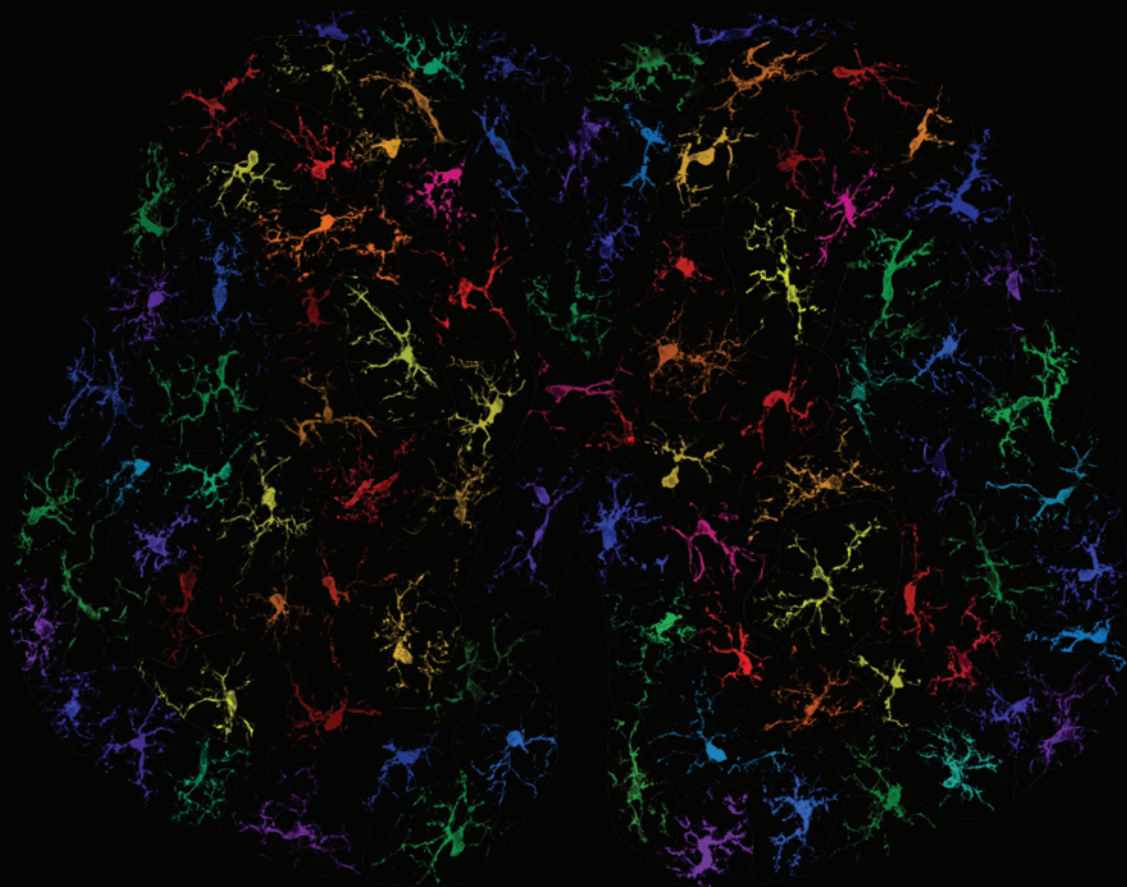


The Rita Allen Foundation and the
American Pain Society

CELEBRATING 10 YEARS OF SCHOLARS ADVANCING BASIC PAIN RESEARCH



COVER: Tuan Trang, a 2014 Rita Allen Foundation Scholar, has investigated mechanisms of opioid tolerance and withdrawal. Trang and his research group have found that immune cells in the central nervous system, known as microglia, play a key role in the development of morphine tolerance in an animal model. This image, a compilation of spinal microglia forming a cross section of the lumbar spinal cord, appeared on the cover of the October 18, 2017, issue of *The Journal of Neuroscience* in conjunction with the research article "Site-Specific Regulation of P2X7 Receptor Function in Microglia Gates Morphine Analgesic Tolerance." (Image by Heather Leduc-Pessah, Trang Laboratory)

A NETWORK OF HOPE



Elizabeth G. Christopherson
*President and
Chief Executive Officer
Rita Allen Foundation*

Tonight we celebrate 20 pioneering early-career pain Scholars as well as our partnership with the American Pain Society over the past decade. As we welcome our newest class of Scholars, we reflect on the accomplishments of these researchers and the profound questions that drive them forward to new discoveries.

These scientists are leading efforts to map the neural circuits of chronic pain, define the roles of immune signals, and examine the connections between pain and itch. Their findings point to approaches for combating opioid tolerance and withdrawal, as well as targets for completely novel pain therapies with the potential to improve safety and specificity. And they are part of teams creating and combining new tools and knowledge, brought together by a deep commitment to seeing this field into the future.

Fueled by that commitment, we also now are working to rally more support for a future where pain is better managed and better understood.

When the Rita Allen Foundation Scholars program began supporting high-promise, innovative research more than 40 years ago, pain research was identified as one of the most difficult and critical biological problems. Our partnership with the American Pain Society began with the inspiration and encouragement of Dr. Kathleen Foley. One of the early Rita Allen Foundation Scholars, Dr. Foley has since helped advance pain research and treatment globally. As the Foundation's Medical Adviser, Dr. Foley introduced the idea of a partnership with the American Pain Society, through which we now work together to identify and support promising early-career pain scientists. With the valued, important contributions of the American Pain Society, a community of exceptional researchers has grown.



Dr. Kathleen Foley
*Rita Allen Foundation
Medical Adviser*

In addition to celebrating the efforts of the Rita Allen Foundation Award in Pain Scholars, we express gratitude to the scientists—many of whom also are Rita Allen Scholars—who have advised our work and served on selection committees over the years. This year's selection committee, chaired by Dr. Charles Inturrisi, includes 21 distinguished scientists. Please join us in special appreciation for the committee members, for the leaders of the American Pain Society, and for all who contribute to advancing the vital work of basic research in pain.

The portfolio of the Rita Allen Foundation has expanded in the decade since the Foundation opened its first office and hired professional staff. We are deeply invested in supporting remarkable scientists as well as increasing awareness about the importance of this work. We have funded the International Association for the Study of Pain/Pain Research Forum's

"RELIEF" website, which presents the science of pain for a non-specialist audience. Some of our other partners include the Science Philanthropy Alliance, the American Association for the Advancement of Science, the National Academy of Sciences, the American Academy of Arts and Sciences, and others who seek to increase public and philanthropic support for science—particularly the cross-disciplinary, complex, emergent and profoundly important science that pain research represents.

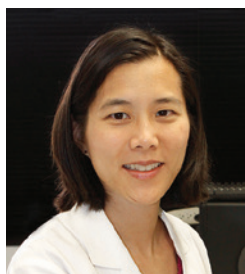
The message we are sharing about pain research is one of great promise. The scientists in the pages that follow represent a vibrant, growing community of pain researchers. Together—whether by way of neuroscience, genetics, cell biology or clinical practice—pain scientists represent, in the face of great challenges, a network of hope.

Their work grows only more urgent as we face an aging population and widespread experiences of pain—with more than 25 million Americans reporting daily pain, and chronic pain affecting some 100 million adults in the country, at the cost of hundreds of billions of dollars and suffering impossible to quantify. As we are acutely aware, we also confront an epidemic of drug overdose deaths—with more Americans now dying from drug overdoses than from car accidents and gun homicides combined. Investing in the research necessary to develop more effective and less addictive pain treatments is a vital priority.

With profound appreciation for our partnership with the American Pain Society and to the outstanding scientists who are dedicated to making essential discoveries,

A handwritten signature in black ink, reading "Elizabeth G. Christopherson". The script is fluid and cursive, with a large, stylized initial 'E'.

Elizabeth G. Christopherson
President and Chief Executive Officer
Rita Allen Foundation



HELEN LAI, PH.D.

Assistant Professor
Department of Neuroscience
The University of Texas Southwestern Medical Center

Project: Understanding the Molecular and Developmental Basis of Painlessness

Helen Lai earned a B.A. in chemistry at Cornell University and a Ph.D. in biophysics at the University of California, San Francisco, where she worked with Lily Jan to investigate the structural mechanisms of voltage-gated potassium channels, which help to define the signaling characteristics of neurons. As a postdoctoral fellow in Jane Johnson's lab at The University of Texas Southwestern Medical Center, Lai studied transcriptional mechanisms of differentiation and cell type specification in spinal cord and cerebellar neurons. She was a Sara and Frank McKnight Fellow at UT Southwestern from 2012 to 2015, when she became an assistant professor.

Somatosensation consists of three main sensory modalities: nociception (thermal sensation/pain), mechanosensation (touch) and proprioception (sense of limb and body position). Our understanding of how these senses are relayed through the dorsal spinal cord up to supraspinal regions is rapidly progressing due to the advent of multiple genetic manipulations and optogenetic techniques in mice. Lai's research aims to understand the circuits that form the basis of somatosensory behavior, how they integrate somatosensory information, how they form their connections, and what plastic changes may occur upon differential sensory input. With support from the Rita Allen Foundation, Lai will examine the molecular basis of congenital insensitivity to pain (CIP). The identification of genes that underlie painlessness in human patients has led to the development of new analgesics to treat people with chronic or neuropathic pain. Recently, another genetic cause of CIP in humans has been linked to recessive mutations in the chromatin-modifying factor PRDM12. To understand the molecular basis of this disease, Lai plans to generate a mouse model of PRDM12-associated CIP. Understanding the mechanisms of how painlessness develops in this mouse model will guide future endeavors aimed at developing improved analgesics.



CANDICE PAULSEN, PH.D.

Assistant Professor
Department of Molecular Biophysics and Biochemistry
Yale University

Project: Uncovering the Regulation of TRPA1 by Irritants, Cofactors and Proteins

Candice Paulsen earned a B.S. in genetic biology at Purdue University and a Ph.D. in chemical biology at the University of Michigan. As a graduate student with Kate Carroll at the University of Michigan and The Scripps Research Institute, Paulsen studied redox regulation of signal transduction cascades important to cancer. As a postdoctoral fellow with David Julius at the University of California, San Francisco, she used cryo-electron microscopy to determine the structure of the TRPA1 ion channel, an important detector of noxious chemical agents also known as the "wasabi receptor." Paulsen joined the Yale University faculty in 2018.

Nociception is a process by which distinct, potentially harmful thermal, mechanical or chemical stimuli activate specialized sensory neurons to initiate pain signals and neurogenic inflammation. The wasabi receptor, TRPA1, is expressed in chemosensory neurons innervating the periphery and visceral organs, and is activated by a chemically diverse panel of environmental toxins. TRPA1 is also activated by endogenous electrophiles produced during inflammation, which contribute to chronic pain associated with arthritis, asthma and colitis. The Paulsen laboratory is taking a multidisciplinary approach to understand how TRPA1 is regulated by small molecules, cofactors and proteins, with an eye toward uncovering novel avenues for analgesic and anti-inflammatory agent development that directly target initiation of pain and neurogenic inflammatory signals, reducing or eliminating the side effects and risks of addiction. Initial work in Paulsen's lab will focus on unresolved questions about how TRPA1 is regulated: 1) determining the structure of TRPA1 in its open, active conformation; 2) identifying endogenous cofactor(s) that stabilize functional TRPA1; and 3) finding proteins that interact with TRPA1 in its basal and activated states.



STEVE PRESCOTT, M.D., PH.D.

Senior Scientist
Program in Neurosciences and Mental Health
The Hospital for Sick Children, Toronto
Associate Professor
Department of Physiology and Institute of Biomaterials and
Biomedical Engineering
University of Toronto

Project: Pain Processing by Neural Networks: A Critical Link between Molecular and Perceptual Changes Associated with Neuropathic Pain

Steve Prescott obtained his M.D. and Ph.D. degrees from McGill University. He did postdoctoral training in computational neuroscience at the Salk Institute for Biological Studies with Terry Sejnowski. In 2008 he set up his own lab at the University of Pittsburgh with the intent of combining a range of experimental and computational tools to investigate pain processing. In 2012 his lab moved to The Hospital for Sick Children in Toronto. Prescott was named a Mallinckrodt Scholar and has also received a Canadian Institutes of Health Research New Investigator Award and an Ontario Early Researcher Award. He has received funding from the National Institutes of Health, the Canadian Institutes of Health Research, and the Natural Sciences and Engineering Research Council of Canada.

Prescott's lab combines experiments (electrophysiology, optogenetics, calcium imaging, etc.) with computer simulations and mathematical analysis to uncover how changes in neuronal excitability and synaptic transmission affect neural coding. He is particularly interested in deciphering the nonlinear, systems-level basis for complex phenomena. In this context, his team has demonstrated how pathological changes in neuronal excitability implicated in neuropathic pain can arise through distinct molecular mechanisms; because multiple molecular changes that are individually sufficient to disrupt excitability are induced by nerve injury, no single molecular change is uniquely necessary for injury-induced excitability changes. This so-called degeneracy has important implications for choosing effective drug targets and may help explain why neuropathic pain is so difficult to treat. Moving forward, the lab is testing a theory of combinatorial coding, which posits that somatosensory information is encoded by the combination of cell types coactivated by different stimuli.



THEODORE PRICE, PH.D.

Associate Professor
School of Behavioral and Brain Science
The University of Texas at Dallas

Project: Translation Regulation as a Novel Paradigm for Understanding Nociceptor Sensitization and Developing Analgesic Targets

Theodore Price completed his Ph.D. at The University of Texas Health Science Center in San Antonio and a postdoctoral fellowship at McGill University. He took his first faculty position at the University of Arizona in 2007 and moved to UT Dallas in 2014, where he also directs the undergraduate neuroscience program and the Center for Advanced Pain Studies. Funded by the National Institutes of Health, Price's laboratory focuses on molecular mechanisms involved in pain plasticity, with the goal of developing new therapeutics to reverse chronic pain states in humans. He has received early-career scholar awards from the American Pain Society and the International Association for the Study of Pain. Price is a member of the Somatosensory and Pain Systems Study Section of the NIH and serves on the editorial boards of numerous journals, including PAIN and the European Journal of Pain, where he is the pharmacology section editor.

Chronic pain is a major clinical problem that can persist for decades, but no disease-modifying treatments are available. Price's work has focused on understanding the phenotypic changes that occur after injury that cause pain-sensing neurons to become hyperactive, driving chronic pain. His recent work has focused on how translation control signaling governs these phenotypic changes, which mRNAs are translated in an activity-dependent fashion in these neurons, and how targeting kinases that regulate translation of mRNAs can lead to disease modification resulting in long-lasting relief of chronic pain.



SEENA AJIT, PH.D.

Assistant Professor
Department of Pharmacology and Physiology
Drexel University College of Medicine

Project: MicroRNA Regulation and Its Utility for Biomarkers in Neuropathic Pain

Seena Ajit received her Ph.D. in molecular biology from Rutgers University, and was a scientist in Neuroscience Discovery at Wyeth Research from 2001 to 2009, when she became an assistant professor at Drexel University College of Medicine.

Epigenetics is now recognized as an important aspect of gene regulation, and epigenetic analysis is likely to play an increasingly important role in the diagnosis, prognosis and treatment of diseases. Ajit is interested in pursuing various aspects of epigenetics, including DNA methylation, histone modifications and RNA-mediated gene silencing, all aimed at understanding the molecular mechanisms underlying pain. Currently her group is studying the role of noncoding RNAs in mediating pain, as well as their utility for biomarkers. They have identified differentially expressed circulating miRNAs in whole blood from patients with complex regional pain syndrome relative to controls. Additionally, studies using blood samples from good and poor responders to ketamine treatment have identified differential miRNA signatures both before and after therapy. A major focus in the lab now is to understand the significance of miRNA alterations in regulating gene expression leading to inflammation and pain.

Circulating miRNAs in bodily fluids are delivered to recipient cells via exosomes. Intercellular communication once thought to be limited to secreted signals can now be attributed to exosomes. Exosome contents, including miRNAs and mRNAs, are capable of modulating gene expression in the recipient cells. Ajit's lab is investigating the mechanistic basis of pro- and anti-nociceptive roles of exosomes from various sources, including patients and rodent models of pain.



DIANA BAUTISTA, PH.D.

Associate Professor
Department of Molecular and Cell Biology
University of California, Berkeley

Project: Molecular Mechanisms of Somatosensory Mechanotransduction

Diana Bautista earned her B.S. in biology from the University of Oregon and her Ph.D. in neuroscience from Stanford University, where she worked in the laboratory of Richard Lewis. She was a postdoctoral fellow at the University of California, San Francisco, collaborating with David Julius. She joined the Berkeley faculty in 2008. In addition to a Rita Allen Foundation Scholar award, she has received the National Institutes of Health Director's New Innovator Award.

Bautista's lab aims to understand the molecular mechanisms underlying the sensations of itch, touch and pain. Humans rely on these senses for a broad range of essential behaviors. For example, acute pain acts as a warning signal that alerts us to noxious mechanical, chemical and thermal stimuli, which are potentially tissue damaging. Likewise, itch sensations trigger reflexes that may protect us from disease-carrying insects. Despite these essential protective functions, itch and pain can outlast their usefulness and become chronic. Bautista's lab uses cellular physiology, molecular biology, molecular genetics and behavioral studies to elucidate the molecular mechanisms underlying itch and pain transduction under normal and pathophysiological conditions.



E. ALFONSO ROMERO-SANDOVAL, M.D., PH.D.

Associate Professor of Anesthesiology
Wake Forest School of Medicine

Project: Spinal Cord Mechanisms in the Resolution of Postoperative Pain

Alfonso Romero-Sandoval is originally from Guatemala, and received his M.D. degree from Universidad de San Carlos de Guatemala in 1999 and his Ph.D. degree in neuroscience from Universidad de Alcalá de Henares, Spain, in 2003. He did postdoctoral training at Wake Forest University and at Geisel Dartmouth Medical School. He has served on the faculty at Geisel Dartmouth Medical School and Presbyterian College School of Pharmacy. Romero-Sandoval is currently an associate professor of anesthesiology at Wake Forest School of Medicine and is studying the molecular mechanisms of macrophages and their role in wound healing and in the transition from acute to chronic pain, and the use of nanotechnology to promote surgical wound healing and to prevent the development of chronic postoperative pain. Other projects include the role of cannabinoid receptor activation in skin cells for induction of analgesia, the role of endocannabinoids in postoperative pain, and the function of phosphatases and kinases in the spinal cord and periphery in the context of pain.

Romero-Sandoval's lab uses a clinically relevant cell target gene therapy method applying nanotechnology (successfully used in HIV-positive patients for gene induction) in human macrophages. The final goal of this project is to target macrophages to induce a cellular phenotype that drives the efficient resolution of inflammation and prevents the development of chronic pain following major surgeries. His team uses nanoparticles to specifically target macrophages. Romero-Sandoval proposes to induce specific genes that are involved in the resolution of inflammation by driving an M2 macrophage phenotype.



YUAN-XIANG TAO, M.D., PH.D.

Professor
Departments of Cell Biology and Molecular Medicine, of Pharmacology and Physiology, and of Neurology and Neurosciences
Vice Chair for Research and Director of the Center for Pain Medicine Research,
Department of Anesthesiology
Rutgers New Jersey Medical School

Project: Discovery of a Large Non-Coding RNA and Its Regulation by Peripheral Nerve Injury

Yuan-Xiang Tao earned B.Sc., M.Sc. and M.D. degrees from Nanjing Medical University, and holds a Ph.D. in neuroscience from the Shanghai Brain Research Institute of the Chinese Academy of Sciences. He completed a postdoctoral fellowship at the University of Virginia Health Sciences Center, where he studied the role of postsynaptic density proteins in chronic pain and anesthesia. Tao was a faculty member in the Department of Anesthesiology and Critical Care Medicine at Johns Hopkins University School of Medicine from 1999 to 2013, when he became a full professor at Rutgers New Jersey Medical School. Tao has received funding from the National Institutes of Health, the National Natural Science Foundation of China, the Blaustein Pain Research Fund, the David H. Koch Prostate Cancer Research Fund and the Brain Science Institute of Johns Hopkins Medicine. In 2017 he was selected for Rutgers New Jersey Medical School's Faculty of the Year Award, as well as an Excellence in Research Award from the New Jersey Health Foundation.

Tao's research focuses on understanding the molecular and cellular mechanisms that underlie chronic pain and opioid-induced analgesic tolerance and hyperalgesia. Research projects in his laboratory have attempted to address questions regarding different aspects of pain and opioid analgesia: 1) how protein translation is regulated under the conditions of chronic opioid tolerance and hyperalgesia; 2) how epigenetic modifications participate in the development and maintenance of chronic pain; and 3) how acute vaso-occlusive episodes induce and aggravate sickle cell disease-associated pain.



MICHAEL JANKOWSKI, PH.D.

Associate Professor
Department of Anesthesiology
Cincinnati Children's Hospital Medical Center
Department of Pediatrics
University of Cincinnati College of Medicine

Project: Molecular Mechanisms of Musculoskeletal Pain after Ischemic Tissue Injury

Michael Jankowski earned an M.S. in neuroscience and a Ph.D. in neurobiology from the University of Pittsburgh, where he also conducted postdoctoral research. He joined the faculty of the Cincinnati Children's Hospital Medical Center in 2011. Jankowski has received several National Institutes of Health grants from the National Institute of Neurological Disorders and Stroke, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and the National Institute of Arthritis, Musculoskeletal and Skin Diseases. He also is a recipient of an International Association for the Study of Pain (IASP) Early Career Research Grant Award, and was named a Cincinnati Children's Trustee Scholar in addition to being a Rita Allen Scholar. He serves on numerous grant review panels and journal review boards and is an associate editor for the journal *PAIN* and reviewing editor for *Molecular Pain*. He is on the training faculty in the Neuroscience Graduate Program and the Molecular and Developmental Biology Graduate Program at CCHMC. He is also a member of the Society for Neuroscience, the IASP and the American Pain Society.

Jankowski's lab is interested in the peripheral mechanisms of pain development under unique injury conditions. His research has two main focuses: peripheral mechanisms of musculoskeletal pain, specifically in the context of ischemia; and the consequences of neonatal injury on developing sensory neurons. Ischemic muscle pain is a major health issue that occurs in numerous disorders, such as sickle cell anemia, peripheral vascular disease and even fibromyalgia. Many patients experience altered cardiovascular reflexes and musculoskeletal pain as a result of these disease states. Chronic pain in children, however, can arise from multiple sources, including surgery, inflammation or even neonatal intensive care. Yet we do not have a comprehensive understanding of the changes that occur in specific subtypes of sensory fibers after ischemic muscle injury or during postnatal development that modulate these distinctive pain states. Jankowski's group utilizes a multidisciplinary experimental approach to obtain a broad understanding of pain development at the primary afferent level. These studies will hopefully lead to the development of treatments for adverse changes in cardiovascular reflexes or musculoskeletal pain associated with muscle ischemia, or novel therapies for pediatric pain.



SARAH ROSS, PH.D.

Associate Professor
Department of Neurobiology
Pittsburgh Center for Pain Research
University of Pittsburgh

Project: Investigating the Neural Circuits of Itch and Pain

Sarah Ross earned her B.Sc. from the University of Western Ontario and her Ph.D. from the University of Michigan, both in physiology. She was a postdoctoral fellow in the Department of Neurobiology at Harvard Medical School, where she worked with Michael Greenberg. She joined the faculty at the University of Pittsburgh in 2011. In addition to the Rita Allen Foundation, she has received support for her work from the National Institutes of Health.

The spinal cord plays a critical role in processing somatosensory information. To study these spinal microcircuits, the Ross lab has developed a novel somatosensory preparation that allows recording from the output neurons (via retrograde labeling of spinal projection neurons) while controlling somatosensory input (via natural stimulation of the skin) and simultaneously manipulating activity of specific populations of spinal interneurons (via the combination of Cre alleles and optogenetics). Using this physiological preparation, the Ross lab is addressing long-standing questions in the field of somatosensation, such as: How is itch distinguished from pain? Why does scratching relieve itch? and How does pain become abnormally amplified upon injury?



REBECCA SEAL, PH.D.

Associate Professor
Departments of Neurobiology and Otolaryngology
Pittsburgh Center for Pain Research
University of Pittsburgh

Project: Mechanical Pain Circuits in the Dorsal Horn

Rebecca Seal earned her B.S. in chemistry and psychology from the University of Oregon and her Ph.D. in neuroscience from Oregon Health and Science University. Her graduate studies with Susan Amara focused on the structure and function of plasma membrane glutamate transporters. As a postdoctoral scholar at the University of California, San Francisco, she studied the vesicular glutamate transporter 3 in hearing and pain with Robert Edwards. She has received a NARSAD Young Investigator Grant from the Brain and Behavior Research Foundation, an Innovation Award from the American Diabetes Association, a Japanese Society for the Promotion of Science Fellowship and a Whitehall Foundation Research Award.

Seal's laboratory focuses on defining the neural circuitry underlying a wide range of nervous system functions in health and disease, including persistent pain, motor symptoms of Parkinson's disease and audition. A major impediment to identifying new pain treatments is incomplete understanding of the neural networks and mechanisms that underlie the pain. Her team's work, using multiple approaches ranging from cellular and molecular to physiological and behavioral, centers on elucidating the neural circuits and mechanisms that underlie a particular form of persistent pain in which touch becomes painful in the setting of injury, termed mechanical allodynia. The spinal cord dorsal horn is a major site for the integration of somatosensory information and is vital for the induction and maintenance of this form of pain. Their work thus far suggests that the pain is encoded by distinct microcircuits in the dorsal horn, depending on the nature of the injury. This concept not only has important implications for understanding at a basic level how the nervous system encodes mechanical allodynia, but also highlights the need to consider etiology in the design and implementation of therapeutic strategies.



REZA SHARIF-NAEINI, PH.D.

Assistant Professor
Department of Physiology
Cell Information Systems Group
McGill University

Project: Role of Parvalbumin Neurons in Dorsal Horn Pain Circuits

Reza Sharif-Naeini earned his Ph.D. in physiology from McGill University in 2007, and returned there to join the faculty in 2012. In the interim, he was a postdoctoral fellow at Institut Pharmacologie Moléculaire et Cellulaire in Nice, France, and in the Department of Anatomy at the University of California, San Francisco. He has received fellowships from the Canadian Institutes of Health Research, the International Association for the Study of Pain and the Human Frontier Science Program. He has also received the CIHR Brain Star Award for excellence in research and the Peter and Patricia Gruber International Research Award in Neuroscience from the Society for Neuroscience.

Chronic neuropathic pain (NeP) is a debilitating disease that follows nerve injury and persists long after the initial injury has subsided. Despite the plethora of medications and treatment modalities, NeP remains a disease with unmet medical needs that significantly decreases patients' quality of life. Spontaneous pain and mechanical allodynia, two hallmarks of NeP, are due in part to a spinal cord dysfunction characterized by a decrease in inhibitory neurotransmission (or inhibitory tone). Our understanding of how these inhibitory mechanisms function in health and disease remains, however, limited. This indicates a need for novel and innovative experimental approaches to gain a better understanding of inhibitory circuits in the dorsal horn and how changes in these circuits can precipitate NeP symptoms. Sharif-Naeini's group is interested in understanding the function of these inhibitory pathways using transgenic mouse lines combined with opto/pharmacogenetic approaches.



GREGORY SCHERRER, PH.D.

Assistant Professor
Departments of Anesthesiology, Perioperative and Pain Medicine, of
Neurosurgery and of Molecular and Cellular Physiology
Stanford University School of Medicine

*Project: Molecular Mechanisms of Opioid-induced Analgesia,
Tolerance and Hyperalgesia*

Gregory Scherrer earned his Ph.D. in cellular and molecular biology from the University of Strasbourg, France. He completed postdoctoral training at the University of California, San Francisco, and at Columbia University. He joined the faculty at the Stanford University School of Medicine in 2012. In addition to a Rita Allen Foundation Scholar award, he has received an International Association for the Study of Pain Postdoctoral Fellowship, National Institutes of Health/National Institute on Drug Abuse K99R00 Pathway to Independence and R01 Awards, a Department of Defense Neurosensory Research Award, and an International Narcotics Research Conference Young Investigator Award, and most recently was named a New York Stem Cell Foundation – Robertson Neuroscience Investigator.

The members of the Scherrer Laboratory investigate how the nervous system generates the sensory and affective dimensions of pain experience and opioid analgesia to discover novel analgesic therapies. They aim to identify the pathological changes that occur within neural circuits when chronic pain develops, at the neural network, cellular and molecular levels. One of their approaches is to gain understanding of how our endogenous opioid system modulates pain thresholds. Opioid receptors mediate the effects of opioid painkillers, such as morphine. By determining how opioids generate analgesia and detrimental side effects (e.g., tolerance, addiction, respiratory depression), Scherrer and his team hope to develop more efficient and safer analgesics for the treatment of chronic pain. These studies will also identify novel approaches to counteract opioid side effects and battle the current opioid epidemic. To reach these goals, Scherrer's research combines a variety of experimental approaches, including molecular and cellular biology, neuroanatomy, electrophysiology, opto- and pharmacogenetics, in vivo calcium imaging and behavior.



TUAN TRANG, PH.D.

Assistant Professor
Department of Physiology and Pharmacology
University of Calgary

Project: Alleviating Opioid Withdrawal by Blocking Pannexin-1 Channels

Tuan Trang completed a Ph.D. in pharmacology and toxicology at Queen's University, and pursued postdoctoral training as a Canadian Institutes of Health Research (CIHR) fellow in the laboratory of Dr. Michael Salter at the Hospital for Sick Children in Toronto. He has received a CIHR New Investigator Award, as well as young investigator awards from the Canadian Association for Neuroscience and Canadian Society for Pharmacology and Therapeutics. His research has been supported by grants from, in addition to the Rita Allen Foundation, the CIHR, the Natural Sciences and Engineering Research Council of Canada, a Vi Riddell Pain Grant from the University of Calgary, and the Canada Foundation for Innovation.

Opioids are among the most powerful and widely prescribed drugs for treating pain. However, a major problem in terminating opioid pain therapy is the debilitating withdrawal syndrome that can plague chronic opioid users. The mechanisms involved in opioid withdrawal are poorly understood, and the limited clinical strategies for treating withdrawal are ineffective. Trang and his collaborators have identified the pannexin-1 (Pannx1) channel as a novel therapeutic target for treating morphine withdrawal. They discovered that morphine treatment induces synaptic plasticity in spinal lamina I/II neurons, which manifests as long-term synaptic facilitation upon naloxone-precipitated morphine withdrawal. This synaptic facilitation is critically gated by activation of Pannx1 channels expressed on microglia. Pharmacologically blocking Pannx1, or genetically ablating this channel specifically from microglia, blocked spinal synaptic facilitation and alleviated the behavioral sequelae of morphine withdrawal. Trang and his team are now moving these discoveries into the clinic.



ROBERT SORGE, PH.D.

Assistant Professor
Department of Psychology
The University of Alabama at Birmingham

Project: Immune System Modulation of Pain via Diet

Robert Sorge earned his Honors B.Sc. in psychology from McMaster University in Hamilton, Ontario, his M.A. in experimental psychology from Wilfrid Laurier University in Waterloo, Ontario, and his Ph.D. in psychology from Concordia University in Montreal, Quebec. He was a postdoctoral fellow at McGill University before joining the faculty at The University of Alabama at Birmingham in 2012. In addition to being named a Rita Allen Foundation Pain Scholar, he has received a Young Investigator Award from the Sex, Gender and Pain Special Interest Group of the International Association for the Study of Pain. He also has received postdoctoral fellowships from the Alan Edwards Center for Research on Pain at McGill and from the National Sciences and Engineering Research Council of Canada.

Obesity in America is reaching epidemic proportions, with more than one-third of the population classified as obese, and even more as overweight. In addition to the increased risk for metabolic syndromes and cardiovascular disease, obesity is comorbid with chronic pain for a significant number of patients. It is known that adipose tissue and components of the American diet can contribute to a chronic proinflammatory state that may predispose individuals to significant negative health effects. Sorge and his collaborators believe that this state is the result of heightened activity of the immune system. Their previous work has shown that consumption of a Western diet results in changes in acute sensitivity to stimuli, increased systemic inflammation and prolonged recovery from injury. These effects are believed to be the result of chronic immune cell activation in the peripheral and central nervous system. Current work is underway to investigate the temporal profile of immune cell activation following differential exposure to the American diet in rodents. Through examination of the immune-related impact of diet, it may be possible to formulate treatments that will reduce the negative effects of the American diet with respect to pain and other related inflammatory conditions.

YI YE, PH.D.



Assistant Professor
Associate Director of Clinical Research Operations
Bluestone Center for Clinical Research
College of Dentistry, New York University

Project: The Role of Schwann Cells in Neural Invasion and Associated Cancer Pain

Yi Ye holds a Ph.D. in neuroscience from the University of Wyoming, a master's degree in clinical research from New York University and an M.B.A. from NYU's Stern School of Business. She was a research fellow in the Department of Oral and Maxillofacial Surgery in the College of Dentistry at the University of California, San Francisco, and joined the Bluestone Center as an associate research scientist in 2010. She has been in her current position since 2015. She has received a Travel Award and an Early Career Research Grant Award from the International Association for the Study of Pain, and was awarded both a National Institutes of Health-NYU-Clinical and Translational Science Institute Scholarship and an NYU Whitehead Fellowship in 2015.

Ye's research aims to understand the neurobiological basis of cancer pain, with an additional focus on carcinogenesis and tumor progression in head and neck cancer. The ultimate goal of her research is to develop novel therapies that can be used for both cancer and pain treatment by targeting shared mechanisms. In progression toward this goal, she directs a translational research program that uses multiple approaches including in vitro cell culture, animal models and human studies.



STEVE DAVIDSON, PH.D.

Assistant Professor
Department of Anesthesiology
University of Cincinnati College of Medicine

Project: Thalamo-limbic Circuit Control of Pain

Steve Davidson earned a B.S. in psychology from the University of New Orleans and a Ph.D. in neuroscience from the University of Minnesota. He was a postdoctoral scholar in the Department of Anesthesiology at Washington University School of Medicine in St. Louis from 2009 to 2014, and in 2015 he joined the faculty of the University of Cincinnati College of Medicine. In 2010, Davidson received a Future Leader in Pain Research award from the American Pain Society.

Pain has long been recognized as a multidimensional experience. Yet research has focused almost exclusively on the sensory dimension, leaving the emotional and motivational components poorly understood and undertreated. The Davidson lab seeks to elucidate and control a neural circuit responsible for regulating the capacity for pain tolerance, an aspect of pain behavior dependent on emotional and motivational pain processing that occurs in the brain. Davidson's research tests the main hypothesis that effective pain control can be achieved by manipulating neural activity in a thalamo-limbic pathway to enhance pain tolerance. His laboratory has developed a novel operant behavioral model in which rodents may obtain a reward by engaging with (tolerating) a noxious thermal stimulus. Using this approach, analgesics with efficacy for improving the affective measure of pain tolerance vs. reflexive withdrawal may be determined. To determine whether thalamo-limbic projection neurons control pain, virally infected posterior thalamic neurons containing optically gated ion channels will allow direct control of activity through an implanted light source while animals are tested for changes to pain tolerance and reflexive behaviors. Finally, the Davidson lab will test the hypothesis that chronic pain alters synaptic plasticity in the thalamo-limbic circuit. This will include examination of posterior thalamic projection neurons for altered excitability and synaptic plasticity at the posterior thalamus-insula synapse in rodent models of neuropathic and inflammatory chronic pain.



KATHERINE HANLON, PH.D.

Assistant Professor of Pharmaceutical Sciences
Director of Research
Presbyterian College School of Pharmacy

Project: Dorsal Root Ganglion Macrophages: Function and Impact on Nociception

Katherine Hanlon earned a B.S. in biochemistry and molecular biophysics and a Ph.D. in pharmacology from the University of Arizona, where she worked with Todd Vanderah. She went on to complete a postdoctoral fellowship in tumor immunology at the Mount Sinai Medical Center with Joshua Brody and Peter Heeger. Hanlon's primary research interests include macrophage-neuron communication in pain processing and the role of tumor-associated macrophages in cancer development. She also studies the mechanisms of dysregulation of cannabinoid receptor signaling in tumor and immune cells in metastatic disease.

Studies in the Hanlon lab are carried out using multiple in vitro and in vivo models, including leukocytes and neurons isolated from dorsal root ganglia, leukocytes and tumor cells isolated from murine mammary tumors, leukocytes harvested from post-surgical peritoneal adhesions, and human blood monocyte primary cultures. With the support of the Rita Allen Foundation and the American Pain Society, the lab is able to explore the communication that occurs between sensory neurons and macrophages (innate immune cells that are critical in injury response) in dorsal root ganglia (DRG). Macrophages in the DRG are a unique population of cells that bear some resemblance to brain microglia, but are functionally distinct and exhibit specific phenotype differences. In response to peripheral injury, DRG macrophages respond to activity in the ascending pain pathways and may alter pain perception. By evaluating the phenotype and function of this unique population, Hanlon hopes to isolate novel and exploitable mechanisms that may be used to develop non-opioid therapeutics for the treatment of persistent pain.



KYLE BAUMBAUER, PH.D.

Assistant Professor
Center for Advancement in Managing Pain
University of Connecticut School of Nursing

Project: Targeting ASIC3 for Disruption of Nociceptor Sensitization Following Spinal Cord Injury

Kyle Baumbauer earned a B.S. in psychology and a B.A. in sociology from the University of Central Florida. He holds an M.A. and Ph.D. in experimental psychology from Kent State University, where he studied molecular mechanisms that allow neurons in the spinal cord to mediate learning and adaptation to the environment. This research contributed to an emerging view of the spinal cord not merely as a channel for signals traveling to and from the brain, but as a dynamic group of nerves with important effects on behavior. Baumbauer continued this area of research while a postdoctoral fellow at Texas A&M University, and explored how painful stimulation impacts spinal cord function to understand how the presence of pain affects the recovery of function after spinal cord injury. Baumbauer then did a second fellowship at the University of Pittsburgh, where he began examining the impact of injury and inflammation on peripheral sensory neuron function.

In 2014 Baumbauer joined the faculty at the University of Connecticut School of Nursing, where his research focuses on unraveling the relationship between alterations in gene expression and sensory neuron function, and how these processes contribute to chronic pain following spinal cord injury. Through these investigations, Baumbauer and his team aim to make advances that aid in the treatment of pathological pain. In addition to the Rita Allen Foundation Baumbauer's research is supported by the National Institute of Neurological Disorders and Stroke. He is also a recipient of a Mary Lawrence Research Development Award from the UConn School of Nursing and has been honored as a Sigma Theta Tau Friend of Nursing.



ARKADY KHOUTORSKY, D.V.M., PH.D.

Assistant Professor
Alan Edwards Centre for Research on Pain
Department of Anesthesia
McGill University

Project: Extracellular Matrix-Mediated Spinal Cord Plasticity in Neuropathic Pain

Arkady Khoutorsky earned a B.Sc. in biology and an M.Sc. in neurobiology, as well as D.V.M. and Ph.D. degrees, from the Hebrew University of Jerusalem. During a postdoctoral fellowship at McGill University, Khoutorsky investigated how regulation of protein synthesis controls neuronal plasticity in the brain and in the pain pathway. He joined McGill's Alan Edwards Centre for Research on Pain in 2016. In addition to the Rita Allen Foundation, Khoutorsky's work is supported by the Canada Foundation for Innovation, and by a NARSAD Young Investigator Grant and a Louise and Alan Edwards Foundation Grant in Chronic Pain Research.

Khoutorsky's lab is examining how neuronal circuits in the spinal cord are remodeled to promote sensitivity to pain. He is interested in the extracellular matrix, a network of proteins that surrounds neurons. In the brain, this matrix appears to restrict the ability of neurons to form the new structures necessary for learning and memory. Enzymes that degrade the matrix are activated in some chronic pain conditions. Khoutorsky and his team are investigating how such degradation impacts spinal cord neurons that normally inhibit pain signals. They aim to determine how changes in the extracellular matrix might enable the neurons to become "hyperexcitable" and inappropriately propagate pain.

ACKNOWLEDGMENTS

THE AWARD IN PAIN is made possible through the partnership of the **Rita Allen Foundation** and the **American Pain Society**.

We are grateful for the efforts and insights of all those who have served on the award review committee over the past 10 years:

Allan Basbaum, Ph.D.

Diana Bautista, Ph.D.

Robert Coghill, Ph.D.

Kathleen Foley, M.D.*

Robert Gereau, Ph.D.

Peter Goadsby, M.D.

Michael Gold, Ph.D.

Charles Inturrisi, Ph.D.#

Michael Jankowski, Ph.D.

Gilles Lavigne, D.M.D., Ph.D.

Jon Levine, M.D., Ph.D.

Patrick Mantyh, Ph.D.

Jianren Mao, M.D., Ph.D.

Jeffrey Mogil, Ph.D.

Gavril Pasternak, M.D., Ph.D.

Frank Porreca, Ph.D.

Steve Prescott, M.D., Ph.D.

Theodore Price, Ph.D.

E. Alfonso Romero-Sandoval, M.D., Ph.D.

Sarah Ross, Ph.D.

Rebecca Seal, Ph.D.

Gregory Scherrer, Ph.D.

Reza Sharif-Naeini, Ph.D.

Hazel Szeto, M.D., Ph.D.

Todd Vanderah, Ph.D.

George Wilcox, Ph.D.

Tony Yaksh, Ph.D.

* Rita Allen Foundation Medical Adviser

Award in Pain Review Committee Chair

Rita Allen Foundation

Elizabeth G. Christopherson, *President and
Chief Executive Officer*

Robbert Dijkgraaf, Ph.D.

William Gadsden, *Chair*

Andrew Golden

Sivan Hong

Landon Jones

The Honorable Thomas H. Kean

Geneva Overholser

Samuel S.-H. Wang, Ph.D.

American Pain Society

Claudia Campbell, Ph.D.

Robert Coghill, Ph.D.

Patrick Dougherty, Ph.D., *Secretary*

Robert Edwards, Ph.D.

Michael Gold, *Liaison to IASP*

Jennifer Haythornthwaite, Ph.D., *Treasurer*

William Maixner, D.D.S., Ph.D., *President Elect*

Edward Michna, J.D., M.D., Pharm.D.

Theodore Price, Ph.D.

Barbara Rakel, Ph.D., R.N.

Barbara St. Marie, Ph.D.

Gary Alan Walco, Ph.D.

Mark S. Wallace, M.D., *Director-at-Large*

David Williams, Ph.D., *President*

Susan Farrell Stock, *Chief Executive Officer*



Molly Sharlach and Ruth Stevens, *Editors*
Kerstin Vogdes Diehn, *Designer*
Allegra Princeton, *Printer*

92 Nassau Street, 3rd Floor
Princeton, New Jersey 08542
609-683-8010
www.ritaallen.org