NIH Investigator Meeting on

Functional Neurocircuits of Interoception

September 29, 2022

NIH National Institutes of Health

Online Program Book

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Agenda

September 29, 2022, 11:30 a.m. – 5:00 p.m. EDT
Open to the Public with Live Videocast

11:30 a.m. – 11:35 a.m. **Opening Remarks**
Dr. David Shurtleff, Deputy Director, National Center for Complementary and Integrative Health (NCCIH), NIH

11:35 a.m. – 11:55 a.m. **Overview and Update of the NIH Interoception Program**
Dr. Wen Chen, Branch Chief, Division of Extramural Research, NCCIH, NIH

11:55 a.m. – 12:20 p.m. **Keynote: Biologically Inspired Neurotechnology to Probe Brain–Organ Communication**
Dr. Polina O. Anikeeva, Massachusetts Institute of Technology

Progress reports from the PIs of NIH grants (15 minutes per presentation; 25-minute Q&A for each session)

12:20 p.m. – 1:45 p.m. **Session 1: Digestive System–Brain Connections**
Moderator: Dr. Heike Müenzberg-Gruening, Pennington Biomedical Research Center

1. **Functional Neural Circuits of Stomach–Brain Interoception**
   Drs. Zhongming Liu and Jiande Chen, University of Michigan
2. **Spinal Sensory Ganglia and Gut Sensation**
   Dr. Ivan E. de Araujo, Icahn School of Medicine at Mount Sinai
3. **Gut-to-Brain Circuits Underlying Fluid Regulation**
   Dr. Yuki Oka, California Institute of Technology
4. **Functional Identification of Vagal Sensory Neurons Innervating the Liver**
   Dr. Young-Hwan Jo, Albert Einstein College of Medicine

1:45 p.m. – 2:05 p.m. **Break**

2:05 p.m. – 3:30 p.m. **Session 2: Pulmonary–Cardiovascular Systems–Brain Connections**
Moderator: Dr. Mark Andermann, Beth Israel Deaconess Medical Center

1. **Dissecting the Interoception Circuit That Controls Airway Constriction**
   Dr. Xin Sun, University of California, San Diego
2. **Unravelling Lung Interoception and Its Functional Consequence in the Developing Ovine Lung**
   Drs. Arlin B. Blood and Christopher G. Wilson, Loma Linda University
3. **Dissecting Neural Circuits for Breathing Patterns**
   Dr. Peng Li, University of Michigan

4. **Defining Subsets of Sympathetic Neurons Mediating Cardiac Neurotransmission**
   Dr. Olujimi A. Ajijola, University of California, Los Angeles

3:30 p.m. – 4:55 p.m. **Session 3: Metabolic, Immune, Muscular, and Multiple Systems–Brain Connections**
Moderator: Dr. Olujimi Ajijola, University of California, Los Angeles

1. **Insular Cortex Estimates Current and Future Bodily States**
   Dr. Mark L. Andermann, Beth Israel Deaconess Medical Center
2. **Metabolic Changes: Connecting Temperature-Sensing Neurons to Sympathetic Adipose Tissue Stimulation**
   Dr. Heike Müenzberg-Gruening, Pennington Biomedical Research Center
3. **Functional Peripheral and Central Vagal Neural Circuits of Interoception Inhibiting Pain**
   Dr. Yu Shin Kim, The University of Texas Health at San Antonio
   Dr. Man-Kyo Chung, University of Maryland, Baltimore
4. **Descending Innervation and Control of Internal Organ Function**
   Dr. Rui M. Costa, Allen Institute

4:55 p.m. – 5:00 p.m. **Closing Remarks**
Dr. Rita Valentino, Director, Division of Neuroscience and Behavior, National Institute on Drug Abuse, NIH

5:00 p.m. **Adjournment**

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Speaker Abstracts

Biologically Inspired Neurotechnology to Probe Brain-Organ Communication

Polina Anikeeva, Massachusetts Institute of Technology

Communication between the central and peripheral nervous systems is increasingly recognized as critical in understanding the phenomena ranging from immune response and metabolism to stress and social behaviors. Yet the tools capable of interfacing with the signaling pathways spanning the enormity of spatiotemporal scales characteristic of brain-organ communication are scarce. Although, the past decade has delivered a wealth of powerful molecular and engineering tools to probe the signaling complexity in the central nervous system, the implementation of these approaches in the peripheral circuits and organs is impeded by their distributed nature, continuous movement, and substantial immune response. This talk will discuss how mimicking structure of the nerves allows creation of fibers with the ability to interrogate peripheral and central nervous systems in behaving mice. For instance, the function of these fibers will be demonstrated in illuminating the gut-brain circuits of nutrient processing and reward. Finally, the presentation will touch upon our group's efforts in developing nanoscale tools to interrogate organ-brain communication with molecular precision using nanomagnetic approaches. These approaches rely on the ability of magnetic nanoparticles to transduce remotely applied weak magnetic fields into a variety of physiological stimuli, and thus allow for wireless control of physiology in behaving mice. The talk will conclude with the discussion of challenges facing these nanomagnetic approaches in vivo and potential biologically informed solutions.

Session 1: Digestive System-Brain Connections

Functional Neural Circuits of Stomach-Brain Interoception

Drs. Zhongming Liu and Jiande Chen, University of Michigan at Ann Arbor

The stomach and the brain interact through peripheral and central neural circuits. Our project aims to map, characterize, and perturb the stomach-brain interactions using magnetic resonance imaging, electrophysiology, chemogenetics, and neural tracing. In this talk, I will report our progress in mapping and understanding the neural circuits that monitor and regulate gastric electrical and mechanical activity, as well as their dynamic coupling.

Spinal Sensory Ganglia and Gut Sensation

Dr. Ivan E. de Araujo, Icahn School of Medicine at Mount Sinai

Gastrointestinal organs are innervated by both vagal and spinal afferents. While much emphasis has been given to vagal pathways, less is known about the role of spinal signaling in interoception. I will discuss recent evidence supporting the notion that spinal, rather than vagal, afferents are the major conveyors of gut mechanical signals to brain. I will also review candidate medullary and cortical spinal targets involved in the central representation of internal tissues and organ volume.

Gut-to-Brain Circuits Underlying Fluid Regulation

Dr. Yuki Oka, California Institute of Technology

Fluid homeostasis is a vital function that regulates the balance between water and sodium. When this balance shifts in one direction, the brain detects the changes and triggers appetite to drive water or sodium intake for compensation. Defining the neural logic of these processes is critical for understanding brain function underlying normal and abnormal appetite. Our goal is to understand how the brain processes internal state information and peripheral signals to regulate goal-oriented behaviors.

In the mammalian brain, thirst is mainly regulated by the forebrain structure called lamina terminalis (LT). We previously identified that thirst-driving neurons in the LT are rapidly suppressed upon water drinking. This thirst satiation is caused by two factors including oropharyngeal mechanical and gut osmolality signals. In this presentation, I will focus on the sensory mechanisms of gut osmolality detection. We examined sensory representation in sensory ganglia and osmolality detection mechanisms through specific sensory neurons at the periphery. We further investigated how gut osmolality signals affect brain thirst circuits by combining in vivo optical recording and loss-of-function in a peripheral sensory branch. These results reveal an additional piece to understand how our body and brain cooperate to maintain body fluid balance.

Functional Identification of Vagal Sensory Neurons Innervating the Liver

Dr. Young-Hwan Jo, Albert Einstein College of Medicine

The primary goals of our project are to thoroughly examine the molecular and cellular identity of liver-projecting vagal sensory neurons. We use the Advillin (Avil)^{CreERT2} transgenic line and the Calcitonin gene-related peptide 1(Calca)^{Cre} strain to identify liver-projecting vagal sensory neurons. Retrograde tracing reveals that vagal sensory nerves innervate hepatocytes situated primarily around the portal vein. This finding is important because the presence of fenestrations in the sinusoidal capillaries may facilitate sensory nerve endings to sense interoceptive signals. In addition, the central terminals of liver-innervating vagal sensory neurons are found in the nucleus tractus solitarius and the dorsal motor nucleus of the vagus. To determine the functional consequences of the loss of functions of a liver-brain neural circuit, we ablate liver-projecting vagal sensory neurons. Ablating liver-projecting Avil-positive neurons causes a reduction in body weight compared to the control group during high-fat feeding. This reduction is significantly associated with a decrease in fat mass. Moreover, deleting these liver-projecting sensory neurons prevents hepatic steatosis in mice fed a high-fat diet. Interestingly, the open field test that evaluates locomotor activity, anxiety, and willingness to explore reveals that male mice without liver-projecting Avil-positive cells exhibit a significant increase in the duration of time spent in the central square, suggesting that they are more eager to explore the central part of the arena. Taken together, our results support the interpretation that liver-projecting vagal sensory neurons may play a critical role in energy metabolism and brain functions, particularly psychological disorders, including depression and anxiety.

Session 2: Pulmonary-Cardiovascular Systems-Brain Connections

Dissecting the Interoception Circuit that Controls Airway Constriction

Dr. Xin Sun, University of California, San Diego

Chronic allergen exposure is a major cause of asthma featuring exaggerated airway constriction which can be life-threatening. Such hyperreactivity is driven by contraction smooth muscles that wrap around airways. How the neuroimmune axis controls hyperreactivity remains poorly understood. In work supported by NIH, we uncovered molecular, anatomical and functional evidence delineating a complete circuit that is necessary and sufficient for allergen-induced airway hyperreactivity. Molecular definition of this circuit allows for targeted neural modulation of allergen responses.

Unravelling Lung Interoception and its Functional Consequence in the Developing Ovine Lung

Drs. Arlin B. Blood & Christopher G. Wilson, Loma Linda University

The fetal lung is richly innervated during development but it is unknown whether these neurons participate in the orchestration of lung formation and interoceptive communication to and from the central nervous system (CNS). The interoceptive link between the lung and CNS includes the relay of mechano- and chemo-sensitive information to the brainstem—which is critical in the newborn for maintaining pulmonary gas exchange in light of behavioral changes, environmental stressors, and immune responses to inflammatory pathogens. However, we lack a mechanistic understanding of how communication between the fetal CNS and lung is established, and to what extent communication between these organs informs their development. We hypothesize that intrinsic and extrinsic lung interoceptive units play a key role in normal development of the lung and respiratory control centers. To address this hypothesis, we use retrograde tracer technology, cell-specific immuno-labeling, surgical intervention, and histopathological assessment to characterize lung development and innervation. We use physiological signal analyses (time-series and frequency domain) to assess changes in vagus activity and heart-rate variability in developing sheep. Lastly, we assess pulmonary vascular function, airway mechanics, and gas exchange following c-section delivery and in response to acute hypoxia and methacholine challenges. The outcomes of these studies will fill critical knowledge gaps for understanding how interoception affects lung and CNS development and function in sheep, a historically important model of human perinatal lung development and physiology. Our focus for this meeting will be summarizing advantages of the sheep model, our analysis workflow, and progress over the past year.

Dissecting Neural Circuits for Breathing Patterns

Dr. Peng Li, University of Michigan at Ann Arbor

Breathing is a vital function constantly regulated by the interoceptive signals from the body, and breathing patterns are known to impact emotional and cognitive processes. Breathing patterns with essential pulmonary interoception functions, such as sighing and coughing, are relevant to many pathological conditions. Sighing is an augmented breath with a deep, double-size inspiration that is dramatically induced in hypoxia. In contrast, coughing is a protective breathing pattern with a characteristically enlarged expiration phase triggered by tussive agents exposed in the airways. However, how these breathing patterns are regulated by interoceptive signals and how they go awry in diseases are largely unknown. Here we identified two neuronal populations with distinct gene expression, connectivity, neural activity, and function, in the nucleus of the solitary tract (NTS), a relay center in the brain that receives interoceptive afferent signals from the visceral organs. These neurons respectively mediate hypoxia-induced sighing and tussive challenge-induced coughing, two discrete breathing patterns associated with different interoceptive signals. We will integrate state-of-the-art techniques to identify the neural circuits and pathways underlying these two interoceptive processes in vivo in freely moving mice. By focusing on these two distinct NTS neuron populations and neural circuits, we will delineate the distinct interoceptive afferent pathways from the periphery to the brain, identify the brain regions that mediate sighing and coughing, and define the higher brain regions for interpreting and integrating these distinct interoceptive signals.

Defining Subsets of Sympathetic Neurons Mediating Cardiac Neurotransmission

Dr. Olujimi A. Ajijola, University of California Los Angeles

The soma of postganglionic sympathetic neurons innervating the heart primarily reside in the stellate ganglion (SG), along with those of neurons innervating other organs and tissue beds. Whether cardiac-innervating stellate ganglionic neurons (SGNs) exhibit diversity and distinction from those innervating other tissues is not known. We leveraged retrograde tracing techniques using adeno-associated virus (AAV) expressing fluorescent proteins (GFP or Td-tomato) with single cell RNA sequencing to identify and resolve the transcriptomic profiles of SGNs innervating the heart. We investigated electrophysiologic, morphologic, and physiologic roles for subsets of cardiac-specific neurons, and report that these subtypes exhibit distinct morphological, neurochemical, and electrophysiologic characteristics, including differential roles in cardiac physiologic and pathophysiologic control.

Session 3: Metabolic, Immune, Muscular, and Multiple Systems-Brain Connections

Insular Cortex Estimates Current and Future Bodily States

Dr. Mark L. Andermann, Beth Israel Deaconess Medical Center

Insular cortex (InsCtx) is a key site that integrates diverse body signals, and is thus considered a key hub for interoception. Based on human neuroimaging and lesion studies, prevailing models suggest that InsCtx receives sensory information from throughout the body (e.g., following food or water deficits), and integrates this with meaningful sensory cues (e.g., a restaurant logo), planned actions, and expected outcomes (e.g., entering and ingesting a specific food or drink) to help guide decision making. Such theories implicate InsCtx in computing interoceptive predictions. However, the precise InsCtx activity patterns reflecting different physiological states and their potential updating by predictive cues remain unclear. In this talk, I will describe our studies imaging populations of neurons in InsCtx and, more recently, in lateral parabrachial nucleus (LPBN) across natural and artificial states of hunger and thirst. InsCtx neurons were driven by cues predicting food/water, but also showed gradual changes in ongoing activity reflecting physiological state transitions. During hunger/thirst, food/water cues rapidly and transiently shifted the pattern of InsCtx population activity towards representations of the future satiety state. In sated mice, artificial activation of hypothalamic neurons that drive hunger/thirst restored selective behavioral and InsCtx responses to food/water cues, but did not restore InsCtx representations of physiological state. These data suggest that InsCtx integrates visceral-sensory inputs regarding current physiological state with hypothalamus-gated limbic inputs signaling upcoming ingestion of food/water to compute predictions of future physiological states. We are currently investigating whether predictive signals in InsCtx can *simulate* interoceptive sensations via centrifugal projections to the LPBN.

Metabolic Changes: Connecting Temperature Sensing Neurons to Sympathetic Adipose Tissue Stimulation

Dr. Heike Müenzberg-Gruening, Pennington Biomedical Research Center, Baton Rouge

Dynamic changes in the adipose tissue-derived, interoceptive hormone leptin during fasting are well known, and leptin receptor signaling in the CNS importantly maintains metabolic health. However, the precise regulation of adipose tissue to brain circuit is incompletely understood. Some literature suggests the requirement of sympathetic adipose tissue activation via β3-adrenergic receptors to induce energy expenditure and suppress leptin levels, yet fasting robustly suppresses energy expenditure and is thought to require reduced sympathetic tone at least in brown adipose tissue (BAT). In order to directly investigate the role of sympathetic activation of select adipose tissue depots we developed a retrograde tracing system to allow chemogenetic activation of select adipose tissue depots in anesthetized and free moving mice. We further use histological and electrophysiology validation methods to ensure correct targeting and proper activation of sympathetic neurons. Our data show that sympathetic activation of interscapular BAT alone is insufficient to induce BAT thermogenesis and suppress leptin levels, instead it acutely counteracted β3-adrenergic signaling. Conversely, prolonged sympathetic BAT activation enhanced β3-adrenergic signaling and prevented metabolic disease progression in diet induced obese mice. Our data indicates a more complex system of sympathetic adipose tissue activation on metabolism than suggested by the extensive literature using β3-adrenergic stimulation as surrogate for sympathetic activation. Future studies will further study how sympathetic activation of adipose tissue depots contributes to metabolic regulation and changes in leptin levels as an important future goal to understand the metabolic role of adipose tissue to brain circuits in health and disease.

Functional Peripheral and Central Vagal Neural Circuits of Interoception Inhibiting Pain

Dr. Yu Shin Kim, University of Texas Health Science Center

Vagal stimulation modulates intractable chronic pain in patients. However, the road to improving chronic pain management through the regulation of interoceptive inputs is blocked by our ignorance of the neurobiological mechanisms whereby vagal activity modulates chronic pain, posing a significant hurdle. Thus, we focus on the neural mechanisms of vagal modulation in a mouse model of forced mouth opening, a surrogate model of temporomandibular disorders (TMD). Here, we try to determine neural mechanisms by which interoception inhibits pain. Our central hypothesis is that vagal interoceptive circuits intersect with peripheral and central nociceptive pathways to inhibit pain from the temporomandibular joint (TMJ). Our data showed that forced mouth opening (FMO) induces persistent mechanical hyperalgesia from TMJ, and TMJ pain was attenuated by electrical vagal stimulation (eVS) in mice. The TMJ is simultaneously innervated by nociceptive trigeminal afferents and auricular branch vagal afferents, suggesting that TMJ is a unique tissue in which nociception is directly regulated by vagal afferent terminals. Our data showed that vagal afferents contain dopaminergic neurons, and dopamine injection into TMJ suppresses nociception and pain. Finally, interoceptive inputs through vagus nerve are predominantly transmitted to the nucleus tract solitarius (NTS), which relays signals into multiple regions of brain, including regions implicated in chronic pain. The outcomes lead to a better understanding of interoceptive regulation of chronic pain, especially from TMD.

Descending Innervation and Control of Internal Organ Function

Dr. Rui M. Costa, Allen Institute and Columbia University

Adaptive control of behavior is critical for survival. Even a simple movement, like extending an arm, requires the activation of many neuronal populations across the nervous system. For example, picking an apple will trigger both muscle activity and the expectation of food, with conditioned release of insulin by the pancreas. Hence adaptive behavior requires the coordination of an organism's actions (effected through muscles) with its physiological internal states (effected through other organs). To better understand this, we have been studying conditioned insulin release, conditioned immunosuppression, and the physiological stress response, which are controlled by the pancreas, spleen, and adrenal medulla respectively. We have leveraged our expertise to dissect the neuronal circuits and principles governing the learning and adaptive "motor" control of internal organ function. Our high-resolution anatomical mapping of the innervation of these organs revealed that different populations of the celiac-mesenteric ganglia sympathetic neurons innervate pancreas versus spleen, and we have started imaging the activity of these neurons during physiological responses. Remarkably, a large proportion of the neurons innervating the thoracic preganglionic spinal cord targeting these three organs emerges from the cortex. What is more surprising perhaps, is that although there is innervation from sensory and prefrontal cortices much of this descending cortical innervation emanates from the motor cortex. We therefore hypothesize that learning to select the appropriate responses in internal organs is mediated by higher-order brain circuits, and follows principles similar to those used for motor responses.

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Speaker Biographies

Olujimi Ajijola, University of California, Los Angeles School of Medicine
Olujimi Ajijola, M.D., Ph.D. completed his undergraduate studies at the University of Virginia, and received his medical degree from Duke University. He went on to the Massachusetts General Hospital for residency training in internal medicine, and completed clinical fellowships in cardiovascular medicine and cardiac electrophysiology at UCLA. He received a Ph.D. in Molecular, Cellular, and Integrative Physiology at UCLA, as part of the Specialty Training and Advanced Research (STAR) program. He is interested in novel approaches for cardiac arrhythmias, and performs invasive cardiac electrophysiological procedures. His research interests revolve around peripheral neural circuits that control cardiac function in health and disease, including neural interventions that alleviate progressive cardiac dysfunction and arrhythmias. In addition to the NIH Director's New Innovator award, he is a recipient of the Jeremiah Stamler Cardiovascular Research Award, an A. P. Giannini Foundation post-doctoral award, and a Young Physician Scientist Award from the American Society for Clinical Investigation (ASCI). He is a member of the New Voices program of the National Academies of Science, Engineering, and Medicine. of the UCLA Cardiac Arrhythmia Center & EP Programs, and directs the Neurocardiology Research Program at UCLA. He co-directs the NIH-funded UCLA-Caltech Medical Scientist Training Program

Mark Andermann, Beth Israel Deaconess Medical Center (BIDMC)
Mark Andermann, Ph.D. is a Professor at Harvard Medical School in the Division of Endocrinology, Diabetes, and Metabolism, Department of Medicine at BIDMC. Dr. Andermann received undergraduate training in mathematics and physics at McGill University. His Ph.D. training focused on functional maps in rat barrel cortex and trigeminal ganglion at MIT and Harvard. He carried out postdoctoral training at the Helsinki University of Technology, where he used non-invasive brain-computer interfaces to study auditory selective attention in humans. He then completed a second postdoctoral fellowship at Harvard Medical School, where he developed new tools for studying the neural basis of visual perception using cellular imaging methods in behaving mice. Dr. Andermann's lab seeks to understand how the brain senses the needs of the body and manages competing motivational drives including the drives to seek food, water, mates, and safety, and how these drives determine the contents of our imagery and our exteroceptive and interoceptive attentional focus. To achieve these goals, the lab employs cellular and subcellular imaging methods to track the activity of the same brain cells across weeks in brainstem, thalamus, cortex, amygdala, and hypothalamus as mice seek food, water, mates, or safety.

Polina Anikeeva, Massachusetts Institute of Technology
Polina Anikeeva, Ph.D. received her B.S. in Physics from St. Petersburg State Polytechnic University, and a Ph.D. in Materials Science and Engineering from MIT. She completed her postdoctoral training in neuroscience at Stanford, where she created devices for optical stimulation and recording from brain circuits. She joined MIT faculty in 2011 and is currently the Stavros and Matoula Salapatas Professor of Materials Science and Brain and Cognitive Sciences. She serves as the director of the Brain-Body Center at the McGovern Institute for Brain Research. Dr. Anikeeva's Bioelectronics research group focuses on the development of minimally invasive approaches to record and modulate physiology of the nervous system, and particularly in the context of brain-body communication. Dr. Anikeeva is a recipient of NSF CAREER Award, DARPA Young Faculty Award, the TR35, Vilcek Prize for Creative Promise, and the 2021 NIH Director's Pioneer Award.

Ivan de Araujo, Icahn School of Medicine at Mount Sinai
Ivan de Araujo, D.Phil. is a Professor of the Nash Department of Neuroscience at the Icahn School of Medicine at Mount Sinai, New York. His research focuses on identifying and characterizing the large-scale neural networks that link the body to the brain, with an emphasis on the gut-brain axis. One goal of his research is to characterize the spinal circuitry innervating visceral organs, and how this circuitry conveys peripheral information to the brain. Dr. de Araujo majored in Philosophy at the University of Brasilia, followed by postgraduate work in Artificial Intelligence at the University of Edinburgh. He obtained his doctorate (D.Phil.) in Medical Imaging at the University of Oxford.

Arlin B. Blood, Loma Linda University
Arlin B. Blood, Ph.D. is an Associate Professor of Physiology in the Lawrence D. Longo, MD Center for Perinatal Biology at Loma Linda University. His research group specializes in the study of cardiopulmonary physiology of the fetus and newborn, with particular emphasis on the remarkable cardiopulmonary transition that takes place at birth, and pulmonary and cerebral vascular adaptation of the fetus and newborn to chronic stress such as hypoxia. In addition to his 24 years of experience in basic science research in this field, Dr. Blood also spent 15 years as Director of Neonatal Research in the Division of Neonatology at Loma Linda University where he oversaw numerous translational and clinical studies in the neonatal and pediatric ICU. In addition to his research, Dr. Blood is Co-Director of the Pulmonary Block of the medical school curriculum at LLU.

Jiande Chen, University of Michigan

Jiande Chen, Ph.D. is Professor of Medicine and Director of Neuromodulation in the Division of Gastroenterology and Hepatology and Department of Biomedical Engineering at University of Michigan. Dr. Chen has received more than 100 research grants from various government and state agents, such as National Institutes of Health, U.S. Department of Veterans Affairs, Department of Defense, and industries. Dr. Chen has trained more than 100 doctoral students, post-docs, and young scholars, filed more than 30 U.S. patents, and published more than 450 peer-reviewed papers in leading biomedical journals. Dr. Chen's current research interest is in the areas of brain-gut interaction and neuromodulation and its applications for treating obesity, diabetes, and disorders of brain-gut interaction and inflammatory bowel diseases.

Wen Chen, NCCIH

Wen Chen, Ph.D. formerly a program director at NCCIH, now serves as the Branch Chief for the Basic and Mechanistic Research Branch. The branch supports research using a variety of research approaches, ranging from biochemical, cellular, physiological, and imaging to behavioral methods, to investigate the basic science and mechanistic processes of complementary and integrative health in biological systems including cells, tissues and organs, animal models, and humans. Dr. Chen's current portfolio focuses on neurobiology and integrative physiology of complementary approaches ranging from mind and body practices (e.g., acupuncture and meditation) to natural products, including Chinese herbal medicine. Dr. Chen holds a Ph.D. in biological chemistry and molecular pharmacology from Harvard University. Under the tutelage of Dr. Michael E. Greenberg at Harvard Medical School, she studied the epigenetic regulation of activity-dependent expression of brain-derived neurotrophic factor (BDNF). She also earned a master's degree in medical sciences as part of the Harvard-Markey Medical Scientist training program at Harvard Medical School. Dr. Chen did her postdoctoral training in proteomics at Massachusetts Institute of Technology. Prior to joining NCCIH, Dr. Chen worked as a scientific editor at NEURON, a program coordinator at the National Institute of Mental Health, and a program director at the National Institute on Aging, overseeing the research portfolio on sensory and motor disorders of aging.

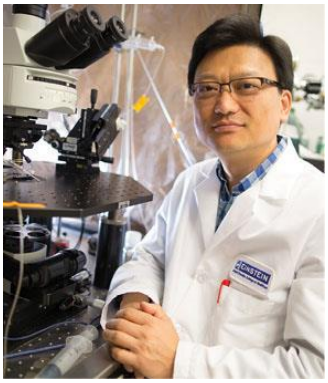
Man-Kyo Chung, University of Maryland School of Dentistry

Man-Kyo Chung, Ph.D., D.M.D. is a Professor in the Department of Neural and Pain Sciences, interim assistant dean of research for the University of Maryland School of Dentistry. He received his D.M.D.-Ph.D from the Kyung Hee University, Seoul Korea. After postdoctoral training at the Johns Hopkins University, Dr. Chung joined the University of Maryland School of Dentistry in 2008. Since then, he has been studying neurobiological mechanisms of craniofacial muscle and neuropathic pain focused on the roles of trigeminal nociceptive afferents. Dr. Chung is an expert in electrophysiological, biophysical, and genetic analysis of nociceptors and nociceptive ion channels including transient receptor potential vanilloid 1 (TRPV1), a receptor for capsaicin. He studies molecular mechanisms and how a capsaicin receptor produces and alleviates craniofacial pain. Dr. Chung is also interested in how pain-sensing nerves modulate remodeling of bone surrounding teeth. His research has been supported by the Federal government, the state of Maryland, and industry. In particular, the innovation and merit of his projects was recognized by the National Institute of Dental and Craniofacial Research

(NIDCR), and Dr. Chung was recently selected as a recipient of the NIDCR Award for Sustaining Outstanding Achievement in Research. Throughout his career at the University of Maryland-Baltimore (UMB), Dr. Chung has been serving to enrich UMB pain research community. Currently, he is serving as a co-director of the University of Maryland Center to Advance Chronic Pain Research to promote multidisciplinary research, education, and management of chronic pain in the UMB campus.

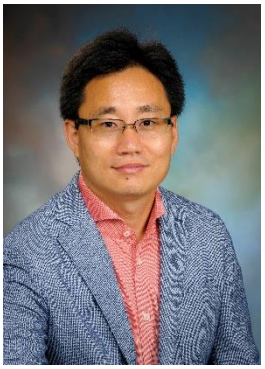
Rui Costa, Allen Institute

Rui Costa, Ph.D. is the President and CEO of the Allen Institute. He did his Ph.D. studies with Dr. Alcino Silva at UCLA and postdoctoral work with Dr. Miguel Nicolelis at Duke University. He became a Section Chief at the National Institutes of Health in 2006, an Investigator of the Champalimaud Neuroscience Program in 2009, and a Professor at Columbia University in 2016. He was co-Director of Champalimaud Research and Director/CEO of the Zuckerman Mind Brain Behavior Institute at Columbia University. He is an elected member of EMBO and the National Academy of Medicine. His laboratory develops and uses genetic, electrophysiological, optical, and behavioral approaches to investigate how the brain adaptively controls overt behavior and internal organ function. His lab uncovered that direct and indirect striatal pathways are concurrently active during movement initiation, that this activity is action-specific and needed for proper movement—challenging the classical Go/NoGo model. They also demonstrated dopaminergic neuron heterogeneity by showing that a sub-population of them are active before movement and critical for initiating and invigorating future movement, but not reward coding. Finally, they revealed distinct cortico-basal ganglia circuit mechanisms mediating goal-directed actions versus habits, and showed that plasticity in basal ganglia is critical to reinforce cortical activity patterns that lead to reward. More recently, he has been investigating the descending mechanisms related to adaptive control of the physiological response of internal organs.



Young-Hwan Jo, Albert Einstein College of Medicine

Young-Hwan Jo, Ph.D. is an Associate Professor of Departments of Medicine and Molecular Pharmacology at Albert Einstein College of Medicine. Dr. Jo received his Ph.D. in Neuroscience from the University of Louis Pasteur in France in 1998. Dr. Jo did his postdoctoral training in Neuroscience at Columbia University. Dr. Jo's research program focuses on studying the neurobiology of energy homeostasis in general and hypothalamic neural mechanisms associated with obesity and metabolic dysregulation in particular.



Yu Shin Kim, University of Texas Health at San Antonio (UTHSA)

Yu Shin Kim, Ph.D., M.S. is an associate professor at the UTHSA. His research is focused on the function and regulation of sensory modalities, including pain, itch, and gentle touch. To delineate underlying mechanisms, his group developed tools to visualize the peripheral neuronal hypersensitivity corresponding to pain and itch through well-validated tissue preparation, excellent spatial resolution, high-efficiency simultaneous imaging of multiple neurons, and finally a stable expression of genetically-encoded Ca^{2+} indicator and voltage sensor. My group developed an imaging technique that allows simultaneous monitoring of the activation of >1,800 neurons in the dorsal root ganglion (DRG) and >2,800 neurons in the trigeminal ganglion (TG) neurons. Using these tools and cutting-edge techniques we developed, we study chronic pain and temporomandibular disorders (TMD) pain. Particularly, we examine coupling activation (adjacent neurons in DRG activate together after certain stimuli) of primary sensory neurons as a novel plasticity mechanism for chronic pain. We currently investigate functional peripheral and central vagal neural circuits of interoception inhibiting pain. The major goal of this project is to determine vagal interoceptive circuits interacting with peripheral and central nociceptive pathways to inhibit pain from TMJ.

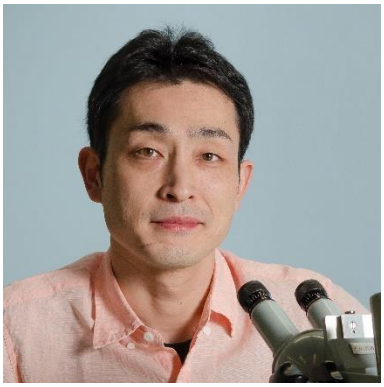
Peng Li, University of Michigan

Peng Li, Ph.D. is an Assistant Professor at the Life Sciences Institute at the University of Michigan. Dr. Li completed his undergraduate study in Biological Sciences at Tsinghua University in China, and then received his Ph.D. degree in Neuroscience from University of Southern California. After completing his graduate work, Dr. Li joined Dr. Mark Krasnow's laboratory at Stanford University and the Howard Hughes Medical Institute to study neural control of breathing. During this time, Dr. Li and his colleagues identified the neuropeptide circuit underlying a breathing pattern variant—sighing. In 2018, Dr. Li joined the Life Sciences Institute faculty at the University of Michigan. His laboratory is working on understanding the molecular and neural basis of how the brain and body interact through respiratory behaviors.

Zhongming Liu, University of Michigan Ann Arbor

Zhongming Liu, Ph.D. is an Associate Professor of Biomedical Engineering, Electrical and Computer Engineering at the University of Michigan Ann Arbor, where he directs the Laboratory of Integrated Brain Imaging and the Engineering Preclinical Imaging Center. His research group develops and uses advanced techniques for imaging, recording, stimulating, and modeling the brain to accelerate progress in neuroscience, neural engineering, and artificial intelligence.

Heike Müenzberg-Gruening, Pennington Biomedical Research Center
Heike Müenzberg-Gruening, Ph.D. is a Professor at the Pennington Biomedical Research Center, and head of the Central Leptin Signaling laboratory in the Division of Neurobiology of Nutrition & Metabolism. She received her Ph.D. at the University of Hamburg, Germany in Endocrinology and Physiology, and did her postdoctoral work at the Beth Israel Deaconess Medical Center/Harvard Medical School in Boston and the University of Michigan in Ann Arbor to research central leptin signaling mechanisms and obesity. Dr. Müenzberg-Gruening studies central and peripheral neuronal circuitries that affect energy homeostasis with specific focus on energy expenditure adaptations. Dr. Müenzberg-Gruening is particularly interested to understand the importance of sympathetic activation of brown and white adipose tissue to regulate the interoceptive hormone leptin and its feedback control of central energy expenditure circuits. Her work uses molecular-genetic viral tools to manipulate neuronal activity or delete leptin receptors from select neuronal populations. Dr. Müenzberg-Gruening's laboratory also spearheaded the use of whole body tissue clearing to highlight profound differential innervation of brown vs. white adipocytes and developed viral tracing techniques to target sympathetic neurons for anatomical, genetic, and functional investigation of adipose tissue depot-specific innervation in metabolism.



Yuki Oka, California Institute of Technology
Yuki Oka, Ph.D. is a professor of Biology and Neuroscience at California Institute of Technology. Dr. Oka received his Ph.D. in neurobiology at the University of Tokyo. Dr. Oka did his postdoctoral training at UC San Diego and Columbia University. The main focus of Dr. Oka's laboratory is to understand molecular and neural mechanisms of body fluid balance.

David Shurtleff, National Center for Complementary and Integrative Health (NCCIH)

David Shurtleff, Ph.D. is Deputy Director of the National Center for Complementary and Integrative Health (NCCIH) at the National Institutes of Health (NIH), the leading Federal agency for research on integrative and complementary health practices. Dr. Shurtleff is also the Acting Scientific Director and Acting Chief for both the Clinical Investigations Branch and the Pain and Integrative Neuroscience Branch, Division of Intramural Research. He served as Acting Director of NCCIH from October 2017 to November 2018. Dr. Shurtleff's career at NIH has focused on providing leadership and fostering an extensive research portfolio in the basic behavioral and neurosciences—cognitive studies, behavioral economics, decision theory, and risk-taking—and a broad spectrum of research that has contributed to cutting-edge research related to drug abuse, addiction, and their treatment. Dr. Shurtleff came to NCCIH from the National Institute on Drug Abuse (NIDA), where he served as the Acting Deputy Director. At NIDA, he helped develop, implement, and manage the Institute's broad grant portfolio covering basic cellular, molecular, and systems neurobiology as well as behavior, treatment, medication development, clinical neuroscience, clinical trials, prevention, and health services research. Dr. Shurtleff began his career at NIDA as a health scientist administrator in the Behavioral Sciences Research Branch (1995 to 1997). He then became Acting Deputy Director of NIDA's Division of Neuroscience and Behavioral Research (1997 to 2000) and later the Division's Deputy Director (2000 to 2001). From 2001 to 2011, Dr. Shurtleff served as the Director of NIDA's Division of Basic Neuroscience and Behavioral Research. Prior to joining NIDA, Dr. Shurtleff was a research psychologist at the Naval Medical Research Institute in Bethesda, Maryland, where he conducted basic behavioral, electrophysiological, cognitive, and field research on a variety of issues related to cognitive performance, environmental stress, and peripheral neuropathy. He also served as a research fellow at the Walter Reed Army Institute of Research in the Department of Medical Neurosciences. Dr. Shurtleff holds a B.S. degree from the University of Massachusetts. He received his M.A. and Ph.D. degrees in experimental psychology from American University. Among his many honors and awards are the NIH Director's Award for outstanding leadership, vision, dedication, and oversight in developing the NIH Blueprint Neurotherapeutics Grand Challenge, and the NIH Director's Award for outstanding contributions to the development and advancement of diverse programs in basic neuroscience and behavioral research.

Xin Sun, University of California, San Diego

Xin Sun, Ph.D. is a Professor of Pediatrics and Biological Sciences at University of California, San Diego. She obtained her Ph.D. at Yale University and conducted postdoctoral training at University of California, San Francisco. The Sun lab studies lung development, stem cells, lung disease mechanisms, as well as lung, neural, and immune crosstalk. The team uses CRISPR/Cas9 genome editing to generate genetic mouse models of human diseases to interrogate disease mechanisms. Dr. Sun leads a research center under the LungMAP consortium to generate open-source single cell transcriptomic and epigenomic datasets of the newborn-pediatric-adult human lung for the community. Dr. Sun has also devoted her time in teaching, and served as a Director of the Cold Spring Harbor Mouse Development, Stem Cells and Cancer course.

Rita Valentino, Division of Neuroscience and Behavior (DNB), National Institute on Drug Abuse (NIDA)

As the director of DNB, Dr. Rita Valentino, Ph.D., leads program staff to set a vision that advances the basic and clinical research mission of NIDA to elucidate the neurobiological underpinnings of substance use disorders from the molecular to behavioral level and to discover approaches for treating it. She bridges DBN with DTMC and DESPR by promoting translation from target discovery to drug development and by using epidemiology to inform research directions. She represents NIDA on trans-NIH initiatives including BRAIN, the Blueprint for Neuroscience Research, and CCRWH. Her career spans 26 years of academic, research, and leadership experience in neuropsychopharmacology and stress neurobiology. She previously directed the Stress Neurobiology Division within the Department of Anesthesiology at The Children's Hospital of Philadelphia, and was a Professor of Anesthesiology and Critical Care at the University of Pennsylvania School of Medicine, Philadelphia. Dr. Valentino is particularly recognized for her research on the neurobiology of stress, the impact of sex, age and coping style on behavioral and cognitive health, and how this can determine vulnerability to substance use. She is a Fellow of the American College of Neuropsychopharmacology and a Fellow of the American Society for Pharmacology and Experimental Therapeutics.

Christopher Wilson, Loma Linda University, School of Medicine

Christopher G. Wilson, Ph.D. is a Professor in the Lawrence D. Longo, MD Center for Perinatal Biology at Loma Linda University, School of Medicine. Dr. Wilson's research interests are focused on mammalian autonomic control networks in the central nervous system. For the past 20 years, he has focused on translational research and worked closely with Pediatricians and Critical Care physicians to study the role that neuroinflammation plays in disrupting cardiorespiratory control in pre-term infants and how this impacts autonomic rhythms more broadly. Dr. Wilson received his Ph.D. in Physiology from the University of California, Davis. He then did post-doctoral work at NINDS in the Laboratory of Neural Control. Before coming to LLU, he worked at Case Western Reserve University and was Director of the Developmental Neurobiology Laboratory, Department of Pediatrics. In addition to heading his own research laboratory, Dr. Wilson is the Associate Director of the Neuroscience, Systems Biology, and Bioengineering graduate program and teaches medical, graduate, and dental students at LLU.