DEPARTMENT OF
PHARMACOLOGY & PHYSIOLOGY

2022 YEAR IN REVIEW

Circuit Breaker: Cracking the Neuronal Codes for Anxiety and Depression

Meet our New Faculty Member: Dr. Manoela Fogaca

Inside the Issue:

SCHOOL OF MEDICINE & DENTISTRY
UNIVERSITY of ROCHESTER

Message From The Chair

As 2022 draws to a close, I am struck with great appreciation for the accomplishments of our faculty, trainees, staff, and alumni this year, as well as the promise for exciting new discoveries and advances in the coming year. Our people continue to push the boundaries of the field by employing rigorous, cutting-edge scientific approaches to better understand how the human body functions, to elucidate mechanisms that result in human disease and to develop new and effective treatments.

Our cover story explores the exciting research program of our newest faculty member, Dr. Manoela Fogaca (p. 2). Dr. Fogaca completed her Ph. D. in Pharmacology at University of São Paulo in Brazil and a highly-productive postdoctoral fellowship at Yale School of Medicine. Her NIH-funded research program focuses on elucidating the role of specific neuronal circuits in controlling stress-induced behavioral changes, as well as the impact of rapid-acting ketamine-like antidepressants on the activity of these critical neuronal circuits. Thus, Dr. Fogaca's recruitment further strengthens the department's and institution's expertise in the neuropharmacology of mental health disorders. In addition to her research expertise and interests, Dr. Fogaca's outgoing nature, quick wit, collaborative spirit, and passion for teaching/mentoring are a perfect fit for our department. We all look forward with great anticipation to Dr. Fogaca joining our department in February.

The department enjoyed a banner year with regard to research funding and output in 2022. Lead by the renewal of Dr. Haber's $15.6M National Institute for Mental Health Silvio O. Conte Center for Neurocircuitry of Obsessive Compulsive Disorder, department faculty and trainees currently hold over $53M in total research funding ($13M for just FY23), including almost $50M in total NIH funding ($12M for just FY23). This work resulted in over 50 peer-reviewed publications in top-tier journals in 2022 alone, as well a new patent application on the use of calcium channel blockers to treat myotonic disorders. As in previous years, our faculty were bestowed with national research, mentorship, and service awards, organized international workshops/symposia in their fields, and served on advisory boards, study sections and editorial boards. Our trainees received numerous research and travel awards. Several of these publications, honors and awards are highlighted in this newsletter (p. 7 – 9).

The department continued the Drug Targets and Mechanisms Collaborative Pilot Grant Program, which is designed to promote grass-roots collaborations between our faculty and other researchers in the institution. This program has dispersed ~$400,000 in pilot grant funds since its inception in 2015. In 2022, the program funded a new collaboration between our own Dr. Angela Glading and Dr. Brain Marples from the Wilmot Cancer Center (p. 3). This project unites Dr. Glading's expertise in the role of scaffolding proteins in mediating vascular permeability with Dr. Marples expertise in conducting localized brain radiation exposure studies in mice. Drs. Glading and Marples employ their unique skills to elucidate the mechanisms that lead to radiation-induced brain injury. Importantly, this pilot project will not only support generation of key preliminary data needed for a collaborative NIH application, but also serves to strengthen our department's growing connection to the Wilmot Cancer Center.

Under Dr. Hocking's steady leadership, the department's Faculty/Staff Diversity and Inclusion Committee has continued its work to foster a more inclusive and welcoming environment within the department. The committee set "DEI Education" as their primary objective in 2022. Working together with the Office for Equity and Inclusion, the committee is offering a series of 6 interactive training sessions throughout the academic year to all members of the Pharmacology and Physiology community. These sessions are providing a framework for us to work together to build an even more welcoming and inclusive environment in the department where all trainees, faculty and staff feel valued and respected (p. 4 – 5).

As always, the newsletter ends with highlighting the Career Stories of several of our successful alumni (p. 9 – 11). This year we highlight two alumni each from both the 1990s (one Physiology Ph.D. and one Pharmacology Ph.D.) and 2000s (both Pharmacology Ph.D.s). These four exceptional alumni are typical of other graduates from our department in that they have continued to excel in basic, translational and clinical research, academic leadership, as well as in the biotechnology and pharmaceutical industries. We are incredibly proud of the graduates of our program and their remarkable success and accomplishments across a wide range of career paths in academia, government, non-profit organizations and the private sector.

From the frozen banks of the Genesee River, I wish you all a festive holiday season and new year full of much success, laughter and good cheer! *Meliora!*

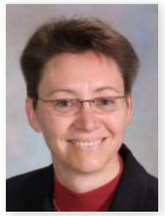
Robert T. Dirksen, Ph.D.

Lewis Pratt Ross Professor
Chair of Pharmacology and Physiology

Department Leadership Team

Jean M. Bidlack, Ph.D.
Professor and Associate Chair

David M. MacLean, Ph.D.
Associate Professor and Director of Graduate Studies



Denise C. Hocking, Ph.D.
Professor and Faculty and Staff Diversity Officer

John D. Lueck, Ph.D.
Assistant Professor and Director of Cellular and Molecular Pharmacology and Physiology Program

Robert S. Freeman, Ph.D.
Professor and Director of Med Pharm Graduate Studies

The research of
Manoela Fogaca, Ph.D.

Dr. Fogaca's research focuses on understanding the molecular basis of behaviors relevant to stress and the actions of antidepressant and anxiolytic drugs, aiming at identifying specific circuits, neuronal subpopulations and synaptic mechanisms involved in these responses, as well as novel pharmacological strategies to treat neuropsychiatric disorders. Dr. Fogaca received her Master's and Ph.D. in Pharmacology from the Department of Pharmacology at the University of São Paulo (Brazil), where she studied molecular mechanisms of action of cannabinoid compounds in multiple brain systems involved in stress-related disorders. As a postdoctoral fellow at Yale University, Dr. Fogaca investigated the cellular and synaptic mechanisms underlying the rapid and sustained effects of fast-acting antidepressants, including ketamine and ketamine-like drugs, with the goal of contributing to the development of more effective medications to treat major depression disorder (MDD). Because currently available antidepressants have serious limitations for treating MDD, including low response rates, a significant number of treatment resistant patients, and a time-lag before there is a therapeutic response, exploring the mechanisms of action of rapid antidepressants is an important strategy to understand the pathophysiology of MDD and to guide efforts to develop safer and better-tolerated drugs. Low doses of ketamine, an NMDA receptor (NMDA-R) blocker, can induce rapid (2 h) and sustained (up to 7 days) antidepressant effects in chronically stressed mice and in patients diagnosed with MDD, even in patients that are refractory to current antidepressants. Early findings suggest that these drugs initially target specific subpopulations of GABA interneurons in the medial prefrontal cortex (mPFC) and promote a fast enhancement of neurotrophic factors release, such as the brain-derived neurotrophic factor (BDNF), as well as glutamate- and GABA-induced neuroplasticity, leading to protein synthesis, synaptogenesis and new spine formation. One hypothesis is that this local re-organization re-establishes the excitation:inhibition balance (E:I) in the mPFC, leading to a restoration of correct firing patterns and the integrity of signal transfer to target regions, and thereby promoting antidepressant effects. At the University of Rochester, research in the Fogaca lab will expand these studies to understand how complex local and long-range neural circuits interact and modulate brain plasticity that culminate in distinct behavioral outcomes. Her lab will combine molecular neuropharmacology, genetic approaches and circuit-level studies of neurobiological systems to investigate how specific subpopulations of GABAergic and glutamatergic neurons crosstalk to modulate the cortical E:I network dynamics that lead to phenotypes relevant to stress disorders. On the long-term, Dr. Fogaca's research will span the mPFC to additional brain circuits, with the objective of mapping downstream regions and neuromodulatory systems to determine how the interaction between the mPFC and its projections promotes stress resilience and rapid antidepressant responses.

Mechanisms underlying rapid antidepressant actions
Chronic stress induces spine loss and dysfunction of the GABAergic and glutamatergic systems, disturbing the optimal excitation:inhibition (E:I) balance in the medial prefrontal cortex (mPFC) and the integrity of local and long-range circuits. Ketamine reverses these effects by initially targeting NMDAR on GABA interneurons and inducing a glutamate burst, leading to a subsequent enhancement of BDNF release, GABA function, protein synthesis and synaptogenesis. VDCC: voltage-dependent calcium channels; AMPA: α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor; NMDAR: N-methyl-D-Aspartate receptor; BDNF: brain-derived neurotrophic factor. Adapted from Fogaça and Duman, 2019.

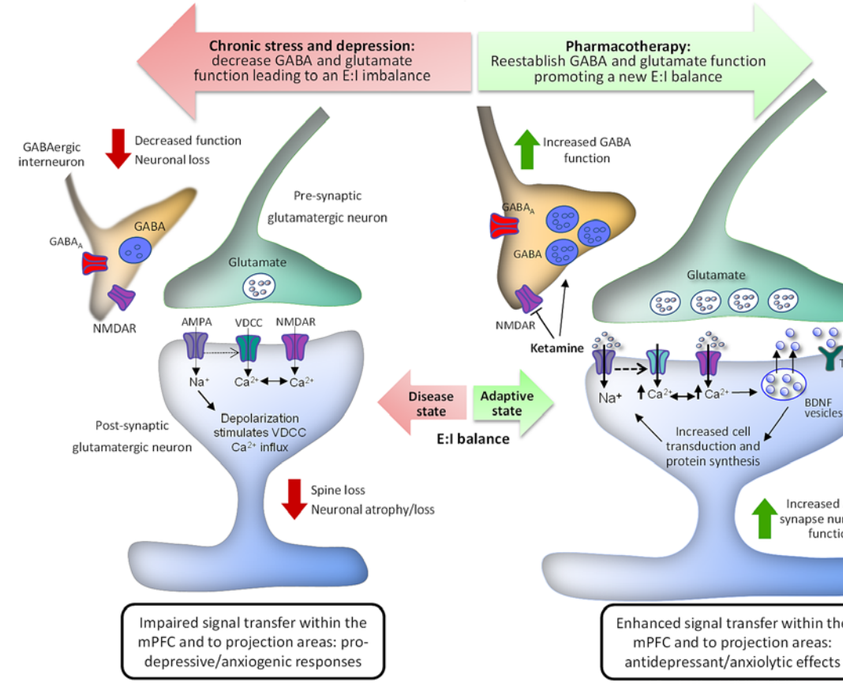


Figure. Common features of RICM and CCM compared to the normal BBB. Both conditions exhibit increased vessel diameter, loss of BBB integrity and vascular leakage, thickened vessel walls and fibrosis, and loss of pericytes and astrocytes. In addition, shared molecular markers include increased endothelial ROS including activation of NADPH oxidases, increased VEGF signaling, and decreased tight junction protein expression.

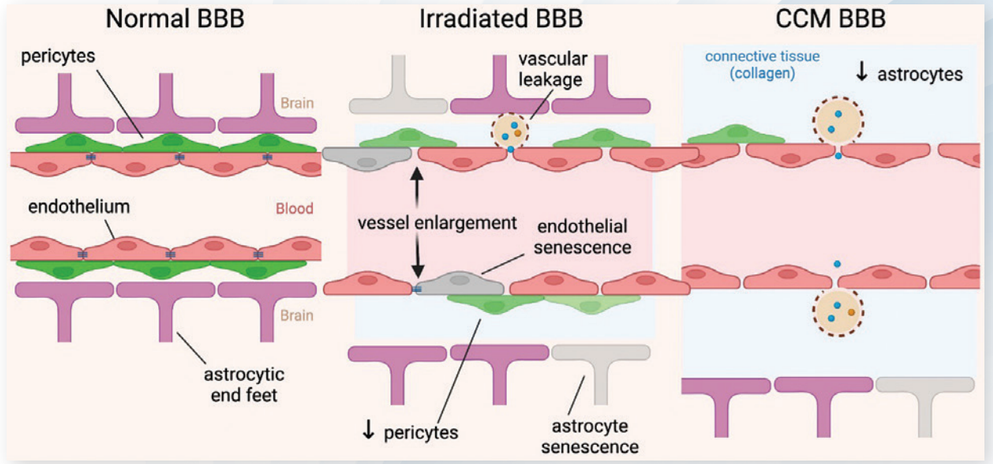
2022 Drug Targets & Mechanisms
Collaborative Pilot Project Award
Angela Glading Ph.D. & Brian Marples Ph.D.

Mechanisms of radiation-induced cavernous malformation development in the brain

Radiation therapy is widely used to effectively treat primary and metastatic brain tumors in adult and pediatric patients, an estimated 84,000 of which are diagnosed every year. However, irradiation of the brain can damage the tissue, leading to long-term side effects including cognitive decline and an increased risk of stroke. Studies suggest that up to 90% of patients that survive more than 6 months after treatment exhibit symptoms of radiation-induced brain injury.

The long-term effects of brain irradiation may be due to changes in several brain cell types, including neurons and glial cells. However, normal brain function is also dependent on the delivery of oxygen and nutrients via the cardiovascular system, thus damage to the cells (endothelial cells) that form the blood vessel wall could significantly contribute to radiation-induced cognitive decline, and the subsequent weakening of the vessel wall could contribute to the increased risk of stroke. Indeed, damage to the endothelial cell layer is now considered to play a primary role in radiation-induced brain injury. Therefore, understanding the effects of radiation on the brain micro-vasculature will be critical to finding new ways to mitigate the negative effects of radiation therapy.

Angela Glading Ph.D. & Brian Marples Ph.D.



It is known that ionizing radiation can cause acute and long-term changes in the smallest vessels of the brain (capillaries), which are not only the most sensitive to radiation, but are critical for oxygen and nutrient supply. These changes include wholesale loss of vessels, microbleeds, and the development of radiation-induced cavernous hemangioma/malformations (RICH/RICM). RICH/RICMs are focal areas of capillary enlargement and increased vessel density often accompanied by a loss of the normal vessel shape and organization. RICH/RICM are striking phenotypically similar to another cerebral vascular disorder, cerebral cavernous malformations (CCM, also called cavernous hemangioma). Both disorders are radiologically defined as blood-filled vascular spaces, exhibit signs of vascular inflammation, are accompanied by increased vascular endothelial growth factor (VEGF) signaling, trigger local fibrosis and changes in extracellular matrix composition, and are marked by a deficient blood-brain barrier.

This significant overlap in molecular and functional phenotypes between radiation-induced vascular changes/RICM and the developmental vascular disorder CCM was noted by Dr. Angela Glading (Pharmacology and Physiology) and Dr. Brian Marples (Radiation Oncology) earlier this year. With the recently awarded Drug Targets and Mechanisms DTM Program of Excellence award, this team will leverage their extensive knowledge of cerebral vascular physiology, radiation biology, endothelial biology and signaling, and CCM mechanism to investigate whether these disorders arise through a common signaling mechanism. Using cutting-edge technologies such as RNA sequencing and CT imaging, they will investigate the molecular changes induced in brain endothelium by radiation and map these to the associated functional changes in the cerebral vasculature.

Fostering an Inclusive Environment in Pharmacology and Physiology

The Diversity and Inclusion Committee of the Department of Pharmacology and Physiology has partnered with the Education and Learning Team within the URMC Office for Equity and Inclusion to provide a series of training sessions related to diversity, equity and inclusion for all members of the Pharmacology and Physiology community. These sessions were designed to:

- Establish common language and expectations surrounding diversity, equity and inclusion work to alleviate fear or shame around saying the wrong thing
- Recognize and introduce tools to mitigate and disrupt microaggressions and bias in the department
- Provide a safe space for participants to practice language and strategies to address microaggressions and bias
- Improve morale and unity across the department
- Teach participants how to have difficult conversations about identity, microaggressions and bias
- Facilitate conversations around restorative justice in academia

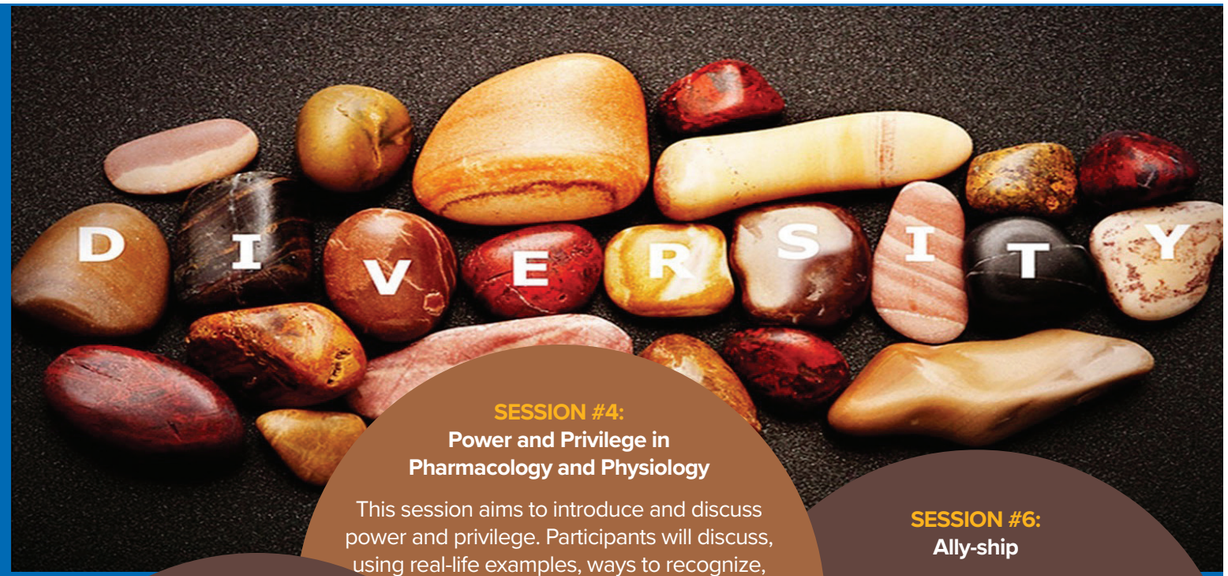
The following sessions are being offered to all members of the department (e.g. faculty, postdoctoral fellows, students, and staff) over the course of the 2022–2023 academic year:

SESSION #1:
Community and Relationship Building

This session focuses on communication, conscious listening, and building relationships within the department. Participants consider how to build an inclusive community within the department while strengthening relationships with colleagues and learners. The goals of this session are to establish trust, highlight similarities and differences, and share feedback in a safe and supportive environment.

SESSION #2:
Unconscious Bias

This session focuses on introducing participants to fundamental terminology and key concepts to create a common language to establish a foundation for DEI work in the department. We learn about microaggressions, bias, and begin to address fears of saying the wrong thing. This session will address knowledge gaps in this topic and help to establish a common language for all members of the department.



SESSION #3:
Recognizing and Addressing Bias in Pharmacology and Physiology

This workshop uses case-based sequential disclosures and storytelling based on real-life scenarios to help participants recognize, respond to, and disrupt incidents of bias or microaggressions. Participants will be asked to identify barriers to diverse learners in their areas.

SESSION #4:
Power and Privilege in Pharmacology and Physiology

This session aims to introduce and discuss power and privilege. Participants will discuss, using real-life examples, ways to recognize, understand and disrupt power and privilege. Participants will discuss best practices for mentoring, managing, and learning to make Pharmacology and Physiology a more inclusive department. This session will also focus on how to have difficult conversations about DEI topics when you are in positions of power and privilege.

SESSION #5:
Restorative Practices in Academia

Participants will learn methods to strengthen individual relationships and social bonds. Episodes of conflict, ranging from arguments to bullying to racial incidents, occur in our society and workplace. In this session, we begin to learn fundamental theory and practices on resolving conflict. The session will explore responses to harm, effective methods to resolve conflict, listening with empathy, and ways to facilitate healing conversations.

SESSION #6:
Ally-ship

The final part of the series builds on the knowledge gained from previous sessions to demonstrate how to partner with others to make change. Ally-ship is an active, consistent, and arduous practice of unlearning and re-evaluating in which a person in a position of power seeks to operate in solidarity with a marginalized group. You will come away with steps you can take to begin your lifelong ally-ship process.

Diversity and Inclusion Committee Members:

Angela Glading
Kaye Thomas
ex officio Robert Dirksen
Robert Freeman
David Delemos
Denise Hocking (Chair)
Emma Norris
Rachel Zapata-Bermudez

Medical Pharmacology Master's Students

Robert Freeman, Ph.D., Program Director, Mikaella Docteur, Efstathia (Anna) Baronos, Mnair Alkhaled, Mashael Alkhaled, Liv Schoenbeck, Ayomide Betiku, Kevin Morabito, Ethan Kaiser

Pharmacology and Physiology First-year Ph.D. and Master's Students

Back row: David MacLean, Ph.D., Program Director, Alireza Mousaei, Martin Garcia, Zahra Mahamed, Kevin Morabito, Ayomide Betiku, Liv Schoenbeck, Michael Malloy, Kathryn Bernier. John Lueck, Ph.D., Program Director; Front row: Emanuelle Chrysilla, Anna Baronos, Fatemeh Alimonhammadi, Mikaella Docteur, Mnair Alkhaled, Mashael Alkhaled, Cih-Li Hong, Kaitlynn Finch

M.S. Degrees Awarded

M.S. Medical Pharmacology Program

MAY 2022

Vivian (Vabby) Baker, M.S.
Megan Berntsen, M.S.
Winni Gao, M.S.
Himal Subramanya, M.S.

DEC 2022

Joshua Agyarko Jr., M.S.
Rachel Christie, M.S.
Katharine French, M.S.
Vivienne Tucker, M.S.

M.S. Pharmacology Program

MAY 2022

Maura Connorton, M.S.
Autumn Helland-Hauser, M.S.

M.S. Physiology Program

DEC 2022

Bryce West, M.S.

Left to Right: Maura Connorton, M.S., Robert Dirksen, Ph.D., Chair, Robert Freeman, Ph.D., Program Director, Vabby Baker, M.S., Megan Berntsen, M.S., Himal Subramanya, M.S., Winni Gao, M.S., Autumn Helland-Hauser, M.S., Angela Glading, Ph.D., Program Director

Ph.D. Degrees Awarded

FEBRUARY 2022

Jing Liu, Ph.D.
"Electroporation Mediated Gene Delivery to Rescue the Alveolar Capillary Barrier Function for ARDS Treatment "
Advisor: Dr. David Dean

MARCH 2022

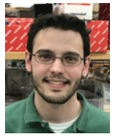
Tyler McCullock, Ph.D.
"A Comprehensive Overview of Metabotropic Glutamate Receptor Dimer Signaling"
Advisor: Dr. Paul Kammermeier

JUNE 2022

Alexander Milliken, Ph.D.
"Investigating Succinate and pH Dynamics in Cardiac Ischemia-Reperfusion Injury"
Advisor: Dr. Paul Brookes

JULY 2022

Tyler A. Couch, Ph.D.
"Topography and Motion of the Acid-sensing Ion Channel 1 Intracellular Domains "
Advisor: Dr. David MacLean



NOVEMBER 2022

Matthew Rook, Ph.D.
"Interrogation into Molecular Mechanisms of Activation and Desensitization in Acid-Sensing Ion Channel 1a "
Advisor: Dr. David MacLean

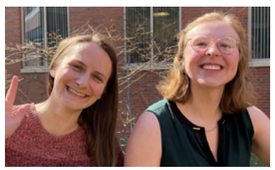
NOVEMBER 2022

Nick Nobiletti, Ph.D.
"KRIT1-mediated Regulation of Cellular Response to Inflammation"
Advisor: Dr. Angela Glading

Student Publications and Awards

Winnie Gao, M.S.
Review paper is accepted at Frontier Journal "The Role of Mechanically-activated Ion Channels Piezo1, Piezo 2, and TRPV4 in Chondrocyte Mechanotransduction and Mechano-Therapeutics for Osteoarthritis."
*Winni Gao, Hamza Hasan, Devon E Anderson, Whasil Lee, Ph.D.**

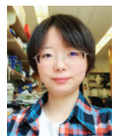
Lily Cisco, M.S. (right), Christina Heil, Ph.D. (left)
Recipients of two-year research fellowships from the Myotonic Dystrophy Foundation. Lily's Predoctoral Fellowship is titled "Identification of altered muscle calcium handling as a potential DM1 therapeutic target". Christina's Postdoctoral Fellowship is "Genetic characterization of DM1 models".
Lueck Lab



Vikas Arige, Ph.D.
Recipient of a two-year AHA Postdoctoral Fellowship Award entitled, "Succinate dynamics and pH in cardiac ischemia-reperfusion injury".
Yule Lab

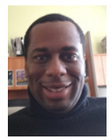
Louben Dorval, Ph.D.
Published research paper in Journal of Neuropharmacology "Mice with high FGF21 serum levels had a reduced preference for morphine and an attenuated development of acute antinociceptive tolerance and physical dependence."
Bidlack Lab

Chongyang Zhang, Ph.D.
Recipient of the prestigious Vincent du Vigneaud Award for a Ph.D. thesis
Yan Lab



Nicholas Nobiletti, M.S.
Published research paper in Journal of FEBS "KRIT1-mediated regulation of neutrophil adhesion and motility."
Glading Lab

Nada Ahmed Selim, B.A., Chidozie Okoye, Ph.D.
Recipients of Travel Awards to attend and present at the 29th Annual Society for Redox Biology and Medicine Conference.
Wojtovich Lab



SELECTED PUBLICATIONS

Bidlack, J.M., Chang, S.L., Fitting, S., Gendelman, H.E., Sorantla, S., Kumar, S., Marcondes, M.C.G., Meigs, D.D., Melendez, L.M., Sariyer, I.K., and Yelamanchili, S. The COVID-19 pandemic: Reflections of science, person, and challenge in academic research settings. J. Neuroimmune Pharmacol. 16(4): 706-717, 2021.

Milliken AS, Nadtochiy SM, Brookes PS. Inhibiting succinate release worsens cardiac reperfusion injury by enhancing mitochondrial reactive oxygen species generation. J. Am. Hrt. Assoc. e026135, 2022.

García-Castañeda M, Michelucci A, Zhao N, Malik S, Dirksen RT. Postdevelopmental knockout of Orai1 improves muscle pathology in a mouse model of Duchenne muscular dystrophy. J. Gen. Physiol, 154(9):e202213081, 2022.

RYR-1-related diseases international research workshop: from mechanisms to treatments. O'Connor TN, van den Bersselaar LR, Chen YS, Nicolau S, Simon B, Huseth A, Todd JJ, Van Petegem F, Sarkozy A, Goldberg MF, Voermans NC, Dirksen RT. J Neuromuscul Dis. doi: 10.3233/JND-221609, 2022.

Nobiletti N, Liu J, Glading AJ. KRIT1-mediated regulation of neutrophil adhesion and motility. FEBS J. doi: 10.1111/febs.16627, 2022.

Perrelli A, Ferraris C, Berni E, Glading AJ, Retta SF. KRIT1: A traffic warden at the busy crossroads between redox signaling and the pathogenesis of cerebral cavernous malformation disease. Antioxid Redox Signal. doi: 10.1089/ars.2021.0263, 2022.

Swamy H, Glading AJ. Contribution of protein-protein interactions to the endothelial-barrier-stabilizing function of KRIT1. J Cell Sci. 135(2):jcs258816, 2022.

Trambaiolli, L.R., Xiaolong Peng, X., Lehman, J.F., Linn, G., Russ, B.E., Schroeder, C.E.Liu, H., Haber, S.N. Anatomical and functional connectivity support the existence of a salience network node within the caudal ventrolateral prefrontal cortex. Elife, 11:e76334, 2022.

Haber SN, Liu H, Seidlitz J, Bullmore E. Prefrontal connectonics: from anatomy to human imaging. Neuropsychpharmacology: 47:20-40, 2022.

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Gao W, Hasan H, Anderson DE, Lee W. The role of mechanically-activated ion channels piezo1, piezo2, and TRPV4 in chondrocyte mechanotransduction and mechano-therapeutics for osteoarthritis. Front Cell Dev Biol. 4;10:885224, 2022.

Ko, W., Porter, J.J., Sipple, M.T., Edwards, K.E., Lueck, J.D. Efficient suppression of endogenous CFTR nonsense mutations using anticodon engineered transfer RNAs. Molecular therapy. Nucleic acids; Vol 28. 2022.

MacLean DM, Soto E. Editorial: ASICs: Structure, Function and Pharmacology. Frontiers in Physiology. 13:831830, 2022.

Onukwufor, J.O. Dirksen, R.T. Wojtovich, A.P. Iron dysregulation in mitochondrial dysfunction and Alzheimer's disease. Antioxidants, 11, 692, 2022.

Fu W, Franchini L, Orlandi C. Comprehensive spatial profile of the orphan G protein coupled receptor GPRC5B expression in mouse brain. Front Neurosci. 16:891544, 2022.

Foley K, Altimimi H, Hou H, Zhang Y, McKee C, Papasergi-Scott MM, Yang H, Mayer A, Ward N, MacLean DM, Nairn AC, Stellwagen D, Xia H. Protein phosphatase-1 inhibitor-2 promotes PP1γ positive regulation of synaptic transmission. Front Synaptic Neurosci. 14:1021832, 2022.

McKee C, Shrager P, Mazumder AG, Ganguly A, Mayer A, Foley K, Ward N, Youngman M, Hou H, Xia H. Nuclear inhibitor of protein phosphatase 1 (NIPP1) regulates CNS tau phosphorylation and myelination during development. Mol Neurobiol. 59(12):7486-7494, 2022.

Onukwufor JO, Farooqi MA, Vodičková A, Koren SA, Baldzizhar A, Berry BJ, Beutner G, Porter GA Jr, Belousov V, Grossfield A, Wojtovich AP. A reversible mitochondrial complex I thiol switch mediates hypoxic avoidance behavior in C. elegans. Nat Commun 13, 2403, 2022.

Lara E. Terry, Vikas Arige, Julika Neumann, Amanda M. Wahl,Taylor R. Knebel, James W. Chaffer, Sundeep Malik, Adrian Liston, Stephanie Humblet-Baron, Geert Bultynck and David I. Yule. Missense mutations in inositol 1,4,5-trisphosphate receptor type 3 result in leaky Ca2+ channels and activation of store-operated Ca2+ entry. iScience 25, 105523, 2022.

Fan G, Baker MR, Terry LE, Arige V, Chen M, Seryshev AB, Baker ML, Ludtke SJ, Yule DI, Serysheva II. Conformational motions and ligand-binding underlying gating and regulation in IP3R channel. Nat Commun. 13(1):6942, 2022.

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Sneyd J, Rugis J, Su S, Suresh V, Wahl AM, Yule DI. Simulation of Calcium Dynamics in Realistic Three-Dimensional Domains. Biomolecules. 12(10):1455, 2022.

Arige V, Terry LE, Wagner LE 2nd, Malik S, Baker MR, Fan G, Joseph SK, Serysheva II, Yule DI. Functional determination of calcium-binding sites required for the activation of inositol 1,4,5-trisphosphate receptors. Proc Natl Acad Sci U S A. 119(39):e2209267119, 2022

Yuan Y, Jaślan D, Rahman T, Bolsover SR, Arige V, Wagner LE 2nd, Abrahamian C, Tang R, Keller M, Hartmann J, Rosato AS, Weiden EM, Bracher F, Yule DI, Grimm C, Patel S. Segregated cation flux by TPC2 biases Ca2+ signaling through lysosomes. Nat Commun. 13(1):4481, 2022.

Arige V, Yule DI. Spatial and temporal crosstalk between the cAMP and Ca2+ signaling systems. Biochim Biophys Acta Mol Cell Res. 1869(9):119293, 2022.

Takano T, Yule DI. In vivo Ca2+ Imaging in Mouse Salivary Glands. Bio Protoc. 5;12(7):e4380, 2022.

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Ahmad M, Ong HL, Saadi H, Son GY, Shokatian Z, Terry LE, Trebak M, Yule DI, Ambudkar I. Functional communication between IP3R and STIM2 at subthreshold stimuli is a critical checkpoint for initiation of SOCE. Proc Natl Acad Sci U S A. 119(3):e2114928118, 2022.

Awards and Honors 2022

Goldstein pilot award to study Piezo-dependent mechanobiology using human RC cartilage
Dr. Whasil Lee, Dr. Sandeep Mannava

Major Grant Funds Research to Understand Key Features of OCD: Inflexibility and Avoidance

NIMH Silvio O. Conte Center Grant: Neurocircuitry of OCD: Effects of Modulation, PI.
Dr. Suzanne Haber

Drug Targets & Mechanisms Collaborative Pilot Project Award
Dr. Angela Glading, Dr. Brian Marples

NIH Pathway to Independence Award (K99)
Dr. Romeo Blanc

National Institutes of Health, NHLBI: "Acid, Succinate and Glyoxal Metabolism in Cardiac Ischemia"
Dr. Paul Brookes

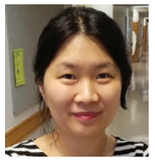
National Institutes of Health, NIH-NCATS: "Orphan Receptor Gprc5b in Retinoci Acid-induced Affective Behaviors"
Dr. Cesare Orlandi


Dr. Romeo Blanc


Dr. Paul Brookes


Dr. Angela Glading


Dr. Suzanne Haber


Dr. Whasil Lee


Dr. Sandeep Mannava


Dr. Brian Marples


Dr. Cesare Orlandi

Alumni Career Stories

Jeff Holt, Ph.D.
(1995 Physiology)
Harvard Medical School; Professor of Otolaryngology and Neurology


Dr. Jeff Holt

I recall Saturday afternoon, September 2, 1989 with great clarity. I was sitting on the banks of the Genesee River at the edge of the University of Rochester, River Campus. I wrote in my journal: "The next chapter of my life begins on Tuesday. The years ahead will be the toughest, most challenging, and most demanding I have ever faced. I have no idea where my life will go from here, but I am committed to make the most of it." I had been accepted as a Ph.D. graduate student in the Department of Physiology at the University of Rochester and my life in science was about to begin. Ted Begenisich, a professor in the Department of Physiology, had encouraged me to apply and I will be forever grateful for his advice. Accepting his advice was a life changing decision and one of the best I ever made.

My journal entry was correct, graduate school challenged me in ways I could not have imagined and opened opportunities beyond my wildest expectations. I am now a tenured professor at Harvard Medical School. I love my job. Teaching graduate students and medical students, running a research lab, making important scientific discoveries, and traveling the world to present my lab's findings are all thrilling and more satisfying than I could have imagined sitting on the shores of the Genesee River.

My lab uses molecular, genetic, and electrophysiological techniques to study the sensory hair cells of the inner ear. We discovered the mechanosensory ion channel proteins, TMC1 and TMC2, which convert sound into electrical signals. My life-long passion for ion channel physiology began with coursework, lessons and lab work led by Department of Physiology faculty, including Ted Begenisich, Peter Shrager, Rocky Kass, Trever Shuttleworth and others.

The Department of Physiology provided a welcoming and nurturing environment. Despite the challenges of graduate education and scientific research, I felt supported by my fellow graduate students, Pat, Bill, Lisa, Patricia, Tara and others and my Department faculty. My academic advisor, Peter Shrager, my thesis advisor, Ruth Anne Eatock, department chair, Paul Horowitz, Camillo Peracchia and numerous other faculty were always supportive and willing to lend a hand. Whether it was

Alumni Career Stories

in the classroom, in the lab, or out and about the University or Rochester, it was a close-knit group and we all supported each other. Those were formative years for my scientific career, and I am so thankful to have been raised by such a wonderful scientific family. The University of Rochester, Department of Physiology will always hold a special place in my heart.

Suzanne Kennedy, Ph.D.

(1998 Pharmacology)
UNC School of Medicine; Administrative Director, Children's Research Institute


Dr. Suzanne Kennedy

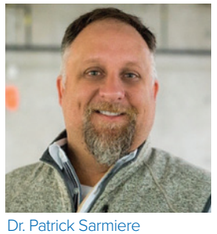
Running my own lab to help find the cure for cancer was my naïve career plan before attending graduate school. Once that vision ended, I used my research and networking skills to figure out what my new path would be. This was in the days before myidp.sciencecareers.org. I had the good fortune to attend U of R when my home Department of Pharmacology combined with the Department of Physiology, providing me with a firm foundation that could be applied to not only basic, but translational and clinical trial research, medical communications, and scientific liaison positions. I learned about these non-traditional paths through the spouse of a new professor to the department, Dr. Sharon Dirksen (wife of the now Chair). My first position out of graduate school was with a medical communications center at U of R. We were awarded funding from the Robert Wood Johnson Foundation to develop a readable guide on the diagnosis and management of asthma. This led to my 20-year engagement working in the field of asthma alongside the leaders in the country, including basic scientists, biostatisticians, and psychologists. Along the way I was exposed to clinical and pragmatic trials, and behavioral interventions with funding from the NIH, foundations, and industry. The connections and experience I gained provided me the opportunity to work in business, academia, and as a contractor, in locations across the country, including Hawaii as well as post Katrina New Orleans. Through the incredible participants, who live in some of the poorest areas, opening their homes to receive an environmental asthma intervention, I was able to learn about self-empowerment, brief motivational interviewing, and mindset in navigating behavior change.

My latest experience is with the University of North Carolina as the Administrative Director for the Department of Pediatrics Clinical Research Institute (CRI) and Interim COO of the School of Medicine Clinical Research Alliance (CRA). I was the first full-time hire for the CRI. During the pandemic we were able to grow the exceptional CRI team from 3 to 15 to provide: support for early career research faculty, outreach to the community we serve, network opportunities, support for large NIH-funded collaborative research projects pre and post award, and infrastructure and resources for our growing human subjects research portfolio to promote evidence-based treatments to our pediatric population (including COVID studies). The department also supported the development of a Pediatrician Wellbeing Program, where I was able to apply my experience as a Principal Investigator to design a pilot study, along with my credentials as a National Board of Health and Wellness Coach, to offer coaching support for early career faculty in pediatrics. My most recent opportunity is with the development of a new endeavor, the UNC CRA, which is an Academic Research Organization to support coordination of multi-center clinical trials. It is drawing upon all my experiences, from graduate school to developing the CRI. My career path is nowhere near what I had thought when I entered graduate school, but I had no idea the possibilities of what I could do with a Ph.D. in Pharmacology Physiology.

Publications: www.ncbi.nlm.nih.gov/myncbi/1lKK1ZK-WlCk1/bibliography/public/

Patrick Sarmiere, Ph.D.

(2001 Pharmacology)
Ovid Therapeutics; Vice President,


Dr. Patrick Sarmiere

I came to the Department of Pharmacology and Physiology back in 1996 because I knew that I wanted to discover and develop new medicines. Simple as that. What I could not have predicted was falling in love with neuroscience. It was never on my radar until my graduate rotation in Robert Freeman's lab. Bob taught me neuroscience basics, how to grow and study neurons, and understand molecular aspects of neurobiology. He stood next to me at the bench, and we did science together. I am extremely grateful for having the opportunity to have a mentor like that. Because of that experience, mentorship and training are still and always will be one of the most important, and rewarding, aspects of my career. I often tell my family and friends how much fun graduate school was. Whether it was drinking morning coffee with my classmates in Trevor Shuttleworth's office, playing softball with the Really Rottens, enjoying a good scotch ale at Rohrbachs Brewing Company taking in a late-night movie at Tinseltown, going to Red Wings, Muckdogs, and Doubleday baseball games, traveling to SfN meetings or Gordon Conferences or even getting snowed in at the Medical Center for a couple days. It was an extremely memorable time in life, and I would not trade it for the world. I hope all those who have and will come through Rochester graduate programs get to have an equally wonderful time.

After leaving Bob's lab in 2001, I went on to do a post-doc at Colorado State University to continue to study neurobiology. I was lucky enough to be supported by a grant from the Christopher and Dana Reeve Paralysis Foundation while studying the biology of axon guidance in James Bamburg's lab. I will never forget traveling to the Foundation's meeting in Chicago and meeting with individuals living every day with spinal cord injuries. At these meetings, I enjoyed hearing their excitement for the research that was happening, but also learning about their concerns. Working with patient advocacy groups and the families and friends of those affected by disease, listening to them, and helping them understand the science we do are arguably just as important as the research itself.

I have worked for non-profit organizations (Spinal Cord Society), small and medium sized biotech (Ovid Therapeutics and Acorda Therapeutics), and even consulted for larger pharma companies (Celgene). I have worked on projects ranging from small molecules to antibodies, growth factors and enzymes, and even cell therapies. I have studied spinal cord injury, multiple sclerosis, neurodegenerative diseases, stroke, peripheral nerve injury, cardiac failure, oncology, and most recently, rare neurodevelopmental diseases, seizures and epilepsy. Each of these programs have had their challenges, some failed outright scientifically, some had great potential but were side-lined for business reasons, some are actual medicines people are using, and some are just starting their journey in the clinic. As an industry we are reaching an inflection point where more and better medicines are coming for those dealing with diseases of the nervous system and I am still very excited to be part of that.

Jennifer Mathews, Ph.D.

(2007 Pharmacology)
University of Rochester; Associate Vice Provost for Academic Administration and Chief Assessment Officer

I'd have to say that my career story has taken some twists and turns that I would not have anticipated. After graduating with my Ph.D. from Jean Bidlack's lab I took a position with the Wegmans School of Pharmacy at St. John Fisher University. I earned tenure and promotion in that faculty role and was fortunate to be able to focus my teaching on pharmacology with a clinical focus. Being in any new School requires people to take on roles that may not be in their area of expertise. That was certainly the case for me when I was elected to Chair the assessment committee. It's worth noting that the election occurred while I was teaching my class. I'm sure there's a lesson here. Overseeing that committee was a steep learning curve but forced me to use many of the skills I had developed in analyzing data and looking for trends. While in my role at St. John Fisher University I had the opportunity to collaborate with Dr. Bidlack as a colleague on a teaching grant focused on the education of future clinicians. After 10 years as both a faculty member and administrator at SJFU I took on a short-term role as an Associate Dean at SUNY Stonybrook assisting in preparation for a new School they were opening. After that I spent 4 years as the Regional Dean for the Vermont campus of Albany College of Pharmacy and Health Sciences. In each role my administrative responsibilities have grown. I continued to teach a few classes in neuropharmacology, but my primary focus was programmatic assessment, faculty development and retention, and student recruitment. The opportunity to return to Rochester presented itself in 2021 and it was hard to pass up the chance to come back to my alma mater. I currently serve as the Associate Vice Provost for Academic Administration and the University's Chief Assessment Officer. This role allows me to continue to use my assessment skills, to build relationships across all our schools, and to serve as the liaison to NYSED. I look back fondly on the time I spent in pharm/phys and as a member of the Bidlack lab. Dr. Bidlack's support allowed me to travel and present my research at both national and international conferences. I keep in touch with many classmates and appreciate the bonds that were formed as we supported each other. Having been at a few different institutions I can appreciate the time and energy the faculty and staff of the pharm/phys department invested in getting to know each of us and for the guidance they provided as we developed the skills needed to be successful in whatever role we took after graduation.


Dr. Jennifer Mathews

Editor: Rachel Zapata-Bermudez

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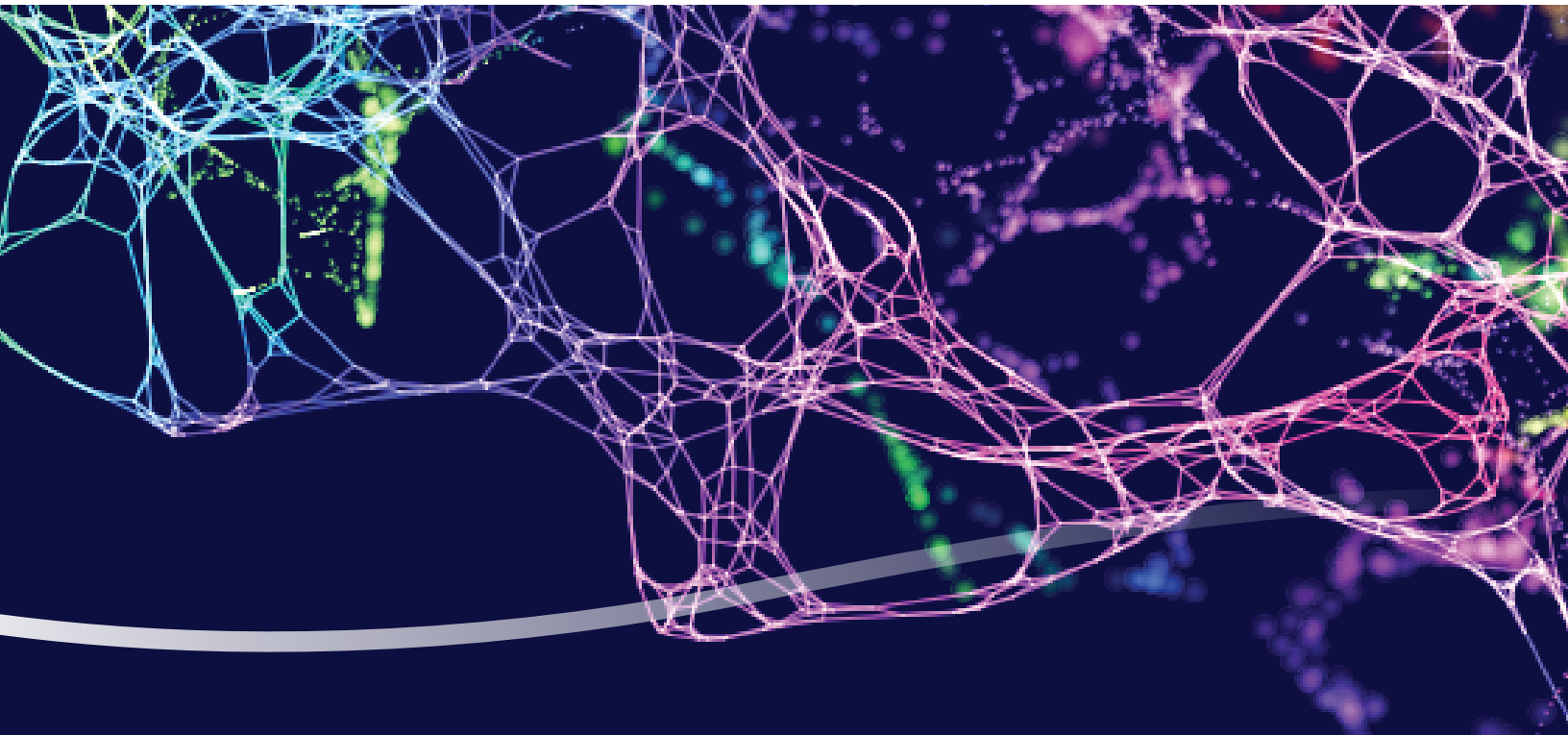

PHARMACOLOGY & PHYSIOLOGY
2022 Year in Review

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