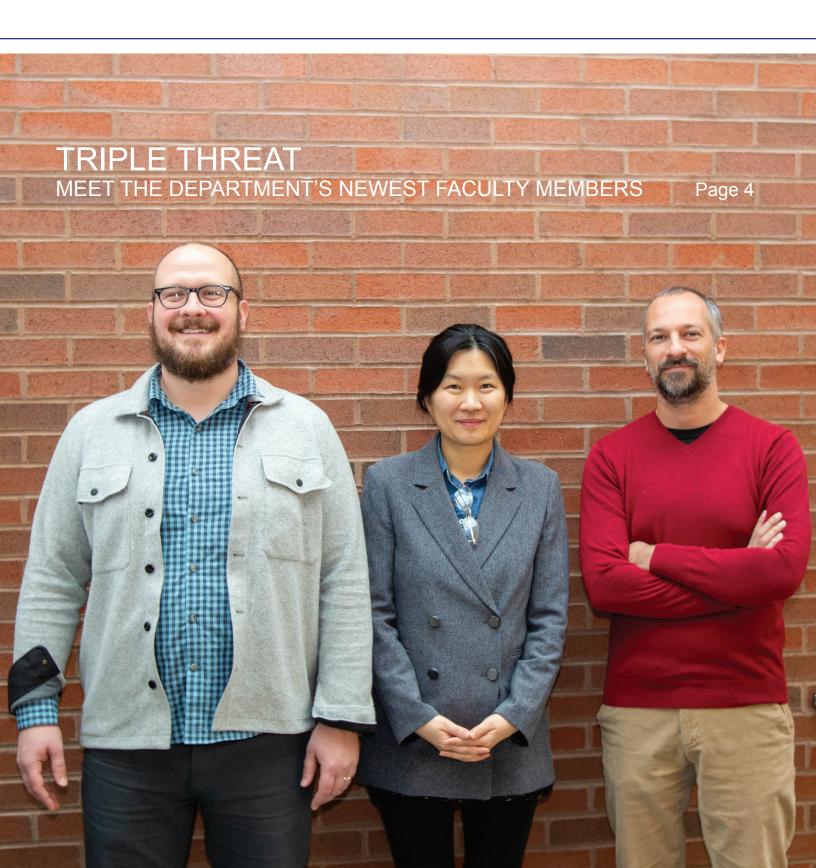
# PHARMACOLOGY AND PHYSIOLOGY

UNIVERSITY OF ROCHESTER SCHOOL OF MEDICINE & DENTISTRY 2019 ISSUE | SUMMER 2018-FALL 2019



## MESSAGE FROM THE CHAIR

With the holiday season now in the rearview mirror and the New Year upon us, this represents an opportune time to reflect on the many accomplishments of the faculty, trainees and staff in the Department of Pharmacology and Physiology over the past year.

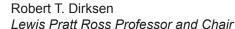
As highlighted on the cover page of this newsletter, the Department of Pharmacology and Physiology welcomed three new tenure-track Assistant Professors in FY2019; Drs. Whasil Lee, John Lueck, and Cesare Orlandi. This represents the largest single-year faculty recruitment cohort for the department in over two decades; dating all the way back to 1998 when Drs. Yule, Hocking and myself joined the department. The cover story of this newsletter describes the unique backgrounds and exciting research programs of Drs. Lee, Lueck, and Orlandi.

The department also significantly expanded our capabilities in advanced imaging approaches in 2019. With the help of a NIH shared equipment grant obtained by Dr. Yule, the institution was able to purchase the first super resolution (Abberior Expert Line 3D STED) microscope in Western New York, which is now fully operational and housed in the Department of Pharmacology and Physiology. In addition to super resolution imaging, Drs. MacLean and Xia recently established a fluorescence lifetime imaging system as an additional module on the two-photon imaging microscope in Dr. Yule's laboratory. Together, these advanced imaging technologies enable unprecedented spatial and temporal resolution of cellular fluorescence signals, which opens up new research questions and directions for our faculty and trainees.

Beyond the addition of new faculty and advanced imaging technologies, the department enjoyed a number of other noted milestones this year. For the first time since its inception in 1997, the department hosted two Paul Horowicz Lectures (Drs. Stephen C. Cannon on 3/7/19 and Trevor J. Shuttleworth on 9/27/19) in the same calendar year. In addition, our students received numerous conference awards and fellowships, six students successfully defended their Ph.D. thesis, and we welcomed three new first year students to our graduate program. Our faculty, students, and staff were selected for several prestigious awards over the past year. As just a few examples, Dr. Bidlack was awarded the Herman Friedman Founder's Award from the Society on NeuroImmune Pharmacology, Dr. Liwei Wang was presented with the 2019 Wallace O. Fenn Award at Commencement, and Debra Andreaccchi-Roth was given the Witmer Award for Distinguished Service, the highest staff award given at the University of Rochester. All of these accomplishments (and more!) are detailed in this newsletter. Finally, we are also excited to highlight the highly successful and unique careers paths of four of our distinguished alumni in the Career Stories section of the newsletter.

Indeed, it has been quite an exciting and successful year for the department. We look forward to more of the same in 2020!







Robert T. Dirksen, Ph.D. Lewis Pratt Ross Professor and Chair



Jean M. Bidlack, Ph.D.

Professor and Associate Chair



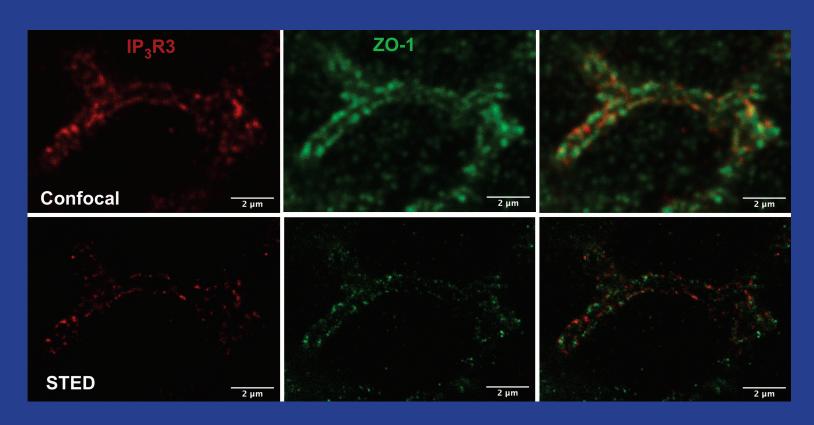
Angela J. Glading, Ph.D.
Associate Professor and
Director of Graduate Studies

### RESEARCH SPOTLIGHT

Conventional fluorescence microscopy can resolve structures separated by more than 250 nm at which point the diffraction limited optics will obscure further detail. Many biological structures and processes occur on a scale smaller than the resolution of light, thus limiting the amount of information that can be collected through conventional fluorescent imaging methods. STED microscopy is a super-resolution imaging technique that allows researchers to image beyond this theoretical resolution limit. Superresolution techniques are thus considered to break the diffraction barrier posed by Ernst Abbe in 1873. A STED microscope can resolve objects located less than 20 nm (0.00002 mm) apart, enabling researchers to visualize individual components and complex structures. For this significant contribution to microscopy, the inventor of STED, Dr. Stefan W. Hell, Director at the Max Planck Institute for Biophysical Chemistry, was awarded the 2014 Nobel Prize in Chemistry.

An Abberior Instruments Stimulated Emission Depletion (STED) microscope was installed in the facility in August 2018 and is giving researchers the opportunity to take a closer look at important spatial relationships. Dr. David Yule, who led the effort to bring this technology to the University, has already made use of the STED microscope to further resolve the relationship between junctional complexes and intracellular Ca2+ release channels present on specialized portions of endoplasmic reticulum in exocrine cells. As can be seen in the image below, staining the tight junction protein zona occludins 1 (ZO-1) and the type 3 Inositol 1,4,5-trisphosphate receptor (IP3R3), STED imaging allows the discrete visualization of individual puncta of each protein in higher resolution than achievable by conventional confocal microscopy.

Image collected by Amanda Wahl, Graduate Student in the Laboratory of Dr. David Yule.



# THE PAUL HOROWICZ LECTURE FUND

The Paul Horowicz Lecture Fund was established to honor the legacy of Dr. Paul Horowicz. An internationally recognized authority in muscle and membrane physiology, Dr. Horowicz was active in many professional organizations, and the recipient of numerous awards and honors. For twenty-six

years Dr. Horowicz served as Chair of the Department of Physiology. An exemplary leader and highly respected member of the medical school faculty, he was known by his colleagues not just as an outstanding scientist, but also as a superb mentor who trained some of the very best muscle physiologists, many of who have assumed leadership positions in physiology around the world. This year the department held two named lectures in honor of Dr. Horowicz.

MARCH 7, 2019 - STEPHEN C. CANNON, M.D., PH.D.

"Muscle mayhem – a shifting CI gradient in attacks of periodic paralysis"

Dr. Cannon is Professor and Chair of the Department of Physiology at the David Geffen School of Medicine



Pictured above (left to right): John Lueck, Stephen Cannon, Bob Dirksen, Kari Horowicz

at the University of California in Los Angeles.

A leading expert on channelopathies, the Cannon lab has elucidated fundamental mechanisms underlying myotonia and periodic paralysis that have guided approaches to disease management. Currently, his lab is now using genetically-engineered mouse models and computational methods to investigate the mechanisms by which environmental triggers (K+, pH, exercise) transiently reduce muscle excitability to cause episodes of weakness in periodic paralysis.

# SEPTEMBER 27, 2019 - TREVOR J. SHUTTLEWORTH, PH.D. "From Fish Gills . . . to the Keepers of the Gates of Heaven"

The lecture was followed by a reception to celebrate Dr. Shuttleworth's retirement and appointment as Professor Emeritus on September 1, 2019.

Dr. Shuttleworth was recruited by Dr. Horowicz to the Department of Physiology at the University of Rochester in 1987. Dr. Shuttleworth's research has centered on the origin and roles of agonist-induced Ca2+ signaling in non-excitable cells, particularly in various exocrine secretory cells. He has made significant contributions to the educational missions of the department, teaching in both the graduate and medical school curriculums and serving on numerous University committees.



Pictured above (left to right): Bob Dirksen, Trevor Shuttleworth, Kari Horowicz, Peter Horowicz



Pictured above (left to right): David Yule, Trevor Shuttleworth, Bob Dirksen

Dr. Shuttleworth has received many professional honors and awards, and served on numerous advisory committees, review panels and editorial boards throughout his career.

#### DEBRA ANDREACCHI-ROTH RECEIVES WITMER AWARD FOR DISTINGUISHED SERVICE

Debra
AndreacchiRoth, Senior
Administrator
and Research
Program
Manager, was
one of three
University staff



presented with the Witmer Award on April 25, 2019, at a ceremony honoring the University's 2019 Staff Award recipients. The Witmer Award for Distinguished Service is presented to a select number of staff members for careers characterized by outstanding and sustained contributions to the University.

Debe began her career at the University in 1976, and has since made significant contributions to the University and to the Departments of Pharmacology & Physiology and Anesthesiology & Perioperative Medicine. Debe oversees the fiscal and operational activities of the Department of Pharmacology and Physiology, and is responsible for all proposal submissions and grant post-award activities for the Department and Anesthesiology and Perioperative Medicine. She has served on numerous committees and special interest groups and has used her many years of experience to contribute to University initiatives. Debe is also dedicated to creating a friendly and welcoming work environment, and is deeply supportive of the growth of her staff. As former Chair Dr. A. William Tank stated, "Debe's dedication, hard work, loyalty and expertise in all areas of administrative leadership is of the highest quality". Congratulations Debe on this most-deserved award!

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University of Rochester photo / J. J. Adam Fenster

# THREE NEW INVESTIGATORS BRING MULTI-DISCIPLINARY RESEARCH TO THE DEPARTMENT

The past year has been a busy one for the department with regard to recruitment of new tenure-track faculty. We are excited to welcome three new junior faculty members. Each recruitment served to strengthen both the Drug Targets and Mechanisms Program of Excellence and key collaborative interactions with other UR departments and centers. Dr. John Lueck was a joint recruitment with the Department of Neurology. Dr. Lueck strengthens our connections with the Departments of Neurology and Neuroscience, as well as the Paul D. Wellstone Muscular Dystrophy Cooperative Research Center, the Center for RNA Biology and the Lung Biology and Disease Program. Dr. Whasil Lee was a joint recruitment with the Department of Biomedical Engineering (BME) on the River Campus who also links the department with the Center for Musculoskeletal Research (CMSR). Finally, Dr. Cesare Orlandi further enhances core departmental strengths in G-protein coupled receptor signaling and neuropharmacology, as well as both fortifying long-standing interactions with the Department of Neuroscience and establishing new connections with the Center for Visual Science and the Flaum Eve Institute.



JOHN LUECK, PH.D.
ASSISTANT PROFESSOR
OF PHARMACOLOGY
AND PHYSIOLOGY;
AND OF NEUROLOGY

Dr. John D. Lueck received his Ph.D. in Physiology from the Department of Pharmacology and Physiology at the University of

Rochester and went on to do two postdocs at the University of Iowa. With Dr. Kevin P. Campbell, Dr. Lueck continued his work on muscular dystrophy and honed his skills in protein biochemistry and muscle physiology. He then joined Dr. Christopher A. Ahern's lab to learn the ins and outs of genetic code expansion for the purpose of studying ion channel structure function. John returned home in July of 2018, as an Assistant Professor in the Departments of Pharmacology and Physiology and Neurology at the University of Rochester. Here, the Lueck Lab employs a multidisciplinary approach to investigate mechanisms that underlie skeletal muscle weakness and degeneration in myotonic dystrophy type 1 (DM1). In a second line of research, Dr. Lueck and his team will determine the therapeutic potential of suppressor tRNAs for cystic fibrosis that is caused by nonsense mutations or premature termination codons (PTCs). To tackle this problem, they will employ cutting edge molecular biology and work to develop novel nucleotide delivery technologies. More broadly, Dr. Lueck is interested in applying his background in membrane biophysics, molecular and cell biology to understanding the molecular underpinnings of physiology in health and disease.

WHASIL LEE, PH.D.
ASSISTANT PROFESSOR OF
BIOMEDICAL ENGINEERING;
AND OF PHARMACOLOGY AND
PHYSIOLOGY

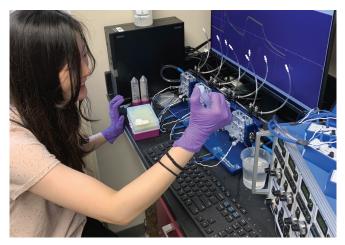
In August 2018, Dr. Whasil Lee joined the faculty of the University of Rochester as an Assistant Professor in the Departments of



Biomedical Engineering (BME) and Pharmacology and Physiology (PHP). With expertise in biophysics, biomedical engineering, and orthopaedics, Dr. Lee's program takes a multi-disciplinary approach to mechanobiology research.

Dr. Lee received her Ph.D. from Duke University where she studied Ankyrin protein mechanics using atomic force microscope (AFM) and molecular dynamics (NAMD) simulations under Dr. Piotr Marszalek and Dr. Vann Bennett. She continued her training at Duke University Medical Center, completing a post-doctoral fellowship with Dr. Wolfgang Liedtke and Dr. Farshid Guilak, leaders in chondrocyte mechanobiology. Using her AFM experience with electrophysiology and molecular biology training, Dr. Lee investigated mechanotransduction mechanisms in chondrocytes, finding that Piezo mechanosensitive ion channels are activated by osteoarthritic stimuli, including mechanical trauma and inflammation. These results opened the door to investigate the role of the mechanosensitive ion channels in pathologic mechanotransduction pathways and to translate these mechanisms for cartilage disease treatment.

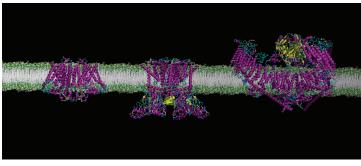
At the University of Rochester, research in the Lee Lab is focused on understanding cellular mechanotransduction mechanisms and their implications on cartilage health, and the development of a rational therapeutic strategy for cartilage degeneration that addresses unmet clinical needs



Wooree Ko, graduate student in the Lueck Lab, performing Ussing chamber experiments on cultured human airway epithelial cells to measure CFTR function

by employing multidisciplinary knowledge and approaches. Early findings have shown an interesting role of Piezo channels under inflammation, which were reported at national annual meetings. Dr. Lee attributes these novel findings due to "the exquisite PHP, BME and CMSR resources, training and mentorships. I and my lab members are thankful for the URMC research environment."

In addition to starting her lab, Dr. Lee designed and taught two new graduate courses for Pharmacology and Physiology and Biomedical Engineering students; BME465/PHP465 Intro to Cell Mechanics and Mechanobiology (4 Credits, fall semester) and BME 468/PHP468 Intro to Structure and Analysis of Biomolecules (2 or 4 Credits, spring semester).



Schematic representation of three Ca2+-permeating Mechanosensitive ion channels inserted in the membrane. The image was prepared using the Cryo-EM Structures of OSCA3.1 (5Z1F), TRPV4 (6BBJ) and Piezo1 (6B3R). Dr. Whasil Lee

# CESARE ORLANDI, PH.D. ASSISTANT PROFESSOR OF PHARMACOLOGY AND PHYSIOLOGY

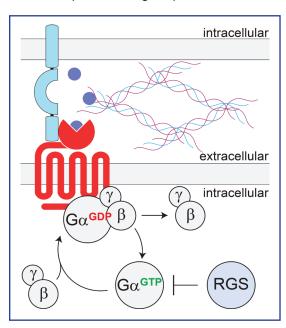


In October 2019, Dr.
Cesare Orlandi, joined the
University as an Assistant
Professor in the Department
of Pharmacology and
Physiology. Born and
raised in Italy, Dr. Orlandi
obtained a B.S./M.S.
in Pharmaceutical
Biotechnology at the
University of Milan and
received his Ph.D. in
Molecular Genetics from
the University of Brescia.

Then, he trained as a postdoctoral fellow with Dr. Kirill Martemyanov in the Department of Neuroscience at Scripps Research Institute in Jupiter, Florida.

Dr. Orlandi lab's research is focused on investigating the biology of a group of understudied G protein coupled receptors (GPCRs) in brain and visual systems. GPCRs represent the largest gene family encoding membrane receptors and they are involved in the regulation of every aspect of human physiology. Because of their physiological relevance and localization at the plasma membrane GPCRs are ideal targets for drug development. The endogenous ligands for a group of ~100 understudied GPCRs are still obscure, thus they are known as "orphan GPCRs". Nonetheless, the identification of disease-causing mutations in patients and studies on animal models have established the involvement of orphan GPCRs in essential physiological processes, and thus, they represent an attractive drug target. Using a multidisciplinary approach that involves proteomics, biochemistry, microscopy imaging, molecular cloning, and pharmacology, Dr. Orlandi discovered a new dimension of orphan GPCR biology. By characterizing

the formation of macromolecular complexes, he identified new molecular mechanisms linking the orphan receptors GPR158 to stress-induced depression, and GPR179 to congenital night blindness. More recently, he also demonstrated the interaction between these orphan receptors and extracellular matrix components illuminating how the extracellular matrix can modulate GPCR signaling. On the long-term, Dr. Orlandi's research will focus on understanding the role that orphan GPCRs play in shaping behavioral responses as well as the ways in which alterations in these complexes can lead to diseases. This exciting and poorly explored area of research has both enormous pharmacological potential and clinical value.



Schematic representation of the G protein coupled receptors (GPCR) signaling cycle. Recent studies indicates that extracellular interactions with cell-surface and secreted proteins such as extracellular matrix components profoundly affect GPCR pharmacology.

Understanding these interactions will be fundamental to uncovering the biology of many GPCRs, especially that of understudied orphan GPCRs.

#### **GRADUATE EDUCATION**

### WELCOME CMPP STUDENTS!

David Delemos, B.S. SUNY Geneseo

Chen Li. B.S. Nanjing University

Nan Zhao, B.S./M.S. University College of London



#### STUDENT AWARDS AND HONORS

Brandon Berry - Poster Award, Translational Research in Mitochondria, Aging, and Disease (TRiMaD) Symposium (September 2018)

Lara Terry - 2nd Place Poster Award, 2018 GSS Annual Poster Session, "Effects of Missense Mutations on Inositol 1,4,5-trisphosphate Receptor Mediated Calcium Release"

Si (Vivian) Chen - 3rd Place Poster Award, 2018 GSS Annual Poster Session, "PDE10A Inhibition and Deficiency Attenuate Pathological Cardiac Remodeling"

Xiaowen (Cindy) Wang - 1st Place Winner of UR CTSI's 2018 America's Got Regulatory Science Talent Competition. Cindy submitted a proposal for a drug repurposing database that could help identify new uses of FDA-approved drugs, and presented her idea to scientists and leaders at the Food and Drug Administration.

Matthew Rook - Recipient of BPS Travel award to attend and present a poster at the 2020 Biophysical Society Annual Meeting in February 2020.

#### STUDENT FELLOWSHIPS AND SUPPORT

Brandon Berry - American Heart Association Predoctoral Fellowship titled, "Optogenetic Control of Mitochondrial Function to Protect Against Ischemia Reperfusion Injury", beginning July 1, 2018

Edward Ayoub - Ruth L. Kirschstein National Research Service Award (NRSA) Individual Predoctoral F31 Fellowship titled, "Therapeutic Strategies for Anemia in 3g26 Rearranged Leukemia", beginning August 1, 2018

Matthew Rook and Alexander Milliken were selected for support by the T32 NIH Training Grant in Cellular, Biochemical & Molecular Sciences for the 2019-2020 academic year.

#### **DEGREES AWARDED**

#### **MARCH 2019**

#### Xiaowen (Cindy) Wang, Ph.D.

"Targeting the c-Cbl Tumor Suppressor Protein as a Novel Therapeutic Approach in Overcoming Acquired Tamoxifen Resistance in Luminal Breast Cancer"

Advisor: Dr. Mark D. Noble

#### OCTOBER 2019

#### Emma Grygotis Norris, Ph.D.

"Development of Acoustically-Modified Collagen-Based Biomaterials for Regenerative Medicine Applications" Advisor: Dr. Denise C. Hocking

#### Kevin Tylock, Ph.D.

"Biophysical and Molecular Mechanisms for QRS- and QTc-Interval Prolongation in Mice with Cardiac Expression of Expanded CUG repeat RNA"

Advisor: Dr. Robert T. Dirksen

#### Edward Ayoub, Ph.D.

"The Role of EVI1 in Hematopoietic Stem Cell Differentiation"

Advisors: Drs. Archibald S. Perkins and

David I. Yule

#### **DECEMBER 2019**

#### Chen Braun, Ph.D.

"Chronic PKCBIIII Activation Inhibits IKs Channel Membrane Localization via Phosphatidylinositol 4-phosphate: Implications for Long-QT1 Treatment" Advisor: Dr. Coeli M. Lopes

# **MARCH 2020**

#### Manisha Taya, Ph.D.

"Neutrophil Elastase and GPNMB as Novel Potential Therapeutic Targets in a Tsc2-null Mouse Model for Lymphangioleiomyomatosis (LAM) Tumor Growth"

Advisor: Dr. Stephen R. Hammes



Liwei Wang, Ph.D. (right) and his Faculty Advisor, Dr. David I. Yule (left)

Liwei Wang, Ph.D. was presented with the Wallace O. Fenn Award at the 2019 Commencement Dinner by Richard Libby, Senior Associate Dean for Graduate Education and Postdoctoral Affairs, for his thesis titled "Region-specific Proteolysis Differentially Regulates Inositol 1,4,5-trisphosphate Receptor Activity". The Fenn award is given annually to a graduating student judged to have performed especially meritorious research. Dr. Wang completed his graduate research in the laboratory of Dr. David I. Yule.

Dr. Wang is currently a Postdoctoral Fellow in the laboratory of Dr. Stefan Feske at NYU, Langone Medical School. His current research involves investigating the role of ion channels in immunological tolerance and immunity.

# FACULTY ACCOMPLISHMENTS

#### **AWARDS AND HONORS**

The department currently manages \$9.8M in extramural research funds annually and has an additional \$6.0M in pending proposals.

**Dr. Jean M. Bidlack** received the Herman Friedman Founder's Award from the Society on NeuroImmune Pharmacology. This award was given for "Visionary Contributions in Establishment and Continued Development of the Society." The award was presented at the 25th Annual Meeting of the Society on NeuroImmune Pharmacology in Portland, Oregon in April 2019.

**Dr. Denise C. Hocking** and **Dr. Michelle Dziejman** (Microbiology and Immunology)
received a 2019 University Research Award
for their project titled "Bacterial Pathogens,
Fibronectin Mimicry and
Intestinal Permeability."

**Dr. Whasil Lee** received Center for Musculoskeletal Research (CMSR) pilot funding for her project with **Dr. Sandeep Mannava** (Orthopaedics) titled, "Targeting mechanosensitive ion channels for anterior cruciate ligament (ACL)-injury associated osteoarthritis: Evaluation in a mouse model."

**Dr. John D. Lueck** received funding through the UR CTSI Incubatory Program for his project "Muscle calcium dysregulation as a therapeutic target in myotonic dystrophy."

**Dr. Angela J. Glading** was named Director of Graduate Studies in July 2018.

**Dr. David I. Yule** was nominated Chair of the Board of Scientific Councilors for NIDCR (National Institute of Dental and Craniofacial Research) for 2020.

Dr. Paul J. Kammermeier and Dr. Christoph Pröschel (Biomedical Genetics) were recipients of the 2019 Drug Targets and Mechanisms of Excellence Award for their project "Homer proteins in post-traumatic epilepsy."



Dr. Paul Kammermeier

#### SELECTED PUBLICATIONS

Bidlack, JM, Knapp, BI, Deaver, DR, Plotnikava, M, Arnelle, D, Quinn, AM, Toh, MF, Pin, SS, Namchuk, MN. "In vitro pharmacological characterization of buprenorphine, samidorphan, and combinations being developed as an adjunctive treatment for major depressive disorder." J. Pharmacol. Exp. Ther. 2018; 367:267-281

Bachman JF, Klose A, Liu W, Paris ND, Blanc RS, Schmalz M, Knapp E, Chakkalakal JV. "Prepubertal skeletal muscle growth requires Pax7-expressing satellite cell-derived myonuclear contribution." Development 2018; 145(20).

Michelucci A, Boncompagni S, Pietrangelo L, García-Castañeda M, Takano T, Malik S, Dirksen RT, Protasi F. "Transverse tubule remodeling enhances Orai1-dependent Ca entry in skeletal muscle." eLife 2019: 8:e47576.

Tang W, Jbabdi S, Zhu Z, Cottaar M, Grisot G, Lehman JF, Yendiki A, Haber SN. "A connectional hub in the rostral anterior cingulate cortex links areas of emotion and cognitive control." eLife 2019; 8:e43761.

Farrar CS, Rouin GT, Miller BL, Raeman CH, Mooney NA, Hocking DC. "A matricryptic conformation of the integrin-binding domain of fibronectin regulates platelet-derived growth factor-induced intracellular calcium release." Cells 2019; 8(11):1351.

McCullock TW, Kammermeier PJ. "Target validation: Weak selectivity of LY341495 for mGluR2 over mGluR4 makes glutamate a less selective agonist." Pharmacol Res Perspect 2019;7(3):e00471.

Lueck JD, Yoon JS, Perales-Puchalt A, Mackey AL, Infield DT, Behlke MA, Pope MR, Weiner DB, Skach WR, McCray PB, Ahern CA. "Engineered transfer RNAs for suppression of premature termination codons." Nature Communications 2019; 10(1):822.

Orlandi, C, Sutton, LP, Muntean, BS et al. Homeostatic cAMP regulation by the RGS7 complex controls depression-related behaviors. Neuropsychopharmacology 2019; 44, 642–653.

Bartok A, Weaver D, Golenár T, Nichtova Z, Katona M, Bánsághi S, Alzayady KJ, Thomas VK, Ando H, Mikoshiba K, Joseph SK, Yule DI, Csordás G, Hajnóczky. "G.IP3 receptor isoforms differently regulate ER-mitochondrial contacts and local calcium transfer." Nature Communications 2019; 10(1):3726.

#### IN THE NEWS

**Dr. Jean M. Bidlack** - was featured on WXXI's Second Opinion. The segment aired with episode 1509 "Alcoholism" on WXXI, where Dr. Bidlack described the effects of dopamine levels spikes in the brain, and how they lead to the very strong reinforcing properties of addiction.

**Dr. John D. Lueck** raised funds for Emily's Entourage to support research toward developing a cure for cystic fibrosis by climbing >15,000 feet to reach the top of the Matterhorn in the Swiss Alps in August, 2019. As a two-time EE grantee, John flipped the typical researcher's script by committing to raise funds for the foundation that has supported his research program.

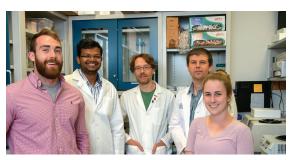
## COLLABORATION CORNER

A unique aspect of the research programs in the Department of Pharmacology and Physiology are the number of longstanding collaborative interactions with other departments and centers across the university. Indeed, the overall objective of the Drug Targets and Mechanisms Program of Excellence Pilot Grant program is to organically stimulate and grow these interdepartmental collaborations. These pilot grants have fostered collaborations with the Departments of Pediatrics, Genetics, Environmental Medicine, Biomedical Engineering and the Center for Oral Biology. In this section of the newsletter, we highlight our collaborative interactions with the research faulty in the

Department of Anesthesiology and Perioperative Medicine. The collaboration between the two departments dates back to 2001 and includes three basic science faculty (Drs. Brookes, Johnson, and Wojtovitch) whose labs are located in Pharm/Phys space in the medical center, as well as several clinical research faculty located on the 5th floor. All three basic science faculty members hold secondary appointments in the department, their research grants are managed by the department's superior administrative staff, and they are all very active in the Department's teaching and mentoring programs.

## ANESTHESIOLOGY MITOCHONDRIAL RESEARCH GROUP

Paul S. Brookes, Ph.D. Research in the Brookes' lab (www.psblab.org) is funded by grants from NIH and the American Heart Association, and is focused on protection of the heart from ischemia-reperfusion injury (heart attack). In particular we are interested in cardiac mitochondria and metabolism, and manipulation of these processes for therapeutic benefit. To this end, we employ organic synthesis to generate mitochondrially targeted drugs. We also use model systems including isolated perfused mouse hearts and primary cardiomyocytes, and state-of-the art analytical tools including LC-MS/MS based metabolomics and a Seahorse XF96 analyzer for high-throughput bioenergetic screening. The lab comprises the PI, a research faculty, post-doctoral fellow, graduate student and technician.



Brookes Lab

Gail V.W. Johnson. Ph.D. Dr. Johnson's primary research focus is molecular mechanisms of neurological disease, using approaches ranging from in-vitro enzyme assays with purified proteins, to studies in whole animals. A key area of interest in Alzheimer's disease, a hallmark of which is the presence of intracellular neurofibrillary tangles comprised of pathologically modified tau protein. The lab is interested in posttranslational modifications that regulate tau function, as well as toxic soluble forms of tau protein, and the clearance mechanisms responsible for tau removal from neurons. The lab also has a longstanding interest in the regulation and function of transglutaminase 2 (TG2) in neuron and astrocyte cell death and survival, particularly in the context of CNS injury. They have found that TG2 facilitates neuronal survival and can limit stroke damage when overexpressed in neurons. However, in astrocytes, TG2 does the opposite, enhancing cell death following injury. Ongoing studies are aimed at developing pharmacologic tools to target TG2 to improve outcomes after spinal injury or stroke.



Johnson Lab

Andrew P. Wojtovich, Ph.D. The Wojtovich lab focuses on the roles of Reactive Oxygen Species (ROS) in mitochondrial physiology and stress signaling. Although mitochondria are mediators of cell death and are a major site of ROS production, antioxidant treatments have so far been ineffective in clinical trials for diseases associated with oxidative stress. Using optogenetic tools, we can manipulate ROS generation precisely, controlling its dose, timing, and location, to gain a better understanding of ROS on a nano-scale. We use a wide variety of approaches from C. elegans to mammals, with CRISPR and other genetic tools. The lab consists of the PI, a post-doctoral fellow, a graduate student, two technicians and two undergraduate students, and our research is funded by NIH, the AHA, and internal (CTSI) projects.



Wojtovich Lab

#### **ALUMNI CAREER STORIES**

Laurie B. Cook, Ph.D. (Ph.D. '04)

I really love the idea of constantly pursuing knowledge because you never get bored! I guess that's one of the reasons I pursued my Ph.D. right out of undergrad. My thesis advisor, Dr. Patty Hinkle (now emeriti), was so much more than an advisor to me – she was to become a lifelong mentor in my professional life. She knew early on that I had a strong interest in teaching, and



I credit her with putting me in touch with my first adjunct teaching experience; in my final graduate year, while 3 months pregnant, I was able to teach a Cell Biology lecture class at Roberts Wesleyan for one semester to cover a sabbatical leave. It was my first independent teaching experience, and it reinforced my career trajectory. The next big question for me was whether to pursue an R01 or PUI (basically research-focused or teaching-focused)-type job. I really struggled with that, so I purposefully pursued postdoctoral opportunities with research projects that I might be able to take with me to a smaller college just in case. I landed at Cornell University's Molecular Biology & Genetics Department in the lab of Dr. Tim Huffaker, studying yeast microtubule genetics. After writing several

small grants and missing the funding line by just that much, I was told my position could not be funded for the original three-year commitment they made to me. I guess that comes with the territory, and so after a 12-month postdoc I put myself on the faculty-job market, with the caveat that if I did not land a job in 3 months of searching, I'd pursue another postdoc at Cornell Vet School. Once again, Patty had an in: a connection at SUNY Brockport told her a position was coming available in their Biology Department. Patty cautioned me though: Brockport had a reputation for sort of bridging the line between R01 and PUI, and the scholarship requirements for tenure were high compared to other smaller colleges. I thought long and hard about it and decided that as fate would have it this was actually quite perfect, since I couldn't really decide on research-focused or teaching-focused and wanted ultimately to do both. I was hired at Brockport in 2005 as a tenure-track Assistant Professor, received tenure and promotion to Associate Professor in 2012, and I plan on applying for Full Professor in September 2020. My path here at The College has recently taken me into administrative roles, and I've credentialed myself with a Graduate Certificate in Higher Education Administration (2016, Stonybrook U). Originally, I thought I'd be a faculty member until I retired, but my skillset has broadened widely and I'm opening up myself to the possibility of pursuing leadership positions in higher education.

#### Monicah Otieno, Ph.D. (Ph.D. '96)

Monicah received her Ph.D. in Pharmacology from Dr. Drag Anders' laboratory at the University of Rochester, Rochester NY, where she studied mechanisms of bioactivation of halogenated alkenes. The training from Dr. Ander's lab built a strong foundation for her success as a toxicologist. It was here that she learned to sharpen her critical thinking and scientific writing skills, develop hypotheses, and to identify key scientific questions. After her Ph.D., she cemented her training in toxicology as a post-doctoral fellow at Johns Hopkins University in Baltimore, M.D., where she studied mechanisms of carcinogenesis with Dr. Thomas Kensler. She then joined the pharmaceutical industry where she has held diverse positions of increasing responsibility in toxicology over the last 18 years with the latest position as a senior scientific director at Janssen pharmaceutical companies of Johnson & Johnson. In addition to supporting projects as a toxicologist through the drug development pipeline, Monicah also led the Mechanistic & Investigative Toxicology group at Janssen with the primary remit of addressing toxicology issues encountered during drug



discovery and development. She is keen on identifying innovative tools and approaches for solving key toxicology issues, and as such developed partnerships with key investigators in academia where she sponsored original research and post-

doctoral fellows. She has authored and co-authored over 40 scientific articles and book chapters and is a co-inventor on two patents on the Organ-on-Chip technology as the future for in vitro testing. She was instrumental in the development of the Liver-Chip model for safety testing that was recently published in Science Translational Medicine. Monicah has also been active in several scientific and industry organizations.

#### Christopher East, M.D., Ph.D. (Ph.D. '91)

Chris received his Ph.D. in Pharmacology from the University of Rochester in 1991, where he studied the mechanisms of diethyldithiocarbamate myeloprotection under the mentorship of Dr. Richard F. Borch. He attributes the program to teaching him "how to be a much better critical thinker" and "significantly improving my ability (and comfort level) to speak to an audience of scientific colleagues". His time at Rochester also gave him great memories of softball and post-game beers at the Elmwood Inn.

Chris went on to attend medical school at the University at Buffalo School of Medicine & Biomedical Sciences, graduating in 1995. He then completed an internship at Sisters of Charity Hospital in Buffalo, NY, and residency

at Duke University Medical Center.

From 2000-2013 Chris specialized in Cardiac Anesthesia in a tertiary hospital setting, and is currently a private practice anesthesiologist with Anesthesia Medical Group in Nashville, TN, specializing in regional anesthesia for orthopedic patients in a community hospital setting.



#### Maya Desai, Ph.D. (Ph.D. '11)



I graduated with a Ph.D. from the pharmacology and physiology department at URMC in 2011. My time during my graduate years has been very memorable and is reflective of the faculty, the mentors, the colleagues and friends that I made during this time. The aspect I appreciate

the most is the faculty encouraged us to build on our strengths without expecting us to fit a certain preconceived mold. This allowed creativity and growth which is fundamental to confidence as we approach the real-world. With time I have grown to further appreciate the in-depth coursework, the rigor during the qualifying exams, and the departmental requirements we were expected to complete. All of these equipped me and I am sure my colleagues as well to be stronger scientists and leaders.

After graduation, I completed my postdoc at Stanford University studying neuro-regenerative mechanisms in Multiple Sclerosis. During this time, I also completed the Program in Innovation and Entrepreneurship at

Stanford Graduate School of Business (GSB). I also served as a strategic advisor for start-ups where I conceived, designed and developed innovative capabilities (patentpathway mapping, sequence dashboard) that engaged biopharmaceutical and biotechnology clients. I established a high-performing team of over 50 scientists and successfully directed global teams business analysts and computer/life scientists. I continued being involved in the entrepreneurial community in various roles and served on committees/ panels at the Stanford Medical/GSB and UVA Darden GSB. Currently, I am an associate director at Navigant, a Guidehouse company where I lead the launch center of excellence working directly with founders, CEOs, and investors of pharmaceutical, biotechnology, and digital health companies. I have successfully provided product launch readiness and commercialization strategies for companies to remain competitive in the evolving healthcare environment. I also provide leadership to teams across a variety of global client stakeholders, including brand marketing, pipeline/franchise strategy, corporate strategy, new product planning, life cycle management, business development, and valuation. In aggregate, now with over 13 years of experience I have leveraged my academic and business background to provide strategic advise at the company and product level from research stage to commercialization and beyond. I also continue to be active in the entrepreneurial community and GSB.

### **IN MEMORY**

We were saddened to learn that Dr. Leonor T. Rivera-Calimlim passed away on December 2, 2019 at her home in Bridgewater, New Jersey. Leonor joined the University of Rochester, Department of Pharmacology in 1970, where she conducted research, and passionately taught graduate, nursing, and medical education students. She served on numerous departmental and institutional committees, and served as Acting Chair during Dr. M.W. Anders sabbatical, and was later appointed Associate Chair. In 1995 Leonor retired and was appointed Professor Emeritus, and also began her second career as a certified financial planner.



For those honored to have known Leonor, all will agree that she was a caring person as well as an excellent mentor, greatly admired, and a highly-respected member of the department and the University.



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