



BrainStorm

Fall 2023

PROGRAM IN NEUROSCIENCE

University of Maryland School of Medicine
<http://lifesciences.umaryland.edu/neuroscience>

 @UMMedNeuro

Faculty Spotlight:

INSIDE THIS ISSUE

- 1 Faculty Spotlight: Q & A with Todd Gould, MD
- 2 Neuroscience Outreach & Volunteer Association
- 3 Faculty Research Highlights
- 4 Faculty Spotlight: Todd Gould, MD (cont'd)
- 6 Recent PIN Graduates
- 7 New Faculty Researcher: Barbara Juarez, PhD
- 9 Annual PIN Retreat
- 10 Student Highlights
- 11 Photo Gallery



Q&A with Todd Gould, MD

Q: *How did you end up becoming a scientist?*

A: As an undergraduate, I elected to take an upper-level course in Physiological Psychology as my psychology elective. The school was not very research focused, though the professor directing this course ran a small biological psychology laboratory within the department. I started getting involved, and then got the research bug and was completely hooked. We didn't have much of a library, so I would drive about an hour to a university that had a library with medical journals and spend hours there reading. To me, thinking about questions that had no answers available was the most stimulating thing ever. My nucleus accumbens, it seems, really liked research! Thereafter, my first experience with high level research was during an NSF-funded fellowship between my junior and senior years in college researching neurovirology, followed by a one-year position at intramural NIH in Bethesda, MD, studying molecular genetics prior to medical school. Although I had applied to MD/PhD programs, no program would take me, so I spent four long years memorizing stuff in medical school, followed by a 6-year postdoc through the Intramural Research Program at NIH where I trained in neuropharmacology, prior to joining the superb neuroscience community here at UMB in 2007.

Faculty Spotlight continued on page 4

Neuroscience Outreach & Volunteer Association



Blossoming Brains



Fall Lab Tours



Brain Awareness Week



Sidewalk Science

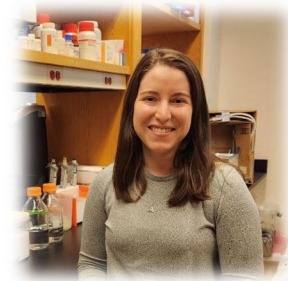


Brewing Biology

by Cassie Stapf,
Program in Neuroscience student and President of NOVA



Neuroscience
Outreach
Volunteer
Association



Neuroscience Outreach and Volunteer Association (NOVA) is a graduate student-led organization that sponsors monthly outreach events to foster a relationship between the Baltimore city public and the scientific community at UMB. NOVA's volunteers accomplish this mission by connecting with community members of all ages through interactive learning demonstrations and public discussions which foster enthusiasm for science.

In the fall semester, NOVA volunteers visit the Maryland Science Center at the Inner Harbor for the Blossoming Brains event. Volunteers conduct neuroscience activities for kids ages 3-8 to introduce basic neuroscience concepts. Additionally, NOVA invites several high school students across Baltimore to participate in yearly Fall Lab Tours. Students meet current graduate students, step into lab spaces, and learn about the path to graduate school. In the spring semester, NOVA participates in Brain Awareness Week (BAW). During BAW, NOVA volunteers visit middle schools and provide lessons and demonstrations on various neuroscience topics. This year, NOVA will continue our Brewing Biology series in the Spring. This event brings together UMB researchers, city councilmembers, and nonprofit groups to host a forum on relevant public health topics such as substance use disorder treatment and COVID-19 prevention. Other events we will host this year are Sidewalk Science, the Brain Bee, and Paul's Place Day. We are also open to new ideas and opportunities for broadening our impact!

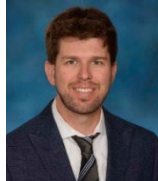
If you have questions about this volunteer organization or are interested in participating, please email Cassie Stapf:

catherine.stapf@som.umaryland.edu

Faculty Research Highlights



Vivek Garg, PhD, Assistant Professor, Department of Physiology received an RO1 grant from the National Institute of General Medical Sciences for “Molecular Physiology of Mitochondrial Calcium Uniporter.” Dr. Garg also authored two publications, including a tutorial “Patch clamp technique to study mitochondrial membrane biophysics,” which was published in the *Journal of General Physiology*.



Seth Ament, PhD, Associate Professor, Department of Psychiatry, received an RO1 grant, “Multi-scale consequences of variants in the neuropsychiatric risk gene SETD1A in a population isolate,” from the National Institute of Mental Health.



Mary Kay Lobo, PhD, Professor, Department of Neurobiology was awarded, in collaboration with **Seth Ament, PhD**, and **Asaf Keller, PhD**, “Lasting Neurological Effects of Perinatal Opioids,” a multi-million-dollar research grant supported by National Institute on Drug Abuse, and authored multiple publications including, “An endogenous opioid alters neuronal plasticity to constrain cognitive flexibility,” found in *Molecular Psychiatry*.



Marco Venniro, PhD, Assistant Professor, Department of Neurobiology received a multi-million dollar RO1 research grant in collaboration with **Seth Ament, PhD**, and **Mary Kay Lobo, PhD**, “Genomic profiling mediating the protective effect of social reward on opioid craving,” from the National Institute on Drug Abuse. Dr. Venniro also coauthored a publication with **Todd Gould, PhD**, “Relative to females, male rats are more willing to forego obtaining sucrose reward in order to prevent harm to their cage mate,” published in *Psychopharmacology*.



Todd Gould, MD, Professor, Department of Psychiatry received a VA Merit award for his work progressing the understanding of “Estradiol treatment of stress-related psychiatric disorders in Veterans,” and authored multiple publications including, “Possible psychedelic therapeutic mechanism: Psychedelics act on intracellular serotonin receptors that are not accessible by serotonin alone,” published in *Science* and including the work of UMB faculty **Sarah Clark, PhD** and **Leonardo Tonelli, PhD**.



Joyce Teixeira Da Silva, PhD, Assistant Professor, Department of Neural and Pain Sciences, authored, “Sex differences in visceral sensitivity and brain activity in a rat model of comorbid pain: A longitudinal study,” in press in *PAIN Journal*, and co-authored “Intraganglionic reactive oxygen species mediate inflammatory pain and hyperalgesia through TRPA1 in the rat,” published in *Frontiers in Pain Research*.



Alexandre Medina, DSci, Associate Professor, Department Pediatrics, published “Development of multisensory processing in ferret parietal cortex” and “Effects of developmental alcohol exposure on cortical multisensory integration: in the European Journal of Neuroscience.



Alexandros Pouloupoulos, PhD, Professor, Department of Pharmacology, published, in collaboration with **Seth Ament, PhD**, “The brain’s dark transcriptome: Sequencing RNA in distal compartments of neurons and glia,” in *Current Opinion in Neurobiology*.



Donna Calu, PhD, Associate Professor, Department of Neurobiology, authored, “Decreased Ventral Tegmental Area CB1R Signaling Reduces Sign Tracking and Shifts Cue-Outcome Dynamics in Rat Nucleus Accumbens,” in collaboration with **Joseph Cheer, PhD**, published in the *Journal of Neuroscience*.



Miroslaw Janowski, MD, PhD, Associate Professor, Department of Diagnostic Radiology and Nuclear Medicine published “Mesenchymal stem cell engineering by ARCA analog-capped mRNA,” in *Molecular Therapy: Nucleic Acid*, and is a collaborator on a the R21 grant “Hyperpolarized ¹³C metabolic imaging in an endovascular swine model of ischemic stroke.”

Faculty Spotlight continued from page 1

Q: *When is the first time you felt like you were a “real” scientist?*

A: Perhaps this is a trick question.... I felt like a real scientist with those first experiences and experiments as an undergraduate. To me, being a scientist is more a process and existence than an outcome. Perhaps this means that I am not yet a real scientist, because I have not reached an epiphany moment when I realized I was a real scientist? Seems like something exciting to look forward to when it happens!

Q: *What do you study?*

A: My research is mostly focused on discovering antidepressant drug mechanisms, and I am particularly interested in the pharmacology underlying effective ‘orphan’ drugs as a route to discovering new drugs. Orphan drugs are drugs that while they are effective as treatment, we do not know how they work. For many years I have explored how the simple monovalent cation lithium could stabilize mood in individuals with bipolar disorder or depression. Lithium has been used as a mood stabilizer for over 70 years, and yet we still do not know how it works. More recently, I have focused on the pharmacology of the anesthetic ketamine, which is used at sub-anesthetic doses for the treatment of depression. In contrast to most antidepressant drugs, ketamine can reverse depressive symptoms rapidly within hours and can work in individuals who do not respond well to other treatments. While some of the pharmacology of ketamine is understood, including inhibition of NMDA glutamate receptors, other drugs that share that pharmacology are not effective. I study the pharmacology of ketamine distinct from NMDA receptor inhibition.

Q: *Why is your research important?*

A: The idea is that if we understand how existing drugs work, we can use those targets to identify more specific drugs with fewer side effects. For example, we have identified that the production of a naturally occurring metabolite of ketamine, hydroxynorketamine, is necessary for ketamine’s antidepressant-relevant effects in animal models (e.g., Zanos *et al.*, *Nature* 2016; Georgiou *et al.*, *Nature Neuroscience* 2022). Furthermore, we showed using electrophysiology combined with behavioral outcomes that this hydroxynorketamine itself is sufficient to exert potent effects to strengthen glutamatergic synapses that we think reverses deficits in these synapses. In contrast to ketamine, side effects including dissociation and abuse potential were not observed in animals treated with hydroxynorketamine. We recently completed human phase I studies confirming no indication of dissociation or misuse potential and anticipate beginning phase II studies in individuals with treatment resistant depression this coming year.

Q: *Do you have an analogy to help people understand your work?*

A: Depression is very common, so most of us have first-hand experience with a friend or family member who is depressed or has experienced depression. We have drugs that work to treat depression in many individuals, however, these drugs typically take weeks or months to be fully effective. Individuals who are treatment resistant do not respond well at all. My work is aimed at discovering and developing new treatments for depression that work faster, and work in individuals who do not respond well to existing drugs. As one example, a new project we are focused on is the process of regulating the capacity for synaptic plasticity by exposing neurons to a stimulation that alters future synaptic plasticity. This is referred to as metaplasticity. We seek to harness such metaplasticity mechanisms to prepare the depressed brain to respond more favorably future stimuli. Such future stimuli could take the form of other drugs, non-invasive neuromodulation approaches such as electroconvulsive therapy and transcranial magnetic stimulation, or talk therapy. An analogy could be using a primer when painting a house; without the primer the robustness and overall durability of the topcoat paint will be reduced.

Q: *What is your favorite thing about your work?*

A: As an academic scientist we have the privilege of being paid to think and dream and are surrounded by a very diverse, interesting, and passionate group of people, both senior scientists and trainees, sharing that same passion. I enjoy being able to conduct basic research for which the translational impact has been realized, rather than just hypothesized.

Q: *What is it like to be in your lab?*

A: I have a mixture of PhD students, research assistants, postdocs, and more senior scientists. Depending on their stage in training, I routinely meet with trainees once every 1 or 2 weeks. This allows for a set-aside time for discussion of experimental results, planned experiments, and everyday life. This is in addition to an open-door policy and communications by e-mail. We have weekly lab meetings and a monthly journal club, which is combined with a couple clinical research groups where we review papers that describe novel antidepressant findings in a translational context.

Q: *Why would a student want to join your lab?*

A: Most students who join my laboratory have an interest in both neuroscience and neuropharmacology, as well as an interest in participating in translational research. We have a collaborative environment in everyday lab activities between students, postdocs, and other faculty. We utilize basic and cutting-edge neuroscience techniques, including opto- and chemo-genetics, fiber photometry, electrophysiology, behavioral pharmacology, et cetera but I also encourage working with other research groups to tackle new problems, which is facilitated by the scientifically robust, diverse, and collaborative neuroscience environment at UMB. There also may, or may not, be a ping pong table hidden on the floor where our laboratory is located.

Q: *What is the next step in your research?*

A: There is work going on related to ketamine's hydroxynorketamine metabolites. One is the drug development, where we are currently seeking FDA approval for the phase II study in treatment resistant depression. The second are mechanistic studies where we aim to understand the unique mechanisms whereby hydroxynorketamine potentiates excitatory synapses and to harness that knowledge for future drug discovery. There are other projects ongoing including a focus on neurohormones and the role of estradiol in mediating stress susceptibility and depression in both men and women, and other antidepressant approaches to target metaplasticity (priming a synapse to respond favorably to a later stimuli). For example, combining pharmacology treatment with neuromodulation or therapy.

Q: *What do you like to do when you're not doing research?*

A: My wife and I have two children in grade school. I spend much of my time helping to guide them to interpret the world around them and being prepared for the future. Otherwise, I live close to Patapsco State Park and am shredding the mountain bike trails as much as possible.



Pictured to the right: Summer 2023 Gould Lab Retreat

Recent PIN Graduates



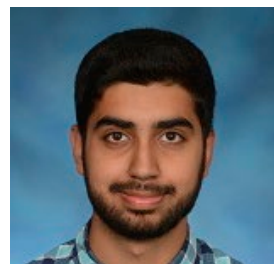
Ashley Marquardt, PhD defended her thesis “Defining the causes and consequences of sex differences in juvenile rat social play,” work she accomplished while in the lab of **Margaret McCarthy, PhD**. We’re pleased to have Ashley remain on campus in her current position as Program Manager of University of Maryland - Medicine Institute for Neuroscience Discovery (UM-MIND)!



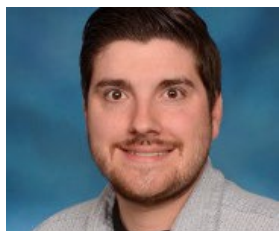
Miriam Menken, PhD defended her thesis “The Neurobehavioral and Brain Morphometric Outcomes Associated with Bullying Victimization,” work she accomplished in the lab of **Linda Chang, PhD**. We wish Miriam the best of luck as she explores employment in secondary education!



Michael Patton, PhD defended his thesis “Striatal Fast-Spiking Interneurons Regulate Compulsive Ethanol; Consumption,” work he accomplished in the lab of **Brian Mathur, PhD**. We wish Michael well in his Postdoctoral Studies at Duke University!



Houman Qadir, PhD defended his thesis “The claustrum: A novel cortical network hub” in the lab of **Brian Mathur, PhD**. We wish Houman the best as he continues his studies as a postdoctoral fellow in the Tarik Haydar lab at Children’s National!



Jesse Smith, PhD defended his thesis “The role of parabrachial in nociception and pain in awake mice,” work he accomplished in the lab of **Asaf Keller, PhD**. Congratulations to Jesse as he continues his studies as a postdoctoral fellow at Boston University!



Andreas Wulff, PhD defended his thesis “A common goal, a common path: Shared mechanisms between psilocybin and SSRI antidepressant actions?” work he accomplished in the labs of **Scott Thompson, PhD** and **Brian Mathur, PhD**. We wish Andreas the best of luck as he continues his studies as a Postdoctoral Fellow in the lab of Dr. Brian Mathur!

New Faculty Researcher:



Barbara Juarez, PhD

Barbara Juarez was always interested in science, but she suggests that she “accidentally” became a career scientist, through a series of serendipitous events. After undergoing the (common) undergraduate student struggle with organic chemistry, she decided to shift gears and take a biological psychiatry class, where she first developed an interest in neuroscience. She became intrigued by understanding how the brain is connected to how we feel and behave. A teaching assistant for this course picked up on Barbara’s curiosity and mentioned that she could volunteer in a research lab to explore this further, so Barbara then sought out the single Neuroanatomy lab at the then ecologically focused Florida International University. The primary investigator of this lab was, incidentally, “super-supportive of whatever crazy thing we wanted to do.” This spark of creative freedom, coupled with hearing about a post-baccalaureate preparation program at Mt. Sinai in New York, unleashed a new world of discovery and opportunity for Barbara. She pursued this preparation program, and later transitioned into the graduate program at Mt. Sinai, where she was introduced to the powerful impact of translational research. The passion evoked by seeing her graduate studies of potassium ion channels be applied to human treatment within a matter of years motivated her to pursue a postdoc and begin her own research program here at UMB.

Her own unanticipated path to becoming a scientist has motivated her to engage in outreach work, such as being a member of the UM-MIND Inclusion, Diversity, Equity and Anti-racism in Science committee and establishing Promoting Belonging in Neurobiology to help, more deliberately, pave the path to a career in research for other individuals from underrepresented backgrounds.

Barbara also promotes this sense of belonging as she works alongside her two laboratory technicians, Bridget Asare-Owusu and Star Fernandez, to lay the groundwork of her newly minted laboratory. Barbara gets excited as she provides perspective on how thrilling it is to set up a lab from scratch, and begin performing experiments under her own domain, citing having taken pictures of the first gel that was run in her lab, and of Bridget running photometry experiments for the first time. As the collaborative, energetic, and dynamic lab environment continues to develop, Barbara hopes to soon bring graduate students into the fold. With work spanning from CRISPR Cas-9 gene knockouts to evaluating how this impacts *in vivo* behavior and neural activity, her lab aims to afford members the opportunity to identify new therapeutic targets, with hope of later establishing collaborations for drug design, recreating the bench-to-bedside process that sparked her own passion as a young scientist.

Barbara hopes to identify potential targets for neuropsychiatric disorders by studying how brain circuitry becomes dysregulated in negative emotional states, induced by chronic stress or drug withdrawal, to impact decision making (such as whether one chooses to prioritize substance use over going to work). Her work is influenced by the neural circuit hypothesis of the progression of substance use disorders, which proposes that through repeated phases of drug intake, withdrawal, and abstinence, distinct neural circuits of reward, stress, and executive function are undergo pathological adaptations. This shift over time causes the motivation for misuse of drugs to shift from seeking pleasure, to being motivated by the expected alleviation of aversive withdrawal symptoms; this latter motivation appears to be an even more difficult pattern to break, making recovery from misuse of drugs more difficult to achieve over time.

Barbara's research into aversion circuitry is uniquely focused on using a neurophysiological perspective and a mouse model to understand the role of the Parabrachial Nucleus (PBN), a newly implicated region in the hindbrain with a direct connection to the amygdala, in this late "drug intoxication phase" of misuse of drugs, and how it might serve as a target for treatment of chronic misuse of drugs. There is evidence to suggest that the PBN may play a role in the development of these aversive withdrawal symptoms, including both the physical, somatic symptoms which take place immediately during withdrawal, and the emotional, affective symptoms which are depressive-like and have a slightly delayed onset and tend to linger, making relapse more likely. She is currently investigating how regulation of potassium channels in the PBN may mitigate withdrawal symptoms triggered by chronic opioid use.

As Barbara uses a two-pronged approach to better understand how to target the changes that take place in both aversion and reward circuitry during substance use, she is also currently studying how the diverse neurons of the dopamine reward system are regulated by opioids. Her approach to studying this is to knock out specific subsets of opioid receptors and measure the impact on dopamine signaling and reward behaviors during various stages of drug abuse and withdrawal.

When Barbara isn't taking pictures of the initial experiments which she hopes will lead to therapeutic breakthroughs, she enjoys getting to know the unique neighborhoods of Baltimore, by visiting farmers markets and buying records, and hiking through the many parks in and near Baltimore, her favorite being Gunpowder Falls State Park.

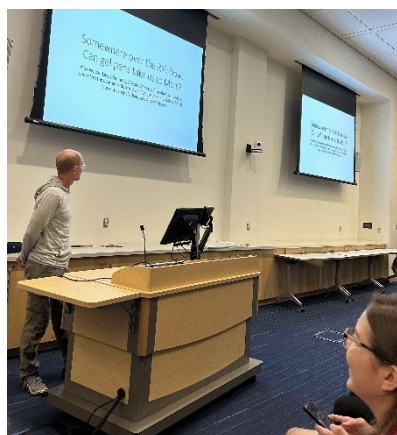
Annual PIN Retreat



The PIN Community was engrossed in a (genuinely) talent-laden scientific jam session performed by PIN students Abby Vigderman (guitar) and Alex Wiltse (ukulele).

This year’s PIN Retreat was centered around community-building and the sharing of science in unconventional ways. Although we aimed to hold the event at a pavilion in a wooded area of nearby Patapsco State Park, a blip in the weather led us to pivot to an on-campus event, so that we could stay dry; but the change in plans was hardly noticed amongst all the fun we were having!

We began the day with lively conversations facilitated by “Scientific Speed Chats,” in which members of the community discussed their work with “partners” of a different scientific background. We were then introduced to the lab work of various students, faculty, and postdocs, as illustrated through the live performance of song (pictured, top left), poetry, and hilarious skits. Trainees then worked in groups to practice generating the various parts of a grant by developing (ridiculous) fictitious grants, one being titled “Somewhere over the Rainbow: Can Gel Pens take us to Mars?” which were later presented by faculty, in a “plea for funding” (pictured, middle left).



Dr. Greg Elmer nearly convinced us that we should fund a project about sending gel pens to space.

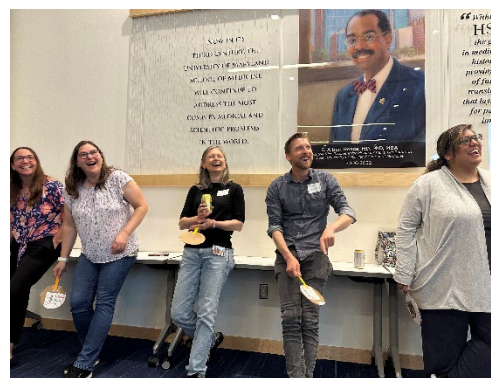
The afternoon brought us bellies full of pizza, booths hosted by community leaders, available to discuss how to get involved in campus life, and “Research Pictionary” where all attendees were challenged to illustrate their science, so that others might guess what they work on (pictured, bottom left). Following this was a “Guess My Paper” game show, in which a panel of faculty (pictured, bottom right) were shown figures (pictured, bottom middle) and had to guess if they were from one of their publications, which lead to some surprised faces, as faculty were (hilariously) stumped by some tricky figures! We ended the day laughing about skit videos created by various groups in the community and a “leadership handover” of the Program in Neuroscience Director position to Dr. Donna Calu.



Dr. Brian Mathur draws a smiley face and some dots, expecting that this will lead onlooking community members to guess precisely what he studies.



Dr. Steffen Wolff (left), Chair of Retreat Committee and “Guess My Paper” Game Show Host. Student and game-planning mastermind Cody Lis assists.



Faculty members (left to right), Drs. Donna Calu, Ivy Dick, Marta Lipinski, Tom Longden, and Mary Kay Lobo laugh as someone is, again, tricked by the clever curators of “Guess My Paper.”



Student Highlights

PIN Graduate Students who are independently funded

Michael Anderson, Maxwell Madden, Cassie Stapf, and Emily DeMarco are currently funded by NRSA (F31) NIH Grants! Congratulations to **Ruchael McNair** for being appointed to the Cardiovascular Biology T32 Training Grant. Additionally, congratulations to **Pedro Rodriguez Rivera, Jewel White, Antonio Figueiredo, Soad Elziny and Daniela Franco** for their support through Diversity Supplements! Further, congratulations to those most recently awarded our Neuroscience T32 training grant: **Laura Ventura, Loryn Johnson, Amanda Pacheco-Spiewak, Neema Moin Afshar, Maisie Ahern and Noury Khim!** Finally, congratulations to **Geralin Virata and Krystal Flores Feliz** for their appointments on the Initiative for Maximizing Student Development (IMSD) T32 Grant.

Some Student Publications

Kali Engel, PIN student in the lab of Dr. Margaret McCarthy, published “Neonatal Zika virus infection causes transient perineuronal net degradation” in *Frontiers in Cellular Neuroscience*.

Cassie Stapf, PIN student, with recent PIN graduate Dr. Sam Bacharach and colleagues published “Decreased Ventral tegmental area CB1R signaling reduces sign-tracking and shifts cue-outcome dynamics in rat nucleus accumbens” in the *Journal of Neuroscience*, work completed in the labs of Dr. Donna Calu and Joe Cheer.

Daniela Franco, PIN Student in the lab of Dr. Mary Kay Lobo, alongside PIN student **Cassie Stapf**, PIN graduate Dr. Kara Cover, , and Molecular Medicine program graduate, Dr. Eric Choi, published “Inducible CRISPR Epigenome Systems Mimic Cocaine Induced Bidirectional Regulation of Nab2 and Egr3” in *The Journal of Neuroscience*.

Roxy Cundiff-O’Sullivan, PIN Student, published “Cultural Influence on Placebo and Nocebo Effects,” in *Journal of Pain*, and published “How negative and positive constructs and comorbid conditions contribute to disability in chronic orofacial pain,” in *European Journal of Pain*. This work was completed in the lab of Dr. Luana Colloca.

Other Student Accomplishments

Ryan Mayers, PIN student in the lab of Dr. Brian Polster, was named one of Global Biotech Revolution’s 35 yearly- appointed “Global Ambassadors.”

Cassie Stapf, PIN student in the lab of Dr. Donna Calu, completed a semester-long Teaching Assistantship, through the Collaborative Teaching Fellows Program, teaching “Introduction to Psychology” at Goucher College. She also received a travel award to attend the Gordon Research Conference: Neurobiology of Addiction. Furthermore, Cassie was invited to present at the “Neuro-RECEPTR Symposium” at Rutgers, presented a poster at three conferences and authored a book chapter this year!

Neuroscience Outreach Volunteer Association leaders, and PIN Students, **Cassie Stapf** and **Garrett Bunce** wrote and received a grant from Research!America to support their “Brewing Biology” event series.

Roxy Cundiff-O’Sullivan, PIN Student in the lab of Dr. Luana Colloca, attended four conferences this year, two of which were international, and one of which she received a travel and accommodation award to attend (the International Association for the Study of Pain conference). She also authored a book chapter.

Photo Gallery



Above: McCarthy Lab students do some high-altitude hiking in Boulder, CO with friends from Duke and Harvard during the Psychoneuroimmunology Society conference



Above: PIN Students and Alumni mingle in San Diego, CA during the Society for Neuroscience conference



Above: Teixeira Da Silva Lab presents at Unites States Association for the Study of Pain in Durham, NC



Left: A PIN student from the Keller lab visits Glacier 3000 in Switzerland, with graduate students from all over the world, while attending the Gordon Research Conference for Inhibition in the CNS



Above: Colloca Lab socializes at Society for Interdisciplinary Placebo Studies conference in Duisburg, Germany

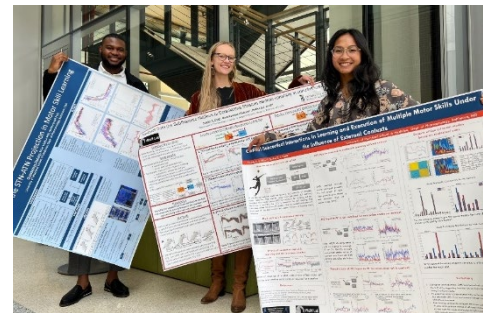


Above: Cheers for the McCarthy Lab as they tour gardens in Tours, France at the Society for Behavioral Neuroendocrinology conference

Below: The Wolff Lab poses proudly with their productive posters at our PIN Program poster session



Above: Are the McCarthy and Mathur Lab members twins, or do great minds merely think alike?



Below: A cluster of PIN faculty members sparkle at this glitter-themed monthly Program social hour hosted by the Juarez and Lobo Labs



Left: PIN Students at the annual Student Training Committee-hosted holiday party



Program in Neuroscience

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