Newsletter
Issue 3, Spring 2016

Photo Credit: Meagan Quinlan

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Faculty Advisor: Ashley E. Brady, Ph.D.

Letter from the Deans

Welcome to the third issue of *Results and Discussion*, a newsletter sponsored by the Biomedical Research Education and Training (BRET) office, which is devoted to highlighting the research accomplishments and activities of our PhD graduate students and postdoctoral fellows.

Spring is a busy time for the BRET office and our trainees. Our first year students are completing their laboratory rotations and will be selecting the labs that they will call home for the duration of their training. Many senior graduate students are setting defense dates and preparing themselves for commencement on May 13th. Recruiting season has been in full force and will be wrapping up soon as we all anticipate welcoming the newest class to campus in the fall. The Office of Career Development will be hosting the annual Career Symposium on June 2, which will draw a large audience of trainees to learn about research and development careers in industry.

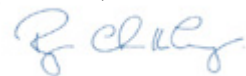
We are excited to once again share our newsletter with you that has been designed, written, and edited completely by current trainees. We sincerely hope that you will enjoy learning about the important research being pursued and published by Vanderbilt's young scientists. In addition, our newsletter features stories about campus events and alumni interviews that will be of particular inter-

est to our alumni, current trainees, and their families.

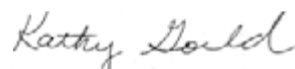
Please let us know if you would like to become more involved with our students and postdoctoral fellows, or with our programs at Vanderbilt University. There are many ways you can support us in our efforts to prepare the next generation of scientists. We would love to have the opportunity to hear your ideas and help find a way to engage you.

For more information, please visit our website or feel free to reach out to either of us directly. We would love to hear from you.

Sincerely,



Roger G. Chalkley, D. Phil.
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Kathy L. Gould, Ph.D.
Associate Dean for Biomedical Sciences
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What's Inside

Trainee Research

by Lorena Infante Lara, Page 2
by Philip Ko, Ph.D., Page 6

ASPIRE Program Highlights

by Ashley E. Brady, Ph.D., Page 3
by Lorena Infante Lara, Page 10

Alumni Spotlights

by Andrew Wiese, Page 4
by Marilyn Holt, Page 8

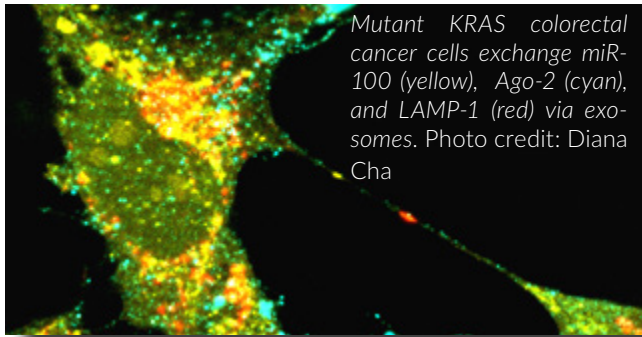
Important Dates, Page 12

Trainee Research

by Courtney Bricker-Anthony, Page 7
by Andrew Wiese, Page 11

Visit us at our website for more information:

<https://medschool.vanderbilt.edu/bret/>



Stimulating results can come from the least likely places. This wisdom guides graduate student Diana Cha, who has published a paper on data she discovered where the field thought there wasn't anything to find.

A native of the Greater Seattle Area, Cha fed her passion for science as an undergraduate student at the University of Washington. She knew she wanted to go to graduate school from the start, so after receiving a B.S. in Biology and Physiology she came straight to Vanderbilt University to pursue a Ph.D.

"I couldn't stay away from the science!" she jokes.

Cha came to Nashville in 2011 as a student in Vanderbilt's Interdisciplinary Graduate Program, and joined the lab of Professor Jim Patton, Ph.D., in the Department of Biological Sciences. Since then, years of hard work have led to a recent publication in *eLIFE* that sheds light on how cancer cells enhance their ability to survive. Although she was co-first author with Research Assistant Professor Jeff Franklin, Ph.D., she is quick to draw the spotlight away from herself and credit the hard work of everyone involved.

While RNA primarily exists in a cell's nucleus as a transition state in the production of protein from DNA, **many RNAs do not code for proteins.** Cha is part of a team of Vanderbilt labs that is involved in the NIH-funded Extracellular RNA Communication program. Their focus is on secreted RNAs that are found in exosomes.

Exosomes are small bubble-like vesicles that carry various cellular cargos into the extracellular space. Initially discovered as carriers of waste products, scientists have since found that exosomes carry proteins that are important in cell-to-cell communication. RNAs are also present in exosomes, but they have been largely ignored since extracellular RNAs are present at low concentrations and are less stable. As a result, the field believed that any regulatory function extracellular RNAs may have was unlikely to have far-reaching or long-lasting effects.

Secreted RNAs: Cancer's Malevolent Messengers

By **Lorena Infante Lara**, Graduate Student

Cha and colleagues found that the status of KRAS, an oncogene associated with colorectal cancer, affects which RNAs are secreted in exosomes. Importantly, they determined that secreted RNAs induced changes in gene expression in recipient cells. In colorectal cancer, the secreted RNAs could discourage other cells from growing too much, thus giving cancer cells a growth advantage.

As this new role for secreted RNAs was highly controversial, the authors backed it up with extensive controls. According to Cha, "You need to learn how to do the right experiment with the right controls. Controls are everything."

Cha's findings have interesting implications for patients as, one day, it might be possible to monitor colorectal cancer progression by taking a blood sample that measures the levels of certain RNAs, rather than through more invasive procedures.

Cha looks toward the future with anticipation. She hopes to stay in the RNA field, perhaps **researching "sexy RNAs like long non-coding RNAs or other secreted RNAs."**

Graduate Student Diana Cha



Learn More:

Cha et al., KRAS-dependent sorting of miRNA to exosomes. *eLIFE* (2015)



Provided by: Life Science TN

AdvaMed Federal Policy Fly-In on March 1. Left to right: biomedical researchers Kirby Wallace and Laura Eckard (St. Jude Children's Research Hospital and UT Health Science Center; Abby Trotter, executive director, Life Science Tennessee; Congressman Marsha Blackburn; Steve Bares, president, Memphis Bioworks; Sam Lynch, president, Lynch Biologics, Rubin Baskir, Vanderbilt University, Alex Cate, Life Science Tennessee

ASPIRE Internships offer a window to the world beyond the lab

This fall, the BRET Office of Career Development launched its internship initiative as part of the **ASPIRE Program**. ASPIRE is funded by a **BEST (Broadening Experiences in Scientific Training)** Award from the NIH Common Fund and is aimed at **empowering and preparing biomedical sciences Ph.D. students and postdoctoral scholars** to make well-informed career decisions.

To this end, the ASPIRE program is facilitating opportunities for graduate students and postdoctoral fellows to gain hands-on experience with a project in a professional work environment. **ASPIRE Internships** are off to a strong start with 18 positions being offered since August in a variety of career areas including policy/advocacy, teaching, biotechnology, healthcare data analytics, and craft beer brewing. Moreover, we have had significant interest from trainees, with 43 applicants for these positions.

So far, internships have all been part-time (8-10 hours per week) for 10-12 weeks at sites in the Nashville area, but we intend to expand beyond Music City.

As the program grows, we plan to increase the variety of internships offered, including full-time positions for 2-3 months, and in areas not currently represented such as non-profit management, venture capital, medical communications, and technology commercialization.

We are also making every effort to support students and postdocs who may wish to pursue established internship opportunities outside of the ASPIRE Program by providing a BRET-curated list of available positions, offering ASPIRE-funded travel awards, and facilitating the application process.

If you would like to **support us in our efforts**, we would be delighted to hear from you. We seek partners from a range of professions to host a graduate student or postdoctoral fellow in the workplace for an internship or a one- to three-day job shadowing externship.

Sincerely,

Kathleen L. Gould, PhD
Associate Dean for Biomedical Sciences

Science Policy Interest Culminates in an ASPIRE Internship

By **Ashley E. Brady, Ph.D.** ASPIRE Program Manager, BRET Office of Career Development

Rubin Baskir is nearing the completion of his Ph.D. training in the Department of Cell and Developmental Biology. However, Baskir isn't only interested in contributing in the academic sphere—he also wants to use his scientific training to effect change on a broader level. To accomplish this goal, he has seized opportunities to learn how he can leverage his scientific training to influence policy decisions.

To gain hands-on-experience in the policy sector, Baskir recently participated in an **ASPIRE Internship with Life Science TN**, the state's industry advocacy organization. As an intern, he performed life science and health care policy research, policy copywriting, and industry and elected official outreach.

During the course of this internship, Baskir joined the Life Science TN team at their legislative "Day on the Hill" in Nashville. There, they met with legislative leadership to discuss **opportunities for industry growth in Tennessee**. Baskir also attended the federal "Day in D.C.," where he met federal industry partners and discussed policy issues in detail with members of Tennessee's Congressional delegation and senior policy staff.

When asked about his experience, Baskir notes, "This opportunity has provided a solid foundation for my long term goals of crafting policies that will improve graduate education, maintain sustainable funding for basic research, and reduce the gaps between basic research and technologies that improve a patient's quality of life."

Learn More:

Interested in participating in an ASPIRE Internship visit <https://medschool.vanderbilt.edu/aspire/aspire-internships>



• Future Directions •

Laura Burns, Ph.D.

the Tennessee brewer uses scientific principles to elevate the beer creation process

By **Andrew Wiese**, Graduate Student

Cell biologist turned brewmaster, Dr. Laura Burns, left an academia-centered career path three years ago for the opportunity to pursue her passion for fermentation and beer creation. Taking advantage of a unique opportunity, Dr. Burns turned a side project of establishing the laboratory and yeast program at Tennessee Brew Works into a full-time position as the company's Brewmaster and Director of Quality Assurance. Dr. Burns credits her time at Vanderbilt University for helping her create a yeast program that is unique to Tennessee Brew Works. Instead of "praying to the yeast gods," Dr. Burns' scientific expertise has informed the creation of a tight, consistent fermentation process that ultimately improves and differentiates the product from competitors. Even as she is raising the profile of Tennessee Brew Works in the Nashville brewery scene, Dr. Burns finds ways to combine her work with her other interests. This is most evident in the yoga class hosted weekly at Tennessee Brew Works known as "The Hair of the Downward Dog."

Recently, Dr. Burns allowed the *BRET Results and Discussion Newsletter* to document a day in her life....



A typical day at Tennessee Brew Works brewery begins at **4:45 a.m.** when Dr. Burns starts an automated program from home to hot water rinse the brew system and mill the grains for brewing. Dr. Burns goes for a morning run at **6:30 a.m.** before she begins a brew day shift.



Dr. Burns spends all day on the brewery floor, but only **20%** of her time is dedicated to actively brewing beer. She is also responsible for responding to emails, in addition to meeting with vendors and Tennessee Brew Works customers. At brewery events, Dr. Burns interacts with about **25** customers.



Photo Credit: Andrew Wiese

Over the past year, Dr. Burns has helped create **7** beers at the brewery, including **2** seasonal and **5** flagship beers.

100%
portion of day
spent on the brew floor

60-80
hours worked
in a typical week

2-3
beers consumed
per standard brewing day

5
barrels of beer
brewed during the day

11-14
hours
required to brew a double
or quadruple batch of beer.

93,000
gallons of beer
brewed in the past year

Clearing Errors in DNA Replication

By **Philip Ko, Ph.D.**, Postdoctoral Fellow

Postdoctoral fellow Huzefa Dungrawala, Ph.D., speaks with the enthusiasm of one who looks to the future. While adjusting to life in the US after moving here from India, this zest may have worked against him. “I had to consciously tell myself to speak slowly,” Dr. Dungrawala said. “I am just used to speaking very fast.” However, this energetic trait also drives his research in DNA replication.

Dr. Dungrawala first studied pharmacology at The University of Pune, in India. Following his studies there, Dr. Dungrawala pursued his passion for genetics by enrolling at Texas Tech University, where he earned his PhD conducting genetic research with yeast cells.

While finishing graduate school, Dr. Dungrawala learned of **iPOND (isolation of proteins on nascent DNA), a groundbreaking protein identification technique** developed in the laboratory of David Cortez, Ph.D.,

Professor of Biochemistry at Vanderbilt. Dr. Dungrawala began working with Dr. Cortez after completing his Ph.D., but the transition from working with yeast to Cortez’s model system, human embryonic kidney cells, was initially daunting. “It took me some time to get used to the techniques and how experiments are done when you work with a different model system,” Dr. Dungrawala said.

Learning quickly, Dr. Dungrawala refined iPOND to more reliably yield proteins of interest. Dr. Dungrawala applied this refined method and paired it with mass spectrometry in a first-authored study, recently published in *Molecular Cell*, that **revealed one of the ways cells regulate DNA replication during added stress.**

Essentially, each cell contains a copy of its blueprint, DNA. During healthy cell growth, billions of base pairs of DNA must be precisely copied, or replicated. This is a delicate process, and errors can result in cancer and other genetic diseases.

One of the first responders during periods of replicative stress is a protein called ATR. Plagued by ineffective DNA repair processes, **cancer cells are particularly vulnerable to interference of DNA replication and “are addicted to having ATR,”** said Dr. Dungrawala. ATR inhibitors are currently in clinical trials testing their ability to kill cancer cells by starving them of ATR.

Biologists believed ATR mitigated the effect of DNA damage by stabilizing the molecular machinery that replicates DNA, called the replisome. However, the results from Dr. Dungrawala’s study suggest the primary role of ATR is to regulate other proteins that repair DNA, rather than to stabilize the replisome as previously thought. Additionally, studying the proteins identified in this study will help us better understand how cells replicate DNA when faced with replication stress.

Dr. Dungrawala looks toward establishing his own lab, and he is unfazed by potential obstacles. “I’m definitely positive and optimistic about it. I just plod along and whatever obstacles I have, I just face it.”

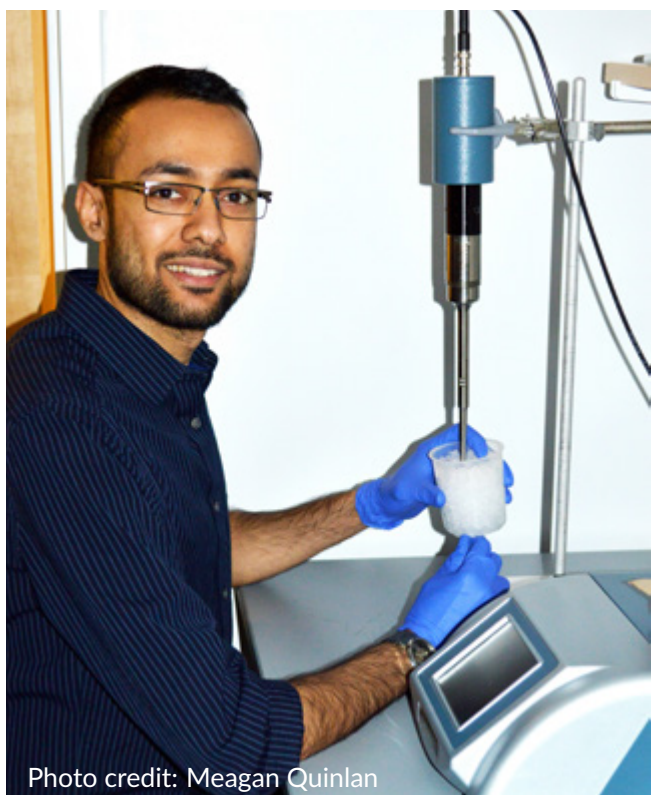
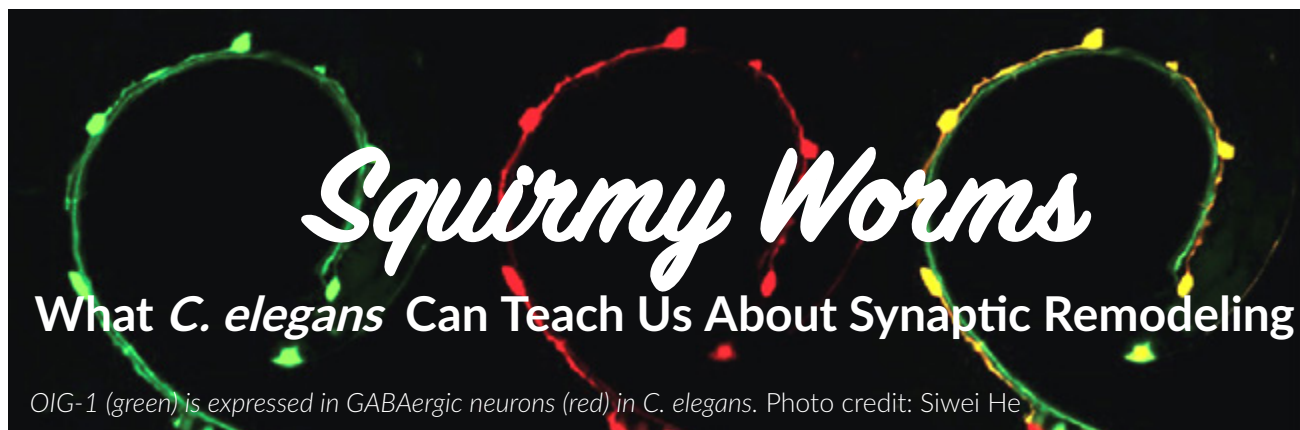


Photo credit: Meagan Quinlan

Dr. Dungrawala in the lab.

Learn More:

Dungrawala et al., The Replication Checkpoint Prevents Two Types of Fork Collapse without Regulating Replisome Stability. *Molecular Cell* (2015)



By **Courtney Bricker-Anthony**, Graduate Student

When he's discussing his research, graduate student Siwei He's passion for neuroscience is palpable. Siwei first became interested in science while attending medical school at Fudan University, where he sated his budding interest by joining a microbiology lab as an intern. When he took a neuroscience course, he was immediately hooked.

"For my thesis, I [joined] a neuroscience lab. **That's how my long romance with neuroscience began,**" said Siwei, grinning.

Siwei is now a Ph.D. candidate in Dr. David Miller's laboratory in the department of Cell and Developmental Biology at Vanderbilt University. The Miller lab focuses on neuronal development and gene expression using the *C. elegans* model system, which attracted Siwei to Dr. Miller's research.

"*C. elegans* is a very powerful model system [because] all of the cellular connections have been clearly mapped and we can study genetic interactions in a very short period of time. Also, most genes in *C. elegans* have a human homologue," explained Siwei.

The advantages of the *C. elegans* model system are evident in Siwei's publication in *Current Biology*, which explores the regulation of developmental synaptic remodeling/plasticity. "Plasticity is important for learning new information and injury responses," said Siwei. "For example, after a stroke, neurons need plasticity to form new connections."

If neurons are unable to form new connections after an injury or make appropriate connections during development, then issues like uncontrollable body movements, abnormal speech or cognitive impairment may occur. Understanding plasticity could lead to the discovery of novel therapeutics. Siwei and colleagues sought to discover the molecular signature of developmental

synaptic remodeling in *C. elegans* motor neurons.

Motor neurons in *C. elegans* innervate muscle cells and produce coordinated movements that allow the worms to navigate their environment and procure food. One class of the motor neurons (GABAergic motor neurons) undergoes synaptic remodeling during development. This provided Siwei and his colleagues with an opportunity to tease out specific **regulators of synaptic remodeling.**

In an elegant series of experiments, Siwei and his colleagues demonstrated that OIG-1, an immunoglobulin superfamily protein, functions as a negative regulator of synaptic remodeling in the GABAergic motor neurons.

According to Siwei, **"OIG-1 inhibits remodeling. If neurons have less OIG-1, then they have more plasticity.** In the future, we want to know how neural activity participates in remodeling and find potential mammalian homologues. We could eventually target [a human homologue] to promote synaptic plasticity."

For now, Siwei is taking time off from the medical field to explore his passion for neuroscience research. In the future, he hopes to combine his medical and doctoral degrees as a physician scientist.

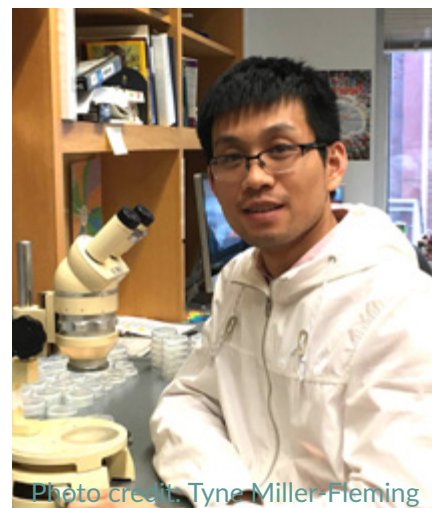


Photo credit: Tyne Miller-Fleming

Graduate Student Siwei He

Learn More:

He et al., Transcriptional Control of Synaptic Remodeling through Regulated Expression of an Immunoglobulin Superfamily Protein. *Current Biology* (2015)

Chemistry, Not Character

By **Marilyn Holt**, Graduate Student

Avielle Richman, Summer 2012
Provided by: The Avielle Foundation



What do you do when your only child is murdered in a brutal, sensationalized act of violence?

For **Jeremy Richman, Ph.D., and his wife, Jennifer Hensel**, the answer was to take positive action. Three days after their 6-year-old daughter, Avielle, was killed in the Sandy Hook Elementary School shooting in December 2012, they had developed the framework for a foundation dedicated to preventing violence.

“This was so, so unimaginably horrible,” Richman said in an interview at Vanderbilt University Medical Center. “We said we don’t want anyone else to suffer this way.”

Rather than focus on gun regulation or public safety issues, the Avielle Foundation, named for their daughter, stresses compassion and mental health, or as Richman put it: **“brain health.”**

“We wanted to play to our strengths,” said Richman, a former postdoctoral fellow in the Department of Pharmacology at Vanderbilt and pharmaceutical company scientist. “We’re scientists. We ask ‘why’ questions all the time. That’s what we do.”

Learn More:

This article is largely reprinted from the November 19th, 2015 issue of the Vanderbilt University Medical Center Reporter.

Twenty-year-old Adam Lanza killed 20 children and six adults at the Sandy Hook school in Newtown, Connecticut, before turning the gun on himself. Stigmatizing the mentally ill as somehow morally flawed will not solve the problem, according to Richman.



Provided by: The Avielle Foundation

“The brain is just another organ — it’s biochemical in nature, and so are our behaviors. It’s chemistry, not character,” he said.

However, Richman also believes that “just because they’re biochemical doesn’t mean we’re fated to them.” Behavior may be biochemical, but we can affect the biochemistry by making good choices — protecting the brain from traumatic injury, staying active and staying connected with others.

In a talk at Vanderbilt University Medical Center, Richman did not focus on the shootings, instead taking a broad approach to violence. According to him, **“We’re really interested in the root cause of violence,** and violence can take on many, many forms, and there are many tools of violence.” Ultimately, preventing violence will require continued investment in brain research, as well as compassionate and engaged communities willing to see violence as an illness that should be treated, not punished. Richman and Hensel created The Avielle Foundation to focus on this very thing.

“The mission is very simple: it’s to prevent violence and build compassion through fostering neuroscience research community engagement and education.”

Toward this goal, the **foundation will soon be announcing the awardees of a number of grants intended to foster neuroscience research.** They also engage in community education projects, including working with interns in high school and college, many of whom are from Sandy Hook.



Dr. Jeremy Richman, Photo credit: Steve Green

“I feel very proud of the legacy that my wife and I are leaving in honor of our daughter Avielle.”

Learn More:

Please visit the Avielle Foundation at <http://www.aviellefoundation.org/>.



Isaiah Hankel Gets Cheeky at Vanderbilt

By **Lorena Infante Lara**, Graduate Student

The term “networking” brings anxiety to many graduate students and post-doctoral fellows, as it is often thought of as an ominous harbinger of professional and social doom.

Much to the appreciation of those who would like to refine their skills, the ASPIRE program brought in a specialist to shed light on the nuances of this process for its 2016 Aspire to Connect event.

He is the Cheeky Scientist – the professional alter ego of Isaiah Hankel, Ph.D. Hankel founded the **Cheeky Scientist, an industry-training platform for Ph.D.s seeking to transition from academia into industry**, in 2012.

Hankel cut through the haziness of how to network during “A2C gets Cheeky.” Speaking to a mixed audience of doctoral students and post-doctoral fellows, he exposed misconceptions and tore down perceived barriers in a three-hour interactive presentation. Hankel focused on how to properly utilize strategies to get hired for industry jobs, but his basic tenets are applicable to any other kind of job search.

“You only have two eyes and two ears, which limits the number of opportunities you can see. **The more you grow your network, the more eyes and ears you have, and the more opportunities you can see,**” Hankel said.



Photo Credit: Ashley E. Brady, Ph.D.



Above: *The Cheeky Scientist, Dr. Isaiah Hankel speaks with an attendee after his seminar. Below:* Seminar attendees perform networking exercises.

According to Hankel, you should try to go to as many networking events as possible, especially if they are outside your field. It is hard to remember one scientist in a room full of scientists, but it is certainly easier in a room full of architects.

Attendee Elizabeth Gibson, a doctoral student in Pharmacology, especially appreciated the tips on introducing oneself at networking events and getting the most out of the professional online networking site LinkedIn. “Who knew that adding something personal to your LinkedIn headline could be so crucial?”

A key takeaway was the necessity of maintaining a healthy network by dedicating a small amount of time to it daily, instead of demanding immediate results following months of neglect.

Hankel said it best,

“Stop being reactive, be proactive.”

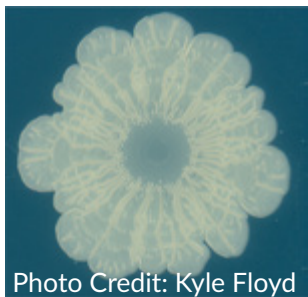


Photo Credit: Kyle Floyd

Uropathogenic E. coli form complex biofilm cities.

Kyle Floyd began his scientific research career at the University of Alabama at Birmingham, where he earned his M.S.P.H. degree and discovered a passion for mass spectrometry technology. While at UAB, Floyd used mass spectrometry to study how the ocular lens develops cataracts. After beginning his graduate studies at Vanderbilt University, Floyd was unsure which scientific question he wanted to tackle next.

Eventually, Floyd's passion for the analytical aspects of mass spectrometry led him to join the lab of Dr. Maria Hadjifrangiskou in the Department of Pathology, Microbiology and Immunology. Floyd and Dr. Hadjifrangiskou forged a co-mentorship with Dr. Richard Caprioli in the Department of Biochemistry and the Mass Spectrometry Research Center, which allowed Floyd to use mass spectrometry technology to better understand how bacteria that cause urinary tract infections (UTIs) form biofilms on surfaces, like catheters.

Latest estimates from the CDC indicate that **UTIs are the fourth most common type of healthcare-associated infection**, with over 93,000 healthcare-associated UTIs. UTIs are also an important issue in women's health as, according to Floyd, "at least 1 in every 2 women will experience a [UTI] in their lifetime." With symptoms including pain and discomfort, UTIs can lead to increased costs and even death among hospitalized patients. "By understanding [bacterial] pathogenesis, we hope to help develop methods to treat UTIs better. In addition, we believe that—using mass spectrometry techniques—we can identify biomarkers for early detection of infections or even patients at high risk for UTI," said Floyd.

When bacteria enter the urinary tract or come into contact with medical equipment, they can come together to form large communities—or cities—of bacteria, known as a biofilm. This can make treating UTIs very difficult. In a study recently published in *PLOS Pathogens*, Floyd and colleagues used matrix-assisted laser desorption/ionization time-of-flight imaging mass spectrometry (MALDI-TOF IMS) to identify mechanisms that support uropathogenic *Escherichia coli* (*E. coli*) biofilm

Study Sheds New Insights into How Bacteria Build Cities

By **Andrew Wiese**, Graduate Student

formation. **"As uropathogenic *E. coli* is the major causative pathogen in urinary tract infections, the ultimate goal was to look at how biofilm formation is regulated by uropathogenic *E. coli*,"** said Floyd.

The study also demonstrated that MALDI-TOF IMS is a promising new tool for studying bacteria. MALDI-TOF IMS was able to identify 60 different proteins at a time, dramatically outperforming current methods that can only study few proteins at a time. "We've adapted a technology that we can use to dig into the building blocks of these multicellular bacterial communities that are crucial for infection. By digging into the individual building blocks, we can look for ways to negate the effects of these bacteria," said Floyd.

Moving forward, Floyd's immediate research plans are to continue studying how bacterial communities form during urinary tract infection. Floyd's long-term plan is to seek academic post-doctoral training and earn a tenure-track faculty position focusing on bacterial pathogenesis. Regardless of where he ends up, he will continue to use mass spectrometry in his work. "I feel that these technologies have a lot to offer for the study of bacterial pathogenesis, and I would like to further their uses for the field," said Floyd.



Photo Credit: Meagan Quinlan

Graduate Student Kyle Floyd

Learn More:

Floyd et al., Adhesive Fiber Stratification in Uropathogenic *Escherichia coli* Biofilms Unveils Oxygen-Mediated Control of Type 1 Pili. *PLOS Pathogens* (2015)

Important Dates Spring 2016

March 14

ASPIRE to Connect

April 20

1st Year Lab
Selection

April 29

PDA Shared
Resources
Symposium

May 9

Annual RCR
Training

May 13

Commencement

June 2

Career Symposium
"R&D Careers
in Industry"

Sept 2

Simple Beginnings
Ceremony

Photo Credit: Meagan Quinlan

RESULTS AND DISCUSSION

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