12th Annual GCC Translational Pain Research Conference

May 24-25, 2023

Houston, Texas

Gulf Coast Consortia
QUANTITATIVE BIOMEDICAL SCIENCES

The Gulf Coast Consortia (GCC), located in Houston, Texas, is a dynamic, multi-institution collaboration of basic and translational scientists, researchers, clinicians, and students in the quantitative biomedical sciences, who benefit from joint training programs, topic-focused research consortia, shared facilities and equipment, and exchange of scientific knowledge. Working together, GCC member institutions provide a cutting-edge collaborative training environment and research infrastructure beyond the capability of any single institution. GCC research consortia gather interested faculty around research foci within the quantitative biomedical sciences and currently include Translational Pain Research, Antimicrobial Resistance, Cellular and Molecular Biophysics, Innovative Drug Discovery and Development, Immunology, Mental Health Research, Regenerative Medicine, Single Cell Omics, Theoretical and Computational Neuroscience. GCC training programs currently focus on Biomedical Informatics, Computational Cancer Biology, Molecular Biophysics, Pharmacological Sciences, Precision Environmental Health Sciences and Antimicrobial Resistance. Current members include Baylor College of Medicine, Rice University, University of Houston, The University of Texas Health Science Center at Houston, The University of Texas Medical Branch at Galveston, The University of Texas M. D. Anderson Cancer Center, Institute of Biosciences and Technology of Texas A&M Health Science Center and Houston Methodist Research Institute.

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For today's conference use hashtag:

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Gulf Coast Consortia - Research

11th Annual GCC Translational Pain Research Conference
May 24-25, 2023

Day 1

1:00	Welcome **Suzanne Tomlinson**, Gulf Coast Consortia **Peter Grace**, Univ. of Texas MD Anderson Cancer Center
Convener:	Andrew Shepherd, Univ. of Texas MD Anderson Cancer Center
1:05	**Keynote Presentation** *Central Pain Processing Circuits* **Fan Wang**, Massachusetts Institute of Technology
Convener:	Shivani Ruparel, Univ. of Texas Health Science Center San Antonio
1:35	*Diversity in Mechanically Activated Current Responses for Trigeminal Ganglion Sensory Neurons Innervating Masseter Muscle* **Karen Lindquist**, Univ. of Texas San Antonio
1:50	*Targeting Peripheral Opioid Receptor Biochemistry to Improve Analgesia* **Nathan Jeske**, Univ. of Texas San Antonio
2:05	*Memory-Related Induction Mechanisms Trigger Persistent Hyperexcitability of Nociceptors* **Alexis Bavencoffe**, Univ. of Texas McGovern Medical School
2:20	*Ginger Root Extract Mitigates Neuropathic Pain Via Gut-Brain-Axis* **Chwan-Li (Leslie) Shen**, Texas Tech Univ. Health Sciences Center
2:35	Break
Convener:	Dorina Papageorgiou, Baylor College of Medicine
2:45	*Neuropathic Pain Induces Microglial Reactivity in Sensory and Affective Brain Regions* **Rafael Cazuza**, Univ. of Texas MD Anderson Cancer Center
3:00	*Electroencephalogram Activity of Participants with Chronic Pain that Use Cannabinoids* **AmberHarris Bozer**, Tarleton State Univ.
3:15	*Sensory Neuron-Specific Transmission and Voltage Dynamics and Neuronal Plasticity Changes* **Yu Shin Kim**, Univ. of Texas Health Science San Antonio
3:30	*Bidirectional Relationship Between Opioid Sensitivity and Neuronal Excitability* **Anibal Garza Carbajal**, Univ. of Texas Health Science Houston

Convener: Pat Dougherty, Univ. of Texas MD Anderson Cancer Center

3:45 Data Blitz Presentations

Student Data Blitz Presenters

Characterization of Trigeminal Sensory Neurons Innervating the Temporomandibular Joint Poster 2
Jessie Alfaro, Univ. of Texas Health San Antonio

Precision Medicine MRI Neuromodulation Enhances Decoding for Swallow Control Targeted for the Alleviation of Lower Cranial Neuropathy Poster 5
Alexandra Bishop, Baylor College of Medicine

The Role of an Extracellular Kinase in NMDAR-Dependent Pain Poster 8
Hajira Elahi, Univ. of Texas at Dallas

Effects of SGC Stimulation on DRG Neurons Poster 10
Chrystine Gallegos, Univ. of Texas Health Science Center Houston

The Role of Meteorin in Cisplatin Induced Peripheral Neuropathy Poster 12
Lucy He, Univ. of Texas at Dallas

The Role of Sigma-2/TMEM97 in the Context of Affective and Pain Behaviors Poster 13
Veronica Hong, Univ. of Texas at Dallas

Sex-Dependent Differences in the Genomic Profile of Lingual Sensory Neurons in Naïve and Tongue-Tumor Bearing Mice Poster 18
Jaclyn Merlo, Univ. of Texas Health San Antonio

Elucidating the Role of IGF2 in the Dorsal Root Ganglion: An Inter-Species Investigation Poster 19
Grace Moore, Univ. of Texas, Dallas

Evaluation of MIF in Mediating hSCAP Analgesia in Orofacial Pain Poster 20
Josue Murillo, Univ. of Texas Health San Antonio

Peripheral Myeloid Cells Control Resolution of Painful Chemotherapy-Induced Peripheral Neuropathy (CIPN) Poster 21
George Naratadam, Univ. of Texas Health San Antonio

Subacute Inhibition of Hmgb1 in the Amygdala Reduces Pain-Related Behaviors in a Rat Model of Chronic Neuropathic Pain Poster 23
Peyton Presto, Texas Tech University Health Sciences Center

MRGPRX2 on Meningeal Mast Cells Drives Migraine-like Pain Poster 25
Sami Sbei, Univ. of Texas Medical Branch Galveston

Postdoc Data Blitz Presenters

Inflammasome Activation in Peripheral Nerve Injury Poster 6
Fisher Cherry, Univ. of Texas MD Anderson Cancer Center

The Integrated Stress Response and Eukaryotic Initiation Factor 2A Mediate Evoked Pain Hypersensitivity in a Model of Multiple Sclerosis Poster 14
Jonathan Iketem, Univ. of Texas, Dallas

The Role of OPRM1 in Neonatal Autoresuscitation and Sudden Infant Death Syndrome (SIDS) Poster 17
Nicoletta Memos, Baylor College of Medicine

Glial Progenitor Heterogeneity and Key Regulators Revealed by Single-Cell RNA-Sequencing Provide Insight to Regeneration in Spinal Cord Injury Poster 27
Haichao Wei, Univ. of Texas Health Science Center Houston

B Cells Drive Mechanical Pain After Nerve Injury Poster 28
Kendal Willcox, Univ. of Texas MD Anderson Cancer Center

4:15 Posters and Reception
4:15-5:15 Poster Presentation
5:15-6:00 Reception

Day 2

9:00 Welcome
Peter Grace, Univ. of Texas MD Anderson Cancer Center

Convener: Terry Walters, Univ. of Texas Health Science Center Houston

9:05 **Keynote Presentation**
Human Molecular Neuroscience Approaches to Developing New Neuropathic Pain Therapies
Ted Price, Univ. of Texas Dallas

Convener: Helen Lai, Univ. of Texas Southwestern

9:35 *Thoracic Spinal Hemisection Produces Chronic Neuropathic Pain in the Contralateral Hindlimb in Mice*
Melissa Henwood, Univ. of Texas Medical Branch at Galveston

9:50 *Getting out of the (Pain) Matrix: TIMP-1 as Regulator of Inflammatory Pain Resolution*
Kyle Baumbauer, Univ. of Kansas Medical Center

10:05 *Role of Peripheral Truncated TrkB in Cancer Pain*
Shivani Ruparel, Univ. of Texas San Antonio

10:20 *Ascending Somatosensory Pathways that Shape the Perception of Touch and Pain*
Seungwon (Sebastian) Choi, Univ. of Texas Southwestern Medical Center

10:35 Break

Convener: Jun-Ho La, Univ. of Texas Medical Branch Galveston

10:45 **Keynote Presentation**
The Cells and Molecules for Sensing Touch and Pain
Alex Chesler, NIH

Convener: Michael Lacagnina, Univ. of Texas MD Anderson Cancer Center

11:15 *The Conserved Synaptic Mechanisms of Chronic Pain*
Lingyong Li, Univ, of Alabama at Birmingham

11:30 *A Mouse Model of Paraneoplastic Neuropathy Driven by Colorectal Cancer*
Andrew Shepherd, Univ. of Texas MD Anderson Cancer Center

11:45 *Amygdala Neuroplasticity in Pain*
Volker Neugebauer, Texas Tech Health Science Center

12:00 *Contulakin-G Unravels Neurotensin Receptor-Calcium Channel Signaling as a Non-Opioid Spinal Analgesic Pathway*
Amol Patwardhan, UT Southwestern

12:15 Presentation of Poster Awards and Closing Remarks
Peter Grace, Univ. of Texas MD Anderson Cancer Center

Presenters in alphabetical order

Kyle Baumbauer, PhD
Assistant Professor
Cell Biology and Physiology and of Anesthesiology
Univ. of Kansas Medical Center

Getting out of the (Pain) Matrix: TIMP-1 as Regulator of Inflammatory Pain Resolution

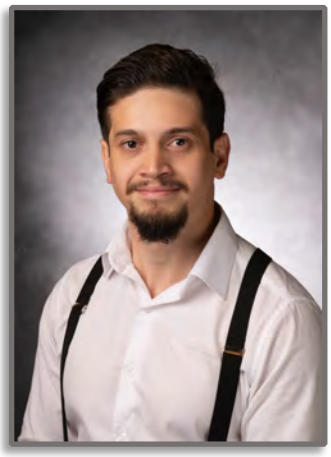
Dr. Kyle Baumbauer received his PhD in Experimental Psychology at Kent State University where he studied mechanisms of spinal plasticity under the mentorship of Robin Joynes. He then went on to do postdoctoral training in the Behavioral and Cellular Neuroscience program at Texas A&M University where he studied how noxious stimuli affected spinal circuits and recovery following spinal cord injury with Jim Grau. He then went on to a second postdoc position in the Pittsburgh Center for Pain Research and the Department of Neurobiology at the University of Pittsburgh School of Medicine where he worked with Rick Koerber studying factors that influenced primary afferent function. After completing his postdoctoral training, Kyle was an Assistant Professor in the School of Nursing at the University of Connecticut and is currently an Assistant Professor in the Department of Cell Biology and Physiology and Department of Anesthesiology at the University of Kansas Medical Center. The work in Kyle's lab broadly focuses on understanding mechanisms that regulate nociceptor sensitivity and subsequent pain following inflammation and spinal cord injury and has been funded by the Craig H. Neilsen Foundation and NIH, and he was a recipient of the Rita Allen Foundation Award in Pain.

Alexis Bavencoffe, PhD
Research Assistant Professor
Univ. of Texas Health Science Center

Memory-Related Induction Mechanisms Trigger Persistent Hyperexcitability of Nociceptors

Dr. Alexis Bavencoffe obtained his License, Master's and PhD degrees from the University of Sciences and Technologies of Lille (France). Developing a strong interest in the roles of ion channels in the generation and maintenance of pain, Alexis came for his postdoctoral training to the Department of Integrative Biology and Pharmacology at McGovern Medical School in 2010. He worked in the Michael Zhu lab and thereafter joined Carmen Dessauer's and Terry Walters' labs where he became instructor and as of today, Research Assistant Professor.

Alexis's research employs electrophysiological (patch-clamp) and behavioral approaches to define intracellular signaling pathways and neuroimmune signals that induce and maintain the pain-related nociceptor hyperactive state that drives neuropathic pain after spinal cord injury or peripheral nerve injury. These efforts have led to 17 scientific articles, 3 book chapters and over 35 communications at national and international meetings.



Rafael Cazuza, PhD
Postdoctoral Fellow
Symptom Research
Univ. of Texas MD Anderson Cancer Center

Neuropathic Pain Induces Microglial Reactivity in Sensory and Affective Brain Regions

Dr. Cazuza is currently a postdoctoral fellow at the University of Texas – M.D Anderson Cancer Center, under mentorship of Dr. Peter Grace. Currently investigating the neuro-glial mechanisms in the brain that underlies chronic neuropathic pain. He received his PhD in Psychobiology at the University of Sao Paulo, Brazil. He received his MSc in Psychobiology at the University of Sao Paulo, Brazil.

Alexander Chesler, PhD
Senior Investigator
Sensory Cells and Circuits Section
National Center for Complementary
and Integrative Health, NIH

The Cells and Molecules for Sensing Touch and Pain

Dr. Chesler is a Senior Investigator at the National Center for Complementary and Integrative Health (NCCIH), NIH. He received his Ph.D. from Columbia University studying the function and development of olfactory sensory neurons. He then completed postdoctoral training investigating the pharmacology of sensory neurons in the laboratory of Dr. David Julius at the University of California San Francisco. At the NCCIH/NIH, his lab aims to elucidate how sensory input is detected and processed by the brain to evoke specific behaviors, focusing on identifying peripheral somatosensory neurons tuned to specific types of stimuli, the molecules they use for transduction, and the neural circuits that they activate, using multiple research tools including mouse genetics, in vitro and in vivo electrophysiology, in vivo two-photon imaging, and behavioral assays. Dr. Chesler has studied patients with a rare inherited disorder affecting mechanosensation due to damaging mutations in the gene PIEZO2. In doing so, he defined the critical role of PIEZO2 in human mechanosensation and probed questions about the role particular sensory inputs play in perception. Dr. Chesler received multiple NCCIH Director's awards for his mentorship and leadership in the Pain Research Center.

Keynote Presenter

Seungwon (Sebastian) Choi, PhD
Assistant Professor
Psychiatry
Univ. of Texas Southwestern Medical Center

Ascending Somatosensory Pathways that Shape the Perception of Touch and Pain

Dr. Choi was born and raised in South Korea and received his B.S. and M.S. from the Korea Advanced Institute of Science and Technology (KAIST), where he studied molecular mechanisms underlying dendritic spine formation. He obtained his Ph.D. at Harvard University, where he studied behavioral arousal and quiescence in C. elegans. As a postdoctoral fellow at Harvard Medical School, Dr. Choi studied ascending spinal pathways that convey touch and pain signals to the brain. Dr. Choi joined the Department of Psychiatry at UT Southwestern Medical Center as an Assistant Professor in July 2022.

Anibal Garza Carbajal, PhD
Instructor
Integrative Biology and Pharmacology
Univ. of Texas Health Science Center

Bidirectional Relationship Between Opioid Sensitivity and Neuronal Excitability

After graduating from Puebla Autonomous University (BUAP, Mexico) in biomedicine, he obtained his PhD in neuroimmunology from the University of Duisburg-Essen (Germany). During his first postdoctoral position, Anibal worked at the Max Planck institute of molecular Genetics (Berlin, Germany) and the University of Cologne (Cologne, Germany) studying neuronal and glial pain-related signaling via high content microscopy. Since April 2016 he joined Carmen Dessauer's group in the department of Integrative Biology and Pharmacology at UTHealth McGovern Medical School (Houston). His work is mostly focused on the crosstalk between signaling pathways in the context of pain sensitization in sensory neurons.

Amber Harris Bozer, PhD
Director, Faculty and Student Research, Center for Educational Excellence
Associate Professor, Psychological Sciences
Tarleton State Univ.

Electroencephalogram Activity of Participants with Chronic Pain that Use Cannabinoids

Dr. Amber Harris Bozer is an Associate Professor in the Department of Psychological Sciences, and serves as the Director of Faculty Scholar Development in the Center for Educational Excellence at Tarleton State University, an R2 university in the Texas A&M system. The Behavioral Neuroscience and Psychophysiology lab at Tarleton has focused on investigating pain behaviors and cognition using electrophysiological methods, specifically concerning pain approach-avoidance conflicts and the cortical effects of using cannabinoids as analgesics.

Melissa Henwood
MD/PhD Student
Univ. of Texas Medical Branch at Galveston

Thoracic Spinal Hemisection Produces Chronic Neuropathic Pain in the Contralateral Hindlimb in Mice

Melissa completed her bachelor's degree in Biomedical Science with a minor in Neuroscience from Texas A&M University in 2017 and went on to join the MD/PhD program at the University of Texas Medical Branch in Galveston, TX in 2019. She is currently working on her PhD on spinal cord injury under Dr. Bo Chen in the Department of Neurobiology. Her research interests include understanding the mechanisms driving not just the loss of normal sensation after SCI, but the gain of abnormal or even painful sensations in body regions below the injury site. Her talk today will outline new evidence for a mouse-model of SCI-induced central pain.

Nathaniel A. Jeske, PhD
Associate Professor, Director of Research
Oral and Maxillofacial Surgery
Center for Biomedical Neuroscience
Univ. of Texas Health San Antonio

Targeting Peripheral Opioid Receptor Biochemistry to Improve Analgesia

Dr. Nathan Jeske's lab conducts research on signaling mechanisms that mediate inflammatory pain and analgesia. Over 100 million Americans suffer from pain annually, and understanding how this sensation graduates to a chronic state, as well as how to treat it efficaciously, are the primary research goals of the Jeske lab. Research in the Jeske lab focuses on biochemical signaling molecules and pathways unique to pain-sensing neurons in the periphery that can be targeted to reduce pain, increase analgesia, and improve the quality of life for pain patients. Researchers combine molecular, biochemical, pharmacological, physiological, and behavioral studies with opportunities for human clinical expertise to provide comprehensive approaches to some of our most important issues related to pain and analgesia in our current society.

Yu Shin Kim, PhD
Associate Professor
Oral & Maxillofacial Surgery
Univ. of Texas Health San Antonio

Sensory Neuron-Specific Transmission and Voltage Dynamics And Neuronal Plasticity Changes

Dr. Kim graduated Johns Hopkins University and did postdoc at Johns Hopkins University. Currently, he is an associate professor in the School of Dentistry at the University of Texas Health at San Antonio (UTHSA) where it is well known for its strong group in pain research. His research is focused on the function and regulation of sensory modalities, including pain, itch, and gentle touch, and on understanding the cellular and molecular mechanisms of pain by studying neural circuit activities evoked by pain in normal and disease conditions like chronic pain and TMD.

Lingyong Li, PhD
Associate Professor
Anesthesiology and Perioperative Medicine
University of Alabama at Birmingham

The Conserved Synaptic Mechanisms of Chronic Pain

Dr. Lingyong Li is an Associate Professor of the Department of Anesthesiology and Perioperative Medicine at the University of Alabama at Birmingham. He received his Ph.D. in biochemistry and molecular biology from Nanjing Agricultural University, China in 2006. After finishing postdoctoral training at Vanderbilt University and MD Anderson Cancer Center, Dr. Li joined Baylor College of Medicine as an Assistant Professor in 2017. In September 2022, Dr. Li moved to the University of Alabama at Birmingham as an Associate Professor. The main research of his lab focuses on synaptic and circuit mechanisms of chronic pain and its modulation by opioids. By using a multidisciplinary approach, such as mouse genetics, Patch-seq, electrophysiology, opto-/chemogenetics, viral-genetic labeling of activated neurons, in vivo recording of neural activity, con-focal imaging, and behavioral experiments, Dr. Li's group studies the underlying mechanisms of chronic pain, chronic pain-induced mood disorders, opioid analgesic tolerance, addiction, and respiratory depression at synaptic and circuit levels. At the 12th GCC conference, Dr. Li will present their unpublished study about the conserved synaptic mechanisms of chronic pain. Dr. Li's group found that Tiam1-coordinated synaptic functional and structural plasticity underlies the pathophysiology of different types of chronic pain and that intervention of Tiam1-mediated maladaptive synaptic plasticity has long-lasting consequences in chronic pain management.

Karen Lindquist
PhD Student
Univ. of Texas San Antonio

Diversity in Mechanically Activated Current Responses for Trigeminal Ganglion Sensory Neurons Innervating Masseter Muscle

Karen Lindquist received her Bachelors and Masters degrees in Neuroscience at the University of Texas at Dallas. She then worked as a research assistant at UT Southwestern for a year and a half. Karen is currently a PhD candidate working in the lab of Armen Akopian, PhD, at UT Health San Antonio. Karen is currently studying chronic masticatory myalgia (muscle pain) in the masseter muscle. This includes unraveling the identity of masseter muscle innervating sensory neurons, with emphasis on their physiological responses to mechanical stimulation.

Volker Neugebauer, PhD
Univ. Distinguished Professor and
Chair of the Department of Pharmacology
Texas Tech Univ. Health Sciences
Center

Amygdala Neuroplasticity in Pain

Dr. Volker Neugebauer is University Distinguished Professor and Chair of the Department of Pharmacology, Founding Director of the Center of Excellence for Translational Neuroscience and Therapeutics, and Executive Director and Chief Scientific Officer of the Garrison Institute on Aging (GIA) at Texas Tech University Health Sciences Center (TTUHSC). Dr. Neugebauer obtained his M.D. and Ph.D. degrees from the University of Würzburg, Germany. He received training in physiology, pharmacology, neuroscience and neurology at the University of Würzburg and the University of Texas Medical Branch (UTMB) at Galveston, TX. Dr. Neugebauer has been studying mechanisms of neuroplasticity and brain functions related to clinically relevant disorders such as chronic pain, neurodegenerative diseases, and various neurological and psychiatric disorders for more than 30 years. The analysis of emotional-affective and cognitive brain mechanisms of pain centered on the amygdala and cortico-limbic interactions is a key contribution to the field of pain research and neuroscience. His team first described neuroplasticity in the amygdala in pain conditions. The current focus on neuroimmune signaling in the brain is pioneering the analysis of neuroplasticity in pain and comorbid disorders. Dr. Neugebauer's research program uses a multidisciplinary approach state-of-the-art in vivo and in vitro electrophysiology, multi-photon imaging in vivo and ex vivo, microendoscopy for in vivo calcium imaging, optogenetics, chemogenetics, viral vector strategies, transgenics, molecular biology, immunohistochemistry, (opto-)pharmacology, and innovative behavioral assays. His work has been continuously funded by NIH since 1999 and published in more than 150 research articles and presented in more than 150 invited lectures and workshops. Since moving to TTUHSC in 2014, Dr. Neugebauer has established collaborative basic science projects and studies in humans on mechanisms, biomarkers and interventions for chronic pain and aging-related health issues such as dementias and Alzheimer's disease in particular. He also oversees the GIA Brain Bank, Project Frontier, a longitudinal epidemiological study that explores the course of chronic disease and cognitive decline in aging in a multi-ethnic sample of adults in rural communities in West Texas, and programs to improve the mental health of informal caregivers of patients with Alzheimer's Disease and Alzheimer's Disease Related Dementias.

Amol Patwardhan, MD, PhD
Associate Professor
Anesthesiology and Pain Management
Univ. of Texas Southwestern Medical Center

Contulakin-G Unravels Neurotensin Receptor-Calcium Channel Signaling as a Non-opioid Spinal Analgesic Pathway

Amol Patwardhan, M.D., Ph.D., is an Associate Professor in the Department of Anesthesiology and Pain Management at UT Southwestern Medical Center and an investigator with the Peter O'donnell Brain Institute. He also serves as a medical director of the 'Core Pain Clinic', a multidisciplinary pain clinic at UTSW.

Dr. Patwardhan earned his medical degree at the University of Mumbai. He completed a residency in anesthesiology at the University of Arizona and a fellowship in interventional pain medicine at the University of California, San Diego. He also holds a doctorate in pharmacology from the University of Texas Health Science Center at San Antonio with a focus on novel analgesic development.

Board certified in anesthesiology with a subspecialty in pain management, he joined the UT Southwestern faculty in 2022. Previously, he served as Co-Director of the Banner University of Arizona Chronic Pain Management Clinic and Vice Chair for Research in the Department of Anesthesiology at the University of Arizona.

Dr. Patwardhan is very active in analgesic research and serves as the principal investigator or co-investigator for several NIH grants. He is also an investigator on many industry-sponsored clinical trials related to pain management. He has published more than 50 manuscripts in peer-reviewed journals and has authored two book chapters.

Dr. Patwardhan serves as a member on a number of NIH, Department of Defense, and other national and international organizations' study sections.

Theodore (Ted) Price, PhD
Ashbel Smith Professor
Neuroscience
Univ. of Texas at Dallas

Human Molecular Neuroscience Approaches to Developing New Neuropathic Pain Therapies

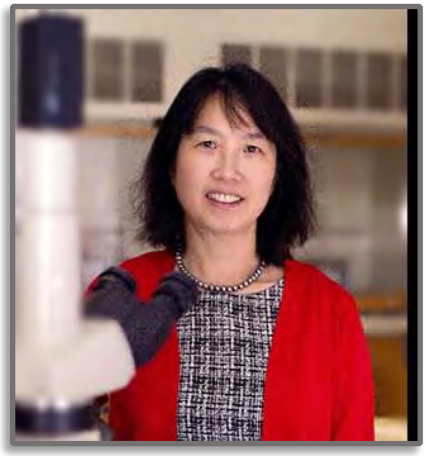
Theodore (Ted) Price is Ashbel Smith Professor in the Department of Neuroscience at University of Texas at Dallas where is the Director of the Center for Advanced Pain Studies. Ted's lab's goal is to identify molecular mechanisms causing chronic pain with emphasis on developing new drugs to treat pain. His lab's focus is on human molecular neuroscience with specialization on dorsal root ganglion and spinal dorsal horn. Ted has published more than 175 peer reviewed studies, and has been continuously funded by NIH for more than 10 years. He is co-founder of many companies, including 4E Therapeutics and Doloromics.

Keynote Presenter

Shivani Ruparel, PhD
Associate Professor and Director of Research, Endodontics
Univ. of Texas Health San Antonio

Role of Truncated TrkB in Lingual Sensory Neurons

Shivani Ruparel, PhD, is Associate Professor and Director of Research in the Department of Endodontics at University of Texas Health San Antonio (UTHSCSA). She obtained her doctoral degree in cancer biology in the Department of Cellular and Structural Biology at UTHSCSA under the guidance of Dr. Robert Marciniak and Dr. Linda deGraffenried in 2009. This was complemented by her postdoctoral training, under the guidance of Dr. Ken Hargreaves, which focused on pain neuropharmacology and biochemistry. She started her independent research program in 2012 on cancer and pain. Alongside, she also obtained a Master of Science in clinical investigation at UTHSCSA. Her research program focuses on peripheral mechanisms of oral tumorigenesis, oral cancer-induced pain, and pain associated with cancer treatment. Her group is the first in the country to develop the tongue-nerve single fiber electrophysiology to test trigeminal nerve discharges. She is authored several peer-reviewed publications in high-impact journals such as Nature Metabolism, Journal of Neuroscience and Pain. She was inducted to the Omikron Kappa Upsilon National Dental Society in 2018. She has been well funded throughout her career by several private and federal agencies.



Chwan-Li (Leslie) Shen, PhD
Associate Dean for Research and
Professor of Pathology and Physiology
Texas Tech Univ.

Ginger Root Extract Mitigates Neuropathic Pain Via Gut-Brain-Axis

Dr. Chwan-Li (Leslie) Shen is an Associate Dean for Research and Professor of Pathology and Physiology, School of Medicine, Texas Tech University Health Sciences Center, Lubbock, Texas, USA. Dr. Shen obtained her B.S. degree from Providence University, Taiwan, her MS degree from Texas Tech University, Texas, and her PhD degree from Purdue University, Indiana, USA. Within her faculty career, she has developed a broad range of expertise in molecular mechanisms, animal models, and clinical trials using bioactive compounds/ phytochemicals in the management of chronic diseases including neuropathic pain, osteoporosis, osteoarthritis, sarcopenia, diabetes, and obesity. Dr. Shen has successfully translated her animal study results into human clinical trials and her translational research program has been funded by federal (NIH and USDA), industry, and foundations. In addition, Dr. Shen's research and presentations are well received by national scientific societies and public media. Dr. Shen has published 123 journal papers, 3 book chapters, and made 120+ national and international conference/invited talks. She served as two associate editors of two journals, an editorial board member of 15 journals in the area of nutrition/exercise and chronic diseases, a reviewer for 140+ journals, and a grant reviewer for private, national, federal (NIH, USDA, NSF, DOD), and foreign funding agencies. She has become a fellow of United States Bone and Joint Initiative in 2006, received a Texas Tech System Chancellor's Council Distinguished Research Award in 2011, and a fellow of NIH Clinical Research Management in 2016, and a fellow of Executive Leadership in Academic Medicine in 2019.

Andrew Shepherd, PhD
Assistant Professor
Symptom Research
Univ. of Texs MD Anderson Cancer Center

A Mouse Model of Paraneoplastic Neuropathy Driven by Colorectal Cancer

Dr. Shepherd received his Bachelors in Molecular Cell Biology and his PhD in Neuroimmunomodulation from the University of Manchester in the UK. I Joined DP Mohapatra's lab in the Department of Pharmacology at the University of Iowa in 2008, where he researched GPCR modulation of ion channel activity in pain and neurodegeneration. In 2015, he joined the Department of Anesthesiology at Washington University in St. Louis as an Instructor, before starting his lab at MD Anderson Cancer Center in 2018 as an Assistant Professor in the Department of Symptom Research.

The research in his lab focuses on chronic pain mechanisms and therapeutic development, with a particular emphasis on neuro-immune interactions in neuropathy. His research is funded by NINDS and the Department of Defense, and he became a Rita Allen Foundation Pain Scholar in 2020.

Fan Wang, PhD
Professor
Brain and Cognitive Sciences
Massachusetts Institute of Technology

Central Pain Processing Circuits

Fan Wang is currently an Investigator of the McGovern Institute for Brain Research, and a Professor of Brain and Cognitive Sciences at Massachusetts Institute of Technology (MIT). She obtained her Ph.D. from Columbia University working with Dr. Richard Axel, and received postdoctoral training at UCSF and Stanford University with Dr. Marc Tessier-Lavigne. She became a faculty member at Duke University in 2003 and was appointed Morris N. Broad Professor of Neurobiology at Duke University before moving to MIT in January 2021. Dr. Wang has made major contributions to our understanding of the assembly and functions of neural circuits in the olfactory, somatosensory (including touch and pain), and motor systems. Dr. Wang was awarded an Alfred Sloan Fellowship, a Klingenstein Fellowship in Neuroscience, a McKnight Scholarship in Neuroscience, an NIH Pioneer Award, and a Keck Foundation research award. She is an AAAS Fellow, and a member of the American Academy of Arts and Sciences.

Keynote Presenter

Poster Presenters
Alphabetical Order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Poster	Poster #
Khalil Ali	Ahmad	Univ. of Texas MD Anderson Cancer Center	Cancer-Induced Pain in an Orthotopic Malignant Peripheral Nerve Sheath Tumor (MPNST) Mouse Model	1
Jessie	Alfaro	Univ. of Texas Health San Antonio	Characterization of Trigeminal Sensory Neurons Innervating the Temporomandibular Joint	2
Anthony	Allam	Baylor College of Medicine	Breaking the Barriers of Linear SVM: 3DCNN for Efficient Neurorehabilitation in Lower Cranial Neuropathy	3
Iniya	Anandan	Univ. of Texas, Dallas	Creating a Virtual Model of Pain-Induced Behavior: Quantifying Cells in the Central Nucleus of the Amygdala that Have PKC-δ, Somatostatin, CGRPR, and CGRP	4
Alexandra	Bishop	Baylor College of Medicine	Precision Medicine MRI Neuromodulation Enhances Decoding for Swallow Control Targeted for the Alleviation of Lower Cranial Neuropathy.	5
Fisher	Cherry	Univ. of Texas MD Anderson Cancer Center	Inflammasome Activation in Peripheral Nerve Injury	6
Hajira	Elahi	Univ. of Texas, Dallas	The Role of an Extracellular Kinase in NMDAR-Dependent Pain	8
Asia	Eter	Univ. of Texas Medical Branch Galveston	Mechanism of Spine Surgery Induced Sensitization in Mice	9
Chrystine	Gallegos	Univ. of Texas Health Science Center Houston	Effects of SGC Stimulation on DRG neurons	10
Ruben	Gomez	Univ. of Texas Health San Antonio	Conditional Deletion of Pannexin 1 Shows Reduced Sensitivity in Chronic Constriction Injury Mice	31
Kali	Hankerd	Univ. of Texas, Dallas	Ion Channels Ensembles in Human Dorsal Root Ganglia	11
Lucy	He	Univ. of Texas, Dallas	The Role of Meteorin in Cisplatin Induced Peripheral Neuropathy	12
Veronica	Hong	Univ. of Texas, Dallas	The Role of Sigma-2/TMEM97 in the Context of Affective and Pain Behaviors	13

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Presenter First Name	Presenter Last Name	Presenter Institution	Title of Poster	Poster #
Jonathan	Iketem	Univ. of Texas, Dallas	The Integrated Stress Response and Eukaryotic Initiation Factor 2A Mediate Evoked Pain Hypersensitivity In A Model Of Multiple Sclerosis	14
Sarah	Jobbins	Univ. of Texas Southwestern Medical Center	The Role of PRDM12 in Axonal Regeneration	15
Marisol	Mancilla Moreno	Univ. of Texas at Dallas	Identification of Neuronal Populations in Dorsal Root Ganglia using Spatial Transcriptomics: Comparison between Pig and Human Species.	16
Nicoletta	Memos	Baylor College of Medicine	The Role of OPRM1 in Neonatal Autoresuscitation and Sudden Infant Death Syndrome (SIDS)	17
Jaclyn	Merlo	Univ. of Texas Health San Antonio	Sex-Dependent Differences in the Genomic Profile of Lingual Sensory Neurons in Naïve and Tongue-Tumor Bearing Mice	18
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Poster 1

Cancer-Induced Pain in an Orthotopic Malignant Peripheral Nerve Sheath Tumor (MPNST) Mouse Model

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Background: Cancer pain can occur at any stage of the disease development and many cancer patients experience moderate to severe pain. Despite advances in cancer treatment, pain management remains limited. Pharmacotherapy of cancer pain has relied mostly on therapeutic approaches in other pain conditions; however, the cellular and molecular mechanisms underlying cancer pain may be distinct and may require new treatment strategies. Animal models have provided insights into the mechanisms of cancer pain, which is thought to result from complex interactions between tumor cells, the immune system, and nervous system. The use of nociceptive behavioral assays in rodent models may help to better reflect the symptoms experienced by patients. Malignant peripheral nerve sheath tumors (MPNSTs) are highly aggressive soft-tissue sarcomas arising in peripheral nerves. Patients with MPNSTs often experience pain but little is known about the mechanisms by which MPNST induces pain.

Hypothesis/Goals: This study aims to characterize pain behaviors and molecular mechanism in murine MPNST models and to identify therapeutic targets.

Methods: Behavioral, cell culture, and immunohistochemistry methods were performed. MPNST cancer pain model was developed by implanting the mouse MPNST cells into the sciatic nerves of either male or female mice. Primary mouse dorsal root ganglion (DRG) neuronal cell cultures were prepared for Calcium imaging experiments.

Results: Mouse MPNST cell line formed tumors within the sciatic nerve following implantation. Mechanical allodynia and thermal hyperalgesia were observed in MPNST-bearing female and male mice after one week of inoculation compared to the sham groups. In addition, MPNST-conditioned medium altered calcium influx in primary cultured mouse DRG neurons, suggesting that MPNST cells secrete factors that change DRG activity.

Conclusions: Using the murine MPNST allograft model, our data demonstrated that MPNST induces pain in the nerve where tumor grows. Future studies will further characterize the pain behaviors in the MPNST pain model and determine the underlying cellular and molecular mechanisms.

Poster 2

Characterization of Trigeminal Sensory Neurons Innervating the Temporomandibular Joint

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Background

Temporomandibular joint (TMJ) disorders (TMJD) are functionally heterogenous conditions of the mastication system affecting jaw joint, masticatory muscles, and ligaments. Despite 40-60% of the population suffering from some type of TMJ pain, treatment remains ineffective (1). Pathophysiology of TMJD is still unknown. However, there is an agreement that TMJD increase responsiveness of sensory neurons innervating TMJ ligament and connected lateral pterygoid muscle.

Hypothesis/Goals

To gain improved and effective treatment, the subtypes of sensory neurons that innervate the TMJ must be functionally phenotyped and thoroughly characterized in naïve and TMJD subjects. Such a study includes the role of specific receptors and mediators as well as sex and age dependent plasticity of sensory neuronal groups that innervate TMJ and determines TMJD disorder pathology. Identification of the sensory neurons innervating the TMJ will allow for the study of cell-specific mechanisms that contribute to TMJD pain.

Methods

As a first step, I used immunohistochemistry with sensory neuronal markers on mouse tissue to identify the specific trigeminal neuronal groups that innervate the TMJ. This initial stage will be followed by electrophysiological characterization of TMJ innervating sensory neuronal groups.

Acknowledgements

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Poster 3

Breaking the Barriers of Linear SVM: 3DCNN for Efficient Neurorehabilitation in Lower Cranial Neuropathy

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Background: The Papageorgiou lab has developed an innovative individualized real-time fMRI closed-loop neuromodulation intervention (iRTfMRI-cNMT) for the alleviation of neuropathic pain relating to cranial nerve (CN) IX and XII lesions, which affect speech, swallowing, and eating. For effective, efficient and sustained neurorehabilitation, it is crucial to decode the entire cortical and subcortical circuit that reflects the underlying physiological functions with high sensitivity and specificity. We used a non-linear 3DCNN deep learning algorithm, as it has demonstrated significant potential in computer vision analysis. We compared 3DCNNs to linear SVMs, which although the latter is commonly used in decoding brain networks, failed to show activation of the medulla oblongata, where the nuclei of the CNIX and XII originate.

Goal/Hypothesis: 3DCNNs will achieve higher classification accuracies, and brain maps with greater biological interpretability when compared to linear SVMs.

Methods: We decoded 30 participants' cortical tongue-motor-sensory-control-direction selectivity generated in response to tongue movement in four directions (up, down, left, and right) using a linear SVM and non-linear 3DCNN decoder. The models were trained to differentiate between cortical selectivity across concatenated cortical directions versus baseline-tongue-at-rest for the cNMT and control conditions. Each model was trained on two run permutations and tested on the remaining run within each condition. Average accuracies across the three permutations were calculated for each subject and across subjects to obtain the overall accuracy for each model.

Results: As hypothesized, the 3DCNN achieved greater classification accuracies: 1. for the control condition with 94.2% compared to 89.6% generated by SVM; 2. for the individualized cNMT condition 97.2% compared to the 94.3% generated by SVM. These findings demonstrate the 3DCNN's enhanced consistency in predicting tongue-motor-sensory-control cortical direction selectivity compared to a linear SVM. In addition, the 3DCNN generated cortical patterns with greater sensitivity as it identified the medulla oblongata, while the SVM did not uncover any brainstem activity.

Conclusions: The 3DCNN decoder has demonstrated superior performance in accurately decoding brain activity and identifying cortical networks associated with tongue sensorimotor control compared to the commonly used linear SVM. Our immediate goal is to incorporate the 3DCNN decoder into the iRTfMRI-cNMT interface, which will allow us to provide more efficacious neurorehabilitation for lower cranial neuropathy patients.

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Poster 4

Creating a Virtual Model of Pain-induced Behavior: Quantifying Cells in the Central Nucleus of the Amygdala that have PKC-δ, Somatostatin, CGRPR, and CGRP

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Background
The amygdala, specifically the central nucleus of the amygdala (CeA), plays an important role in processing neuropathic pain-like behavior. Within the CeA, there are different cell-types with markers such as protein kinase C-δ (PKC-δ), somatostatin (SST), and calcitonin gene-related peptide receptor (CGRPR; also known as CALCRL).

Hypothesis/Goals
Our lab has been working to create a 3D agent-based computational model that will be used to simulate the "virtual brain" to understand pain-induced behavior. To create a fully functioning pain model of the CeA, we need to first define the topographical location of the different cell types within the CeA.

Methods
As a part of this project, we used RNAScope to identify PKC-δ, SST, and CGRPR mRNA in three dimensions, on the dorsal-ventral axis, medial-lateral axis, and in bregma locations (anterior-posterior axis). A grid was overlaid on the stained and imaged brain slices to identify the number of cells with PKC-δ, SST, CGRPR and their location in the brain based on the Allen and Blue Brain Atlases. Second, to provide an additional anatomical reference for these cells, we also probed the brain for calcitonin gene-related peptide (CGRP) protein, which is concentrated in capsular division of the amygdala (CeC).

Results
The wet lab experiments led to quantified results that showed prominent clusters of PKC-δ, SST, and CGRPR throughout the CeA. We showed that the PKC-δ was found mostly in the lateral division of the amygdala (CeL) and CeC, while the SST is mostly found in the CeL and medial division of the amygdala (CeM). The CGRPR was found mostly in the CeC, where the receptor's ligand, CGRP was also found. These distributions did differ though based on the anterior-to-posterior location quantified.

Conclusions
The quantified cell-type specific markers will be used to spatially organize the 3-D model. In the future, additional samples can be quantified and compared to build a more accurate representation of the cell types within the CeA, as well as establish a reliable reference model.

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Poster 5

Precision Medicine MRI Neuromodulation Enhances Decoding for Swallow Control Targeted for the Alleviation of Lower Cranial Neuropathy

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Background: Brain-computer interfaces (BCI) are rapidly developing as neuro-rehabilitative tools in neuroscience and neuroengineering research. The Papageorgiou lab has developed an MRI-BCI, referred to as individualized biomarker-driven neuromodulation (iNMT) intervention for the neuro-rehabilitation of lower cranial neuropathy (LCN), as a sequalae of cranial nerve IX (glossopharyngeal) and XII (hypoglossal) damage following radiation treatment after head and neck cancer or, anterior cervical discectomy and fusion surgery. LCN affects motor and sensory control of the oral, pharyngeal and laryngeal cavities, which in turn impacts swallowing, and speech. Current pharmacotherapies for LCN result in side effects and drug-drug interactions that lead to poor patient adherence. Therefore, new treatments in the management of radiation- or surgery-induced LCN are urgently needed. Here we use support vector machine learning to decode cortical selectivity for swallow under individualized MRI neuromodulation. Decoding the neural substrates for swallow will help us understand the mechanisms of neuromodulation with the goal to aid in the development of more sensitive and specific personalized neurorehabilitation in LCN patients suffering from dysphagia.

Goal/Hypothesis: iNMT will increase the consistency of the intensity and spatial extents of the oxygenated hemoglobin signal compared to the control condition when we decode cortical selectivity for swallow versus tongue motor and sensory control.

Methods: We decoded 30 healthy participants' brain networks in response to swallow and tongue motor and sensory control (up; down; left; right movement) using linear SVMs. The models were trained to distinguish between brain activity during swallow compared to tongue movement under the iNMT and control-NOiNMT conditions. SVM modeling was trained in 29 participants and tested on 1 participant. This was performed in an iterative fashion using a sliding window.

Results: Neuromodulation resulted in higher classification accuracy compared to the control condition. Enhanced activity was noted for motor cerebellum and basal ganglia areas. Neural proprioceptive and pain matrix substrates, such as the insula and claustrum were not activated during iNMT.

Conclusions: The results show that individualized neuromodulation can strengthen the physiologic response of swallow and increase the signal to noise ratio, which is evident in the reduced extent of this network. This suggests that iNMT reinforces the physiology of the swallow to gain greater control during the oral preparatory phase by inhibiting the signal of proprioceptive areas and enhancing motor control. Our findings are in agreement with the literature which shows that neuromodulation of motor control can decrease chronic pain. Understanding the mechanisms of swallow under iNMT will help us delineate optimal neuro-rehabilitative targets for LCN patients suffering of dysphagia.

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Poster 6

Inflammasome Activation in Peripheral Nerve Injury

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Background: Peripheral nerve injury increases levels of interleukin-1β (IL-1β), which contributes to nociceptive hypersensitivity. IL-1β is matured by inflammasomes; e.g., absent in melanoma 2 (AIM2) and NLR family pyrin domain containing 3 (NLRP3), which are activated by a variety of signals like reactive oxygen species (ROS). Inflammasomes also mature gasdermin D which creates pores in the cell membrane, allowing for release of IL-1β. However, it is not fully known which inflammasomes are activated after peripheral nerve injury, where they are activated, and whether GSDMD-dependent pores form to allow IL-1β release.

Hypothesis/Goals: The goal of this present study is to characterize the extent of inflammasome activation after peripheral neuropathic injury. In addition, it is hoped that the results of this study will establish a short-term window of treatment to block inflammasome activation after injury.

Methods: Male and female C57BL/6J mice underwent sciatic nerve chronic constriction injury (CCI). Sciatic nerve (SN), dorsal root ganglion (DRG), and spinal cord were harvested after 0, 1, 5, 7, 14, and 21 days after injury to measure transcription of inflammasome components. Propidium iodide was administered by i.p. injection one hour before taking tissue to measure pore formation.

Results: There was an early increase in gene expression of inflammasome components after injury, with a preference towards NLRP3 in male mice and AIM2 in female mice. This trend was repeated at days 14 and 21. A high expression of caspase 1 and interleukin 1 beta (IL-1B) was observed throughout the SN and DRG, but propidium iodide staining indicated pyroptosis only occurred in the injured SN.

Conclusion: Different inflammasomes may be responsible for IL-1β processing and release in males and females. Although inflammasome components are upregulated in DRG, there is little pore formation, suggesting additional regulation of IL-1β release at this site.

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Poster 8

The Role of an Extracellular Kinase in NMDAR-Dependent Pain

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Background: NMDA receptors play a key role in regulating how nociceptive information is transmitted to the brain through dorsal horn circuits. Changes in NMDAR localization and function contribute to the hyperexcitability of pain pathways after insult or injury. The EphB2 receptor tyrosine kinase interacts in numerous ways with the NMDAR to enhance post-synaptic currents. We recently showed that phosphorylation of an extracellular tyrosine residue on the EphB2 receptor (Y504) is necessary and sufficient to drive increased NMDAR retention at the synapse, and is implicated in post-surgical pain and mechanical hypersensitivity. However, the extracellular kinase responsible for this phosphorylation event is unknown.

Hypothesis: We hypothesize that Vertebrate Lonesome Kinase (VLK) is the effector responsible for extracellular phosphorylation of the EphB2 receptor and the resulting increase in NMDAR activity. As a secreted tyrosine kinase with activity in the extracellular environment, VLK is an ideal candidate for this mechanism.

Methods: VLK was administered intrathecally to mice and its effects on pain-like behaviors were measured as tested by von Frey filaments and the Mouse Grimace Scale. Dependence of its effects on kinase activity and NMDAR activation was tested with kinase-mutation and receptor antagonism, respectively. Endogenous expression of VLK in mouse and human DRG was characterized with RNAscope ISH and immunohistochemistry, and the behavioral effects of VLK knockout in sensory neurons was tested in conditional knockout mice.

Results: VLK administration induces robust mechanical hypersensitivity and spontaneous pain in mice and drives activity in DH neurons. These effects are dependent upon NMDAR activation and are attenuated when VLK is co-administered with APV. VLK is robustly expressed by nociceptors and mechanoreceptors in mouse and human DRG. Conditional knockout of VLK from sensory neurons results in a significant reduction of injury-induced pain in mice and a quicker return to baseline when compared to wild-type controls.

Conclusions: These results provide evidence that VLK has pronociceptive effects dependent upon kinase and NMDAR activation. It is endogenously expressed in the mouse and human pain circuit, and is an essential component of pain signaling after injury. Because NMDA-mediated hyperexcitability is a critical component of pain development and maintenance, this work brings attention to the therapeutic potential for VLK-targeting in the context of pain. Importantly, VLK is the first ectokinase with a clear role in the control of synaptic physiology and pain in response to injury.

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Poster 9

Mechanism of Spine Surgery Induced Sensitization in Mice

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Background: Post-laminectomy syndrome, also called failed back surgery syndrome (FBSS), is defined as the chronic pain experienced by patients after back surgery. The incidence of FBSS is 10-40% after lumbar back surgery and can be extremely difficult to manage. Previously we reported that laminectomy's induce pain hypersensitivity in the hind paws of mice and intraoperative Spinal Cord Stimulation (SCS) significantly reduced hind paw mechanical hypersensitivity. In this study, we will determine the mechanism behind laminectomy-induced central sensitization. We will investigate if the administration of NMDA and NK1 receptor antagonists prior to laminectomy produces similar results to that of intraoperative SCS.

Hypothesis/Goals: The goal of this study is to explore laminectomy-induced central sensitization in mice with the administration of NMDA and NK1 receptor antagonists. We expect these antagonists to provide similar results to intraoperative SCS and reduce hind paw pain hypersensitivity with both ipsi and contralateral administrations.

Methods: To model spine surgery central sensitization, we performed a left sided T13 laminectomy. Fifteen minutes prior to laminectomy, the mice were intrathecally injected at the L5-L6 level with the NMDA receptor antagonist AP5 or the NK1 receptor antagonist L-760735. Von Frey filament testing was conducted on hind paws ipsilateral and contralateral to the surgery side. Measurements were taken at baseline (BL) and at predetermined time points after laminectomy (e.g., 2 hr, 1 day, 2 day, 3 day, 5 day, 7 day, 10 day, and 14 day post-surgery). For statistical analysis, the logarithmic values of paw withdrawal thresholds (PWT) were used, and ANOVA or linear mixed model was used in group comparison.

Results: Both intrathecal injections of NMDA receptor antagonist and NK1 receptor antagonist significantly reduced the development of hind paw mechanical hypersensitivity after laminectomy. There was a difference in the development of pain hypersensitivity between the ipsilateral and the contralateral hind paws. It is noteworthy that there was significant difference in the effects of those antagonists between sex.

Conclusion: Intrathecal injections of NMDA and NK1 receptor antagonists prior to the laminectomy demonstrated a reduced duration and degree of mechanical hypersensitivity in both ipsilateral and contralateral hind paws. These results suggest that both NMDA and NK1 receptors are involved with the development of spine surgery induced central sensitization. This may be associated with the intraoperative SCS therapeutic effect on the spine surgery induced central sensitization. Further investigation is needed to better understand the mechanisms of spine surgery induced sensitization.

Acknowledgments: None to disclose.

Poster 10

Effects of Satellite Glial Cell Stimulation on Isolated DRG Nociceptors

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Background:
An estimated 1.4 million people in the United States report living with spinal cord injury (SCI), and over half of all people with SCI develop chronic pain that is resistant to treatment. Nociceptors in the dorsal root ganglion (DRG) are persistently altered after SCI, exhibiting reduced sensitivity to opioids and hyperexcitability, both of which may contribute to chronic pain. Importantly, SCI is associated with prolonged elevation of neuroactive signaling molecules, including cytokines and growth factors. While neuronal participation in signaling related to ongoing pain is well explored, little is known about the contribution of support cells such as satellite glial cells (SGCs). SGCs in the DRG wrap around neuron somas, and this unique morphology and placement makes them opportune targets for circulating physiological signals or pharmacological manipulation. However, SGC signaling, pharmacology, and the roles of SGCs in driving chronic pain remain mysterious.

Hypothesis/Goals:
We hypothesize that factors upregulated after SCI activate SGCs, driving reduced opioid sensitivity and hyperexcitability of nociceptors. We seek to determine the mechanism of SGC activation and how activated SGCs alter nociceptor signaling by high-content microscopy and confocal imaging.

Methods:
Adult rats were used to prepare primary cultures of mixed cells from dissociated DRGs, and neonatal rats were used to prepare primary cultures of isolated satellite glial cells from whole DRG explants. Cells were treated with different factors, fixed, and stained for cell markers or phosphorylation states of signaling proteins. High content microscopy was used to measure cellular responses after different treatments.

Results:
We have identified a growth factor, which shows sustained elevation after SCI that, alone and in combination with IL-6 family cytokines, increases GFAP staining (a marker of SGC activation) in pure SGCs and in mixed DRG cultures. Additionally, we demonstrate that SMAD2 signaling may play a role in increasing GFAP expression in satellite glial cells, but not STAT3 signaling.

Conclusions:
Ongoing studies are examining the effect of SCI on SGC stimulation and activation, the sensitivity of SGCs and neurons to cytokines, and whether SCI-induced neuronal hyperexcitability and opioid effects require SGC activation and signaling.

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Poster 31

Conditional Deletion of Pannexin 1 Shows Reduced Sensitivity in Chronic Constriction Injury Mice

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Background: Pannexin 1 (Panx1) is a pore protein connecting the intracellular and extracellular space as large transmembrane channels which allow the passage of ions and small molecules between these compartments such as ATP. People assume this pore protein might be involved in pain hypersensitivity following nerve injury and purinergic signaling but it was still controversial. *In vivo* Ca^{2+} imaging of intact dorsal root ganglion (DRG) neurons has consistently found increased neuron activation during states of pain hypersensitivity. **Hypothesis/Goals:** We hypothesized deletion of Panx1 in primary sensory neurons and satellite glial cells would decrease pain sensitivity in animals with nerve injury relative to wild type (WT) animals with nerve injury. **Methods:** WT and Panx1 primary sensory neuron and satellite glial cell conditional knockout mice underwent sciatic nerve chronic constriction injury (CCI) or sham operation. Animals were tested for mechanical, thermal and cold sensitivity using von Frey, Hargreaves, and cold plantar tests. Primary sensory neuron activity in the dorsal root ganglion (DRG) was monitored using the green fluorescent calcium indicator GCaMP3. **Results:** We found that conditional deletion of Panx1 in DRG neurons and satellite glial cells reduces mechanical hypersensitivity after CCI. Panx1 conditional deletion mice in both glia and neuron remain more sensitive to mechanical pain than sham operated control mice. Unexpectedly, conditional deletion of Panx1 in both primary sensory neurons and satellite glial cells results in decreased primary sensory neuron activation in response to mechanical, cold, and thermal stimuli following CCI. Sham control mice with Panx1 conditional deletion retain normal levels of DRG neuron activation in response to stimuli. **Conclusion:** These surprising results suggest a novel mechanism of neuropathic pain hypersensitivity in mice lacking Panx1 in DRG neurons and Plp1 glia. **Acknowledgements:** We would like to thank all members of the Kim Lab, the University of Texas Health and Science Center – San Antonio, NIH (1R01DE031477-01)

Poster 11

Ion Channels Ensembles in Human Dorsal Root Ganglia

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Background: Nociceptor activity, accommodation to stimuli (i.e., rapidly or slowly accommodating), and responsiveness is determined, in part, by ion channel expression and their respective modulators.

Goals: Here, we extracted several ion channels from barcodes corresponding to single nociceptors to gain insight as to functional differences in human nociceptor populations.

Methods: Near single-cell transcriptomics was attained via Visium 10X Spatial Sequencing. Following quality control checks with Seurat and Python code, neuronal populations were segregated via clustering. The expression of multiple ion channels from a single barcode (which corresponded to a single neuron) was extracted using Python.

Results and Conclusions: We characterized ion channel transcripts within each barcode, from donors without diagnosed pain conditions and two donors with painful diabetic neuropathy. Future studies will use this information, along with other datasets, to generate *in silico* models of neuronal activity.

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Poster 12

The Role of Meteorin in Cisplatin Induced Peripheral Neuropathy

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Background:

Cisplatin is a potent therapeutic that induces peripheral neuropathy in cancer patients. This adverse effect severely limits its usefulness as a chemotherapeutic. Cisplatin causes sensory issues by inducing reactive gliosis in dorsal root ganglion (DRG) and the loss of intraepidermal nerve fibers in skin. Previous studies have demonstrated the antinociceptive effects of meteorin in reversing neuropathic pain in rodent models of peripheral nerve injury and paclitaxel induced peripheral neuropathy.

Hypothesis/Goals:

We hypothesize recombinant mouse meteorin (rmMeteorin) can reverse cisplatin induced peripheral neuropathy in a mouse model by decreasing satellite cell gliosis in DRGs and protecting intraepidermal nerve fiber loss in the skin.

Methods:

Female ICR mice were treated with cisplatin (2mg/kg, 5 x i.p.) to induce hind paw mechanical hypersensitivity. After mechanical hypersensitivity was established, rmMeteorin (1.8mg/kg, 5 x s.c.) was administered every other day for 5 doses to reverse mechanical hypersensitivity. Hind paw mechanical hypersensitivity was measured with Von Frey filaments. The animals were euthanized when they returned to baseline and their dorsal root ganglia (DRG) and hind paw skin were collected.

Results:

rmMeteorin treated mice had significantly less hind paw mechanical hypersensitivity compared to vehicle treated mice. Immunohistochemical studies showed rmMeteorin reduced the DRG expression of connexin43 and glutamine synthase, indicating decreased satellite cell gliosis. Intraepidermal nerve fibers in the skin were also protected from cisplatin induced loss by rmMeteorin treatment.

Conclusions:

These results demonstrate rmMeteorin can reverse cisplatin induced peripheral neuropathy in a mouse model. Also, rmMeteorin protects against the cisplatin induced satellite cell gliosis in the DRG and intraepidermal nerve fiber loss in the skin.

Acknowledgements:

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Poster 13

The Role of Sigma-2/TMEM97 in the Context of Affective and Pain Behaviors

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Background: The Sigma-2 receptor, recently identified as *TMEM97*, is a transmembrane protein that is located in the endoplasmic reticulum (ER) and the plasma membrane. Previous studies have shown that ligands that bind to TMEM97 have anxiolytic/antidepressant-like properties and relieve neuropathic pain in rodents. Despite medical interest in TMEM97, little to no affective and pain behavioral characterization has been done using TMEM97 mutant mice, which hinders the development of TMEM97 as a viable therapeutic target.
Hypothesis/Goal: Using wild-type (WT) and global TMEM97 knockout (KO) mice, we aim to investigate the role of TMEM97 in modulating affective and pain behaviors across different assays. We also aim to investigate the contributing role of TMEM97 in regulating neuropathic pain-induced affective behaviors, such as anxiety and depression.
Methods: Adult wild-type (WT) and global TMEM97 knockout (KO) mice on a C57BL6/J background were used. We tested a battery of affective assays - open field, light/dark preference, elevated plus maze, elevated zero maze, forced swim test, and tail suspension test – before surgery to obtain a baseline. At least 10 weeks after a neuropathic spared-nerve injury (or sham treatment), the battery of affective behaviors was repeated. The peripheral paw mechanical sensitivity was performed using von Frey to assess pain hypersensitivity that may develop after the injury.
Results: At baseline, our results demonstrate that TMEM97 KO mice show a trend for less anxiety/depression-like behaviors in light/dark preference and tail suspension test but not in an open field, elevated plus maze, and forced swim test at baseline. We next performed spared nerve injury in WT and TMEM97 KO mice to assess the role of TMEM97 in neuropathic pain-induced anxiety and depression. WT mice, but not TMEM97 KO mice, developed a pain-induced depression phenotype in the forced swim assay.
Conclusion: Our results show that TMEM97 plays a modest role in modulating depression in naïve animals with a significant change in the presence of nerve injury. Overall, these data demonstrate that TMEM97 may be targeted to alleviate pain-affective comorbidities.
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Poster 14

The Integrated Stress Response and Eukaryotic Initiation Factor 2A Mediate Evoked Pain Hypersensitivity in a Model of Multiple Sclerosis

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Background: Multiple sclerosis (MS) is a chronic, autoimmune disease characterized by demyelination, inflammation, and neurodegeneration that results in motor and sensory impairments. As such, chronic pain affects 50-70% of those diagnosed with MS and current treatment for neuropathic pain are not effective in individuals with MS. Most studies investigating neuropathic pain in MS have focused on the central nervous system, particularly in the dorsal horn of the spinal cord. However, increasing evidence points towards a crucial role of the peripheral nervous system (PNS) in the development of pain in MS and in its animal model, experimental autoimmune encephalomyelitis (EAE). In our previous work, dorsal root ganglia (DRG) collected from mice with EAE displayed increased immune activation and evidence of integrated stress response (ISR). The ISR is an adaptive response to various cellular stressors, like protein misfolding and nutrient deprivation, leading to the phosphorylation of eukaryotic initiation factor 2α (eIF2α) leading to decreased protein synthesis and a shift towards eIF2A-mediated translation. eIF2A, not to be confused with eIF2α, is an alternative initiation factor that is dominant under conditions of ISR.

Hypothesis/Goals: I hypothesize that eIF2A regulates evoked mechanical and cold hypersensitivity, but not spontaneous pain, in EAE by modulating the translation of ISR-dependent genes.

Methods: EAE was induced in 12–14-week-old, male wild-type and eIF2A$^{-/-}$ using myelin oligodendrocyte glycoprotein (MOG_{33-55}) emulsified in complete Freud adjuvant (CFA) followed by two injections of pertussis toxin 48 hours apart. Control animals only received CFA and pertussis toxin. Animals were followed for 32 days post induction with their weight and clinical score recorded daily. At the onset of EAE symptoms, defined as a clinical grade 1, mice were tested for mechanical (von Frey test) and cold hypersensitivity (acetone test) as well as spontaneous pain behaviors (mouse grimace scale).

Results: we discovered that the loss of eIF2A did not significantly impact the EAE disease course as compared to wild-type animals. Day of onset of EAE, aggregate disease score, and overall disease burden were comparable in eIF2A$^{-/-}$ and wild-type EAE mice. However, we noted a slightly higher max disease score in eIF2A$^{-/-}$ EAE animals compared to wild-type EAE mice. Interestingly, eIF2A$^{-/-}$ EAE mice had attenuated weight loss than their wild-type EAE littermates.
Using von Frey filaments test and acetone evaporation test, we determined that wild-type EAE animals developed a profound evoked mechanical and cold hypersensitivity at disease onset while eIF2A$^{-/-}$ animals were protected from EAE-induced evoked pain hypersensitivity. Notably, both wild-type and eIF2A$^{-/-}$ mice showed significant grimacing behaviors at the onset of EAE suggesting that eIF2A does not influence spontaneous pain behaviors.

Conclusions: Our data show that the interplay between EAE-induced integrated stress response and eIF2A-mediated translation regulates evoked pain hypersensitivity in EAE. This provides a novel approach to treat neuropathic pain in MS.

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Poster 15

The Role of PRDM12 in Axonal Regeneration

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Background: Peripheral nerves have the amazing ability to regenerate their axons. It is now appreciated that peripheral nerves are made of many cell types with different regenerative capacities. In particular, the regeneration capacity of nociceptors is critical for recovery of nociception after injury. A lack of target tissue reinnervation is associated with insensitivity to noxious stimuli and hyperinnervation with increased sensitivity. Therefore, understanding the molecular mechanisms that modulate nociceptor axonal regeneration is key to discovering pathways that could help reestablish normal nociception after injury.

Preliminary data from our lab suggests a key transcription factor in nociceptor development is involved in adult nociceptor axonal regeneration. Our lab studies PRDM12, a transcription factor linked to a rare genetic disorder called Congenital Insensitivity to Pain. *Prdm12* expression is restricted to nociceptors and PRDM12 has 98-99% amino acid identity between mice and humans, indicating a highly conserved function. Patients with homozygous recessive *Prdm12* mutations cannot sense pain, resulting in serious injuries. *Prdm12* is required during embryogenesis for the development of nociceptors in the dorsal root ganglia, and loss of *Prdm12* results in a painless phenotype. However, the role of *Prdm12* in the adult is currently unknown. When *Prdm12* is knocked out after nociceptor maturation in the adult (*Prdm12* conditional knockout (CKO)), nociceptors survive and nociception is unaffected. Instead, transcriptomic analyses of *Prdm12* CKO DRGs suggest it has a role in reactivating developmental processes, particularly genes linked to axonal regeneration.

Hypothesis: I hypothesize that PRDM12 regulates axonal regeneration of adult mouse nociceptors after injury.

Methods: Methods utilized by this project include *in vivo* axonal regeneration via immunohistochemistry after sciatic nerve crush (SNC), bulk and single nuclear RNA sequencing, and qPCR.

Results: Analysis of bulk RNAseq suggests that developmental pathways are downregulated by *Prdm12* CKO. Nuclei isolation for snRNAseq has been successfully performed and analyzed. qPCR analysis after SNC of control animals indicates decreased injury markers over time.

Conclusions: Experiments are in progress to understand the role of PRDM12 after injury.

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Poster 16

Identification of Neuronal Populations in Dorsal Root Ganglia using Spatial Transcriptomics: Comparison between Pig and Human Species

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Background

Animal models are frequently used to probe basic pain mechanisms in the dorsal root ganglia (DRG) and to test the efficacy of drugs at the preclinical stage. Although rodent models provide invaluable insight for pain research, they often fail to mirror relevant human conditions, leading to poor translatability of promising therapeutic targets. To address this, pigs are considered an alternative model due to their comparability to humans. Pigs and humans share similar neural pathways for Aδ- and C-fibers, distribution of free sensory nerve endings, axonal excitability properties, and conduction velocities of nociceptors. Nevertheless, specific neuronal subpopulations in pig DRGs have not been identified.

Research studies characterizing the molecular profile of DRGs in rodents yield great insight on the heterogenous neuronal populations. Spatial transcriptomic tools offer an advantage over other next generation sequencing technologies because they capture the physical landscape of cell populations, allowing us to localize RNA transcripts within tissue and enhance our understanding of cell-to-cell interactions.

Hypothesis/Goals

This study seeks to comprehensively characterize neuronal subpopulations in pig DRGs and compare their evolutionary divergence from human DRGs to better assess the translatability of our preclinical pain models.

Methods

We sectioned and stained fresh frozen pig DRGs with eosin and hematoxylin (H&E) to assess the quality of the tissue and the morphology of the neurons. We then used the Visium Spatial Gene Expression kit to generate a near single-neuron spatial resolution. After sequencing, we selected barcodes overlapping with neurons using the 10x Loupe Browser platform. Low quality cells demonstrating low counts and high mitochondrial percentages were filtered out during the quality control step. Finally, we performed computational analysis using Seurat to integrate the datasets and perform neuronal clustering.

Results

We used visium spatial transcriptomics and identified distinct clusters corresponding to neuronal populations including nociceptors, proprioceptors, among others. We compared them to those in humans and identified cross-species similarities and differences.

Conclusions

We utilized our lab's recently published spatial transcriptomic dataset on human DRGs from healthy organ donors. Using computational approaches, we characterized neuronal subpopulations in pig DRGs using established markers from the reference human DRG dataset. Different neuronal populations were identified and compared across species. In addition to highlighting evolutionary differences, we also anticipate that this work will allow us to refine pig models, thus increasing translational efficiency of molecular pain research.

Poster 16

Acknowledgements
Genome Center, University of Texas at Dallas

Poster 17

The Role of OPRM1 in the Neonatal Autoresuscitation Reflex and Sudden Infant Death Syndrome

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Background: Opioid receptors are widely expressed throughout the brain and integral in nociception as well as homeostatic regulation of autonomic processes including respiration via modulating respiratory rhythmogenesis and chemosensation. Perturbations to homeostatic mu opioid receptor (MOR) signaling via opiate overdose results in respiratory depression, aberrant breathing, and possibly death. Infants born with Neonatal Abstinence Syndrome (NAS), a congenital respiratory disorder resulting from prenatal exposure to opioids, puts infants at a fourfold increased risk for Sudden Infant Death Syndrome (SIDS). SIDS takes the lives of approximately 1,400 infants annually under the age of one and its etiology remains mostly unknown. Currently SIDS is explained via the triple risk model that proposes that SIDS occurs in a vulnerable infant during a critical developmental period when triggered by an external stressor, including failure of the neonate autoresuscitation reflex. Recently a study identified an association between a mutation in the OPRM1 gene encoding MORs and SIDS cases, however, investigation of how this gene and perturbations in its native function modulates respiratory regulation are poorly understood.
Hypothesis/Goals: We hypothesize that native OPRM1 function is integral to protective neonate respiratory reflexes and that perturbation of native OPRM1 signaling negatively affects the neonatal autoresuscitation reflex. The goal of our research is to determine the requirement of OPRM1 in the protective neonatal autoresuscitation response to elucidate the role MORs in respiratory regulation and dysfunction as well as its potential contribution as a risk factor to congenital diseases, including SIDS and NAS, when expression is perturbed.
Methods: OPRM1 knockout (KO) mice were purchased from JAX and assayed for auto-resuscitation on our novel testbed. Postnatal day 7-8 mice were exposed to 3% CO_2 and 97% N_2 stimuli to induce a state of hypoxia resulting in detection of bradycardia, initial hyperventilation, hypoventilation, and apnea followed by restoration of room air conditions to facilitate the auto-resuscitation reflex and cardio-respiratory recovery. Mice were exposed to repeated bouts of anoxic challenges until death occurred.
Results: Preliminary data suggest that loss of OPRM1 function results in enhanced mortality on the autoresuscitation assay with OPRM1 KO mice surviving significantly less anoxic challenges compared to wild type (WT) controls. Results indicate that OPRM1 KO mice have decreased survival on the autoresuscitation assay compared to WT controls.
Conclusions: Results indicate that perturbation of the native function of OPRM1 produces a vulnerability to autoresuscitation dysfunction and mitigated survival. Our data demonstrate the first functional assessment of OPRM1 in neonatal autoresuscitation and reveal an important risk factor that may be implicated in perpetuating SIDS and NAS phenotypes. Future studies aim to characterize specific splice variants of OPRM1 known to produce neomorphic function to further characterize the implication of OPRM1 and its variants in congenital respiratory diseases. Understanding the role of OPRM1 in respiratory regulation and autoresuscitation will aid in defining potential mechanisms in SIDS etiology that will generate critical insights for the development of prognostics and targeted therapeutic interventions for congenital respiratory disorders.
Acknowledgements: Funding sources NIH/NHLBI R01HLN161142-01 and R01HL130249-07.

Poster 18

Sex-Dependent Differences in the Genomic Profile of Lingual Sensory Neurons in Naïve and Tongue-Tumor Bearing Mice

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Background: While sex-specific prevalence of orofacial pain is established, mechanisms of sex-dependent orofacial pain are widely understudied.

Hypothesis/Goals: To this end, a significant gap in knowledge exists about comprehensive regulation of tissue specific trigeminal sensory neurons in diseased state of males and females.

Methods: Using RNA sequencing of FACS sorted retro-labeled sensory neurons innervating tongue tissue, we determined changes in transcriptomic profiles in male and female mice under naïve as well as tongue-tumor bearing conditions.

Results: Our data revealed the following interesting findings: 1) Tongue tissue of female mice was innervated with higher number of trigeminal neurons compared to males; 2) Naïve female neurons innervating the tongue exclusively expressed immune cell markers such as Csf1R, C1qa and others, that weren't expressed in males. This was validated by Immunohistochemistry. 3) Male neurons were more tightly regulated than female neurons upon tumor growth; 4) While very few differentially expressed genes (DEGs) overlapped between male and female post-tumor growth, several biological processes (BPs) were similar between the two sexes. However, additional distinct processes were sex-specific; 5) Post-tumor growth male DEGs contained an equal mix of transcription factors, ligands, growth factors, receptors and channels, whereas female DEGs predominantly contained channels/receptors, enzymes, cytokines and chemokines.

Conclusion: Taken together, this is the first study to characterize the effect of sex as well as of tongue-tumors on global gene expression, biological pathways, and molecular function of tongue-innervating sensory neurons.

Poster 19

Elucidating the Role of IGF2 in the Dorsal Root Ganglion: An Inter-Species Investigation

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Background: Insulin-like growth factor 2 (IGF2) is a secreted protein involved in signaling pathways critical for neuronal growth and survival. IGF2 and its receptor, IGF1R, are expressed throughout the peripheral nervous system (PNS), but expression in the central nervous system (CNS) is limited to the olfactory bulb and hippocampal stem cells. As these are the only CNS regions known to be able to regenerate damaged axons like the PNS, IGF2 seems to be a common factor that allows for such growth and proliferation. We recently discovered a sparse uncharacterized *Igf2*$^{+}$ neuronal cell type in the adult mouse dorsal root ganglion (DRG), but it is not known what role *Igf2* plays in the DRG or whether this uncharacterized cell type is present in the human DRG.

Hypothesis/Goals: In the present study, we leverage unprecedented access to DRGs from human organ donors to determine whether human DRG neurons express *IGF2* transcript and characterize *IGF2* expression across age and sex. We hypothesized that a discrete neuronal population in human DRGs robustly expresses *IGF2* transcript, like mice.

Methods: For RNAscope experiments, ACD Multiplex V2 RNAscope kits were used per manufacturer instructions. Three 20 μm DRG sections were collected 100 μm apart within each DRG to ensure that no neuron was sampled more than once. Three non overlapping images were taken of each DRG section. Raw image files were analyzed for *IGF2* punctae within *PRDM12*$^{+}$ and *PRDM12*$^{-}$ neurons. Relative *IGF2* expression levels were designated with the following scores for a given neuron: 0 (no punctae), 1 (1-5 punctae), 2 (6-15 punctae), 3 (16-25 punctae), and 4 (26+ punctae). Pairwise statistical comparisons were performed using SPSS v25.

Results: Most *IGF2* expressed in the human DRG is non-neuronal, but there is a substantial population of *PRDM12*$^{+}$ cells with low-level *IGF2* expression. DRGs from female donors and younger donors have significantly more *IGF2*$^{+}$ cells than DRGs from male and older donors.

Conclusions: Our findings suggest a sexual dimorphism in *IGF2* expression and an increased role for IGF2 signaling earlier in life. Future studies will compare the expression level of *IGF2* in patients with painful diabetic neuropathy and patients without a pain disorder.

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Poster 20

Evaluation of MIF in Mediating hSCAP Analgesia in Orofacial Pain

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Background: Despite the efficacy of root canal treatments at eliminating pain associated with apical periodontitis (AP), an estimated 1.8 million patients will experience persistent pain six months after treatment. This pain reduces quality of life and increases the intake of analgesic drugs. However, chronic use of currently available analgesics is accompanied with adverse effects. Therefore, development of a novel class of analgesics that can prevent the development of persistent dental pain, with no adverse effects, will provide relief to millions of patients. Stem cell-induced analgesia is a promising therapeutic that has shown efficacy in pre-clinical and clinical studies. Our preliminary data demonstrates that i.v. injections of human stem cells of the apical papilla (hSCAP) reverses mechanical hypersensitivity in a model of AP. Additionally, our data suggests the cytokine macrophage migration inhibitory factor (MIF) may be mediating this effect.

Hypothesis/Goals: We hypothesis that MIF is mediating hSCAP-induced anti-nociception.

Methods: Pulp exposures of maxillary left 1st molars were performed to induce AP. On day 21 post pulp exposures, orofacial behavior was done to measure AP-induced mechanical allodynia, followed by intra-oral injections of recombinant MIF (0.03μg) on days 22-24. The following day, orofacial behavior was done to evaluate the effect of recombinant MIF on AP-induced mechanical allodynia. A separate group of mice received i.v. injections of hSCAP once a week for three weeks after pulp exposures. On day 22 post-pulp exposures, a MIF antibody (0.15ng/ul) was injected intraorally followed by orofacial behavior the next day.

Results: Intra-oral injection of recombinant MIF for 3 days reversed AP-induced hypersensitivity, while vehicle-treated mice saw no improvement. Mice with AP receiving weekly i.v. hSCAP injections saw their anti-nociception reverse after intra-oral injection of a MIF antibody.

Conclusions: This data provides evidence for a novel, previously undiscovered anti-nociceptive role of MIF in mediating hSCAP-indued pain relief.

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Poster 21

Peripheral Myeloid Cells Control Resolution of Painful Chemotherapy-Induced Peripheral Neuropathy (CIPN)

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BACKGROUND: Chemotherapies contribute to decreased cancer mortality but are associated with severe side effects including Chemotherapy-Induced Peripheral Neuropathy (CIPN). CIPN presents as a distal symmetric polyneuropathy causing numbness, tingling, and in a subset of patients, pain. Painful CIPN is a main cause for chemotherapy dose reduction, treatment cessation and reduced quality of life. A subset of painful CIPN patients will have pain resolution while others maintain pain persistency, however the mechanisms that mediate pain resolution are unknown and constitute a large gap of knowledge.

GOALS: The goals of this study are to identify endogenous mediators controlling CIPN pain resolution.

METHODS: We developed painful CIPN models in mice using the chemotherapeutic paclitaxel, where mice treated with specific injection protocols develop resolving or persistent mechanical hypersensitivity measured via von Frey. Using these models, we performed bulk RNA sequencing on hind paw, whole dorsal root ganglion (DRG), DRG sensory neurons and spinal cord at initiation, pre-resolution, post-resolution, and persistency time points. DEGs were selected (P-adj <0.05, FC > 2, RPKM > 1) and PANTHER analysis was performed to identify biological processes. To investigate the contribution of particular cell types in these tissues, we used the inducible diphtheria toxin receptor ablation model.

RESULTS: PANTHER analysis identified upregulation of immune system related genes in the hind paw during resolution of Model-1 not seen in Model-2. As myeloid cells are known to contribute to immune system related genes in the periphery, we ablated myeloid cells. We identified that CD11b+ peripheral, but not IBA1+ central, myeloid cells are critical for painful CIPN resolution. Further RNA sequencing analysis identified pro-inflammatory pathways correlated with painful CIPN resolution.

CONCLUSIONS: These studies provide mechanistic insights for CIPN pain resolution and identify a unique therapeutic strategy for permanent treatment of painful CIPN. Future studies will focus to delineate the myeloid cell sub-type and factors required for CIPN pain resolution.

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Poster 22

Captopril Loaded Thermo-Responsive Hydrogel Reverses Mechanical Hyposensitivity in the Lepr$^{db/db}$ Type 2 Diabetes Model

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Background: Millions of people worldwide suffer from diabetic peripheral neuropathy (DPN), and current therapeutics for DPN are limited in their efficacy. In light of this our lab has been exploring new therapies for the treatment of DPN with novel biomaterial/pharmaceutical combinations. Previous works have shown inhibition of angiotensin II can be effective in treatment of neuropathic pain after injury to the sciatic nerve. Here we use a novel formulation of the angiotensin converting enzyme (ACE) inhibitor Captopril embedded in a thermo-responsive hydrogel to treat the sensory loss associated with the Lepr$^{db/db}$ model of type 2 diabetes mellitus.

Hypothesis: Based on previous literature we hypothesized that local administration of our Captopril-Hydrogel (Cap-HG) would inhibit the generation of angiotensin II by ACE enzymes and restore sensation to the distal limb of Lepr$^{db/db}$ mice with diabetic peripheral neuropathy.

Methods: As part of our initial examination of safety and efficacy for the novel Cap-HG and drug free hydrogel (DF-HG) formulations, Cap-HG and DF-HG were tested *in vitro* with RAW 264.7 cells for effects on cell viability and inhibition of ACE activity. Once safety and efficacy tests were performed *in vitro* we began *in vivo* testing. For characterization of these hydrogels *in vivo*, Cap-HG and DF-HG were administered to the hind feet of WT or Lepr$^{db/db}$ mice and Von Frey tests were performed to determine the therapeutic window. Once the therapeutic window (approximately 3 days) was identified, Cap-HG and DF-HG were injected into the foot pads of WT or Lepr$^{db/db}$ mice to examine *in vivo* safety and efficacy. As part of determining the safety of these compounds, we examined inflammatory infiltrates in the hind foot, and systemic blood pressure. To determine the effects of Cap-HG and DF-HG on the hind paws we analyzed the proteome profile of hind paw lysate and intra-epidermal nerve fiber (IENF) density from skin samples.

Results: From our *in vitro* testing we were able to conclude that Cap-HG was less cytotoxic than free captopril and had similar inhibition of ACE activity compared to free captopril. *In vivo* testing also showed that our Cap-HG was capable of reversing mechanical hyposensitivity when DF-HG was not. Importantly, this occurred in the absence of any significant inflammatory response in the hind foot or systemic drop in blood pressure, as measured by IVIS imaging and blood pressure cuff respectively. Proteome profiling of hindfoot lysates from uninjected, DF-HG injected, and Cap-HG injected showed a normalization of the proteome from Lepr$^{db/db}$ mice after Cap-HG injection; however analysis of IENF density in the hind foot showed no significant difference compared to DF-HG injected mice.

Conclusions: Taken together, the results from this study show the safety and efficacy of local therapeutic treatment with Cap-HG in DPN and suggest that the therapeutic potential of the treatment lies in the ability to alter the local microenvironment and not in the regrowth of IENFs.

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Poster 23

Subacute Inhibition of Hmgb1 in the Amygdala Reduces Pain-Related Behaviors in a Rat Model of Chronic Neuropathic Pain

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Background
Chronic pain is a prominent healthcare issue that impacts a significant portion of the global population each year. An intricate interplay of sensory, cognitive, and emotional-affective dimensions comprises the highly complex experience of pain, presenting a challenge to identifying effective therapeutic options. Maladaptive neuroplasticity is a key contributor in the transition from acute to chronic pathological pain. This transition may be associated with neuroimmune mechanisms in the brain, which have yet to be elucidated. The amygdala is a key player in the emotional-affective component of pain and pain modulation, and the role of neuroimmune signaling within the amygdala in neuropathic pain states is unknown. High motility group box 1 (Hmgb1) is a pro-inflammatory molecule that is involved in crosstalk between neurons and glial cells in spinal nociception, yet its role in the amygdala in pain conditions is unknown.

Hypothesis/Goals
Here we tested the hypothesis that Hmgb1 is involved in pain-related amygdala plasticity and that inhibition of this molecule can reduce neuropathic pain behaviors.

Methods
Bulk RNA sequencing on right and left central nucleus of the amygdala (CeA) tissues was performed in adult rats at the chronic stage of the spinal nerve ligation (SNL) model of neuropathic pain. siRNA for Hmgb1 was injected stereotaxically into the right CeA of adult male and female rats as either a 2-week pre-treatment or 1-week post-treatment to SNL surgery. Anxiety-like, sensory, and emotional-affective behaviors were measured 4 weeks after SNL.

Results
Transcriptomic analysis revealed an upregulation of Hmgb1 mRNA in the right but not left CeA at the chronic stage of SNL. Hmgb1 silencing reduced mechanical hypersensitivity (von Frey and paw compression tests) and decreased emotional-affective responses (audible and ultrasonic vocalizations) in the post-treatment but not pre-treatment group; anxiety-like behaviors (open field test) were unaffected. Preliminary evidence suggests that neurons are a significant source of Hmgb1 release in the CeA.

Conclusions
Together these findings suggest that Hmgb1 in the amygdala may contribute to the transition from acute to chronic neuropathic pain, and inhibition of this molecule at a subacute time point may serve as a potential therapeutic target for neuropathic pain relief.

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Poster 24

Human, But not Murine, TRPM8^{+} Nociceptors Express PIEZO2

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Background: Piezo-type mechanosensitive ion channel component (PIEZO) 2, a low-force mechano-receptor underlying normal touch, mediates tactile pain induced by inflammation and/or neuropathic injury. Here, we elaborate upon reports that human, but not murine, nociceptors expressing Transient receptor potential cation channel subfamily M member 8 (TRPM8^{+}) possess PIEZO2 transcripts.

Goals: Our primary aim was to characterize PIEZO2 expression in human dorsal root ganglia (DRG).

Methods: Near single-cell transcriptomics was attained via Visium 10X Spatial Sequencing. TRPM8 and PIEZO2 transcripts were assessed by ACD Multiplex V2 RNAscope kits, per manufacturer instructions. Puncta were quantified using ImageJ and all statistical analyses performed using SPSS ver. 25.

Results and Conclusions: We report robust expression of PIEZO2 transcript in TRPM8^{+} nociceptors within human DRG. Future studies will examine the functionality of PIEZO2 protein and consider whether inflammatory pain conditions augment PIEZO2 expression and/or function in TRPM8^{+} nociceptors.

Acknowledgements: These studies were provided for by Allergan Inc.

Poster 25

MRGPRX2 on Meningeal Mast Cells Drives Migraine-like Pain

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Background: As one of the key effector cells in the inflammatory process, mast cells have essential functions in allergies and fighting infections. More recently, mast cells are now recognized to play an important link between the nervous and immune systems. Mast cells can be found in close proximity to peripheral nerve endings and, due to their significant spatial advantages over other immune cells, are one of the first to respond to sensory nerve activation. We recently showed that mast cell specific receptors, MrgprB2 and its human homologue MRGPRX2, are involved in neurogenic inflammation and pain.

Goals: We are interested in translating our previous findings to another pain phenotype; migraine. We generated a humanized mouse line that expresses MRGPRX2 on meningeal mast cells, thus allowing us to study the role receptor of this receptor in migraine pain *in vivo*.

Methods: Calcium imaging was used to study $MRGPRX2^+$ cell activation by PACAP1-38. Calcium imaging and β-hexosaminidase release assays were used to find the dose response. Minimally invasive dural stimulation model was used to apply PACAP1-38 to the MrgprB2-Cre^+ $MRGPRX2^+$ ($X2^+$) or MrgprB2-Cre- $X2^+$ ($X2^-$) mouse meninges. Facial mechanical hypersensitivity was measured in male mice prior to dural injection and then 1hr, 2hrs, 4hrs, and 24hrs after dural stimulation with PACAP1-38 (n=11-10/per group) using Von Frey filaments. Flow Cytometry was utilized to quantify $X2^+$ cells in the extracted meninges of dural-stimulated vs sham $X2^+$ and $X2^-$ mice.

Results: The mast cell receptor MrgprB2/X2 is expressed in the meninges and its activation leads to migraine-like pain behavior. The neuropeptide PACAP1-38 activates of MrgprB2, therefore stimulating mast cell release leading to migraine-like pain. Similarly, PACAP1-38 activates mouse meningeal mast cells that express the human MRGPRX2 receptor.

Conclusions: Here, we demonstrate, for the first time, a novel transgenic mouse line that functionally expresses the human MRGPRX2 in connective tissue mast cells, including meningeal mast cells, and responds to PACAP1-38 to contribute to migraine-like pain, in mice.

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Poster 30

Pannexin 1 Conditional Deletion in Both Primary Sensory Neurons and Satellite Glial Cells Decreases Sensitivity to Cold Behaviorly and in Ca^{2+} Imaging

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Background: Pannexin 1 (Panx1) is a pore protein connecting the intracellular and extracellular space as large transmembrane channels which allow the passage of ions and small molecules between these compartments such as ATP. Glial Panx1 might be involved in sensitivity to mechanical pain but this idea remains controversial. Cold pain hypersensitivity and allodynia are common problems in a variety of medical conditions including chemotherapy-induced peripheral neuropathy, fibromyalgia, post-stroke cerebral pain, and opioid-induced hyperalgesia. **Hypothesis/Goals:** We hypothesized conditional deletion of Panx1 in primary sensory neurons and satellite glial cells would affect basal sensitivity to mechanical, thermal, and cold stimuli. **Methods:** Using floxed Panx1 and Cres driven expressed in primary sensory neurons and satellite glial cells, we tested mechanical, thermal, and cold sensitivity using von Frey filaments, Hargreaves test and cold plantar tests. We imaged dorsal root ganglion (DRG) neurons using green fluorescent Ca^{2+} indicator GCaMP3 and monitored activity in response to cool and cold stimuli. **Results:** We found that conditional deletion of Panx1 in DRG neurons and proteolipid protein 1 (Plp1)-positive glia, including satellite glial cells, reduces sensitivity to noxious cold. Thermal and mechanical pain sensitivity were not altered in nonparametric tests. Furthermore, fewer DRG neurons respond to noxious cold stimulus in Panx1 conditional deletion animals than in wild type animals. **Conclusions:** Panx1 in primary sensory neurons and/or satellite glial cells plays a role in cold sensitivity. The role of Panx1 in noxious cold sensitivity must be further investigated. **Acknowledgements:** We would like to thank all members of the Kim Lab, the University of Texas Health and Science Center – San Antonio, NIH (1R01DE031477-01) and Craniofacial Oral-Biology Student Training in Academic Research (COSTAR) at University of Texas Health and Science Center at San Antonio Dental School.

Poster 26

Morphological Differences Between Human Trigeminal and Dorsal Root Ganglia Sensory Neurons

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Background: Classically, sensory neurons residing in the trigeminal (TG) and dorsal root ganglia (DRG) can be differentiated into three broad classes of neurons based on their cellular diameter and their enrichment of various protein and mRNA markers. For instance, the Aβ mechanoreceptors are large, myelinated neurons that express *KCNS1* and *PVALB* and relay information about touch, while both the myelinated, medium-sized Aδ neurons and the unmyelinated, small-sized C neurons express *PRDM12*, *TRPV1*, *SCN10A* and convey nociceptive information leading to pain. While the distribution of these subtypes has been well-characterized in rodent ganglia and human DRG, there is no information on how these neurons are represented in the human TG.

Methods: To investigate, we first conducted hematoxylin and eosin on mouse and human TG and DRG sections to assess neuronal diameter. We also performed RNAscope for *PRDM12*, *TRPV1*, and *SCN10A* on human TG and compared it to our previously published human DRG data.

Results: We found that almost all human TG sensory neurons are small-diameter (~40-60 μm) and fit the size profile of a C-nociceptor. This is highly unlike human DRG where the neurons have a mixed size profile which can range upwards of 130 μm. Additionally, we found that 97% of all human TG sensory neurons express nociceptive markers like *PRDM12*, *SCN10A*, and *TRPV1*.

Conclusions: These data suggest that human TG neurons are morphologically distinct from human DRG neurons and are potentially comprised mainly of nociceptors. This finding is not recapitulated in mouse TG, evidencing yet another species difference in the sensory system. One alternative conclusion is that human TG neurons have their own unique size-classification within a smaller range of diameters which can be further assessed by additional experiments investigating the distribution of Aβ markers. It is also possible that the Aβ population is located externally in the mesencephalic nucleus of V where proprioceptors that innervate the jaw are located in rodents.

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Poster 27

Glial Progenitor Heterogeneity and Key Regulators Revealed by Single-Cell RNA-Sequencing Provide Insight to Regeneration in Spinal Cord Injury

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Abstract:
Recent studies have revealed the heterogeneous nature of astrocytes; however, how diverse constituents of astrocyte-lineage cells are regulated in adult spinal cord after injury and contribute to regeneration remains elusive. We perform single-cell RNA-sequencing of GFAP-expressing cells from sub-chronic spinal cord injury models, identify and compare with the subpopulations in acute-stage data. We find subpopulations with distinct functional enrichment and their identities defined by subpopulation-specific transcription factors and regulons. Immunohistochemistry, RNAscope experiments and quantification by stereology verify the molecular signature, location and morphology of potential resident neural progenitors or neural stem cells in the adult spinal cord before and after injury, and uncover the populations of the intermediate cells enriched in neuronal genes that could potentially transition into other subpopulations. This study has significantly expanded the knowledge of the heterogeneity and cell state transition of glial progenitors in adult spinal cord before and after injury.

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Poster 28

B Cells Drive Mechanical Pain After Nerve Injury

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Background
Neuropathic pain, caused by damage to the somatosensory system, is a chronic condition that greatly affects quality of life. Previous unbiased transcriptomic analysis revealed upregulation of B cell-associated genes in the spinal cord following peripheral nerve injury. However, the mechanistic role that B cells play in neuropathic pain remains unclear.

Hypothesis/Goals
Here, we investigated if B cells contribute to the development of neuropathic pain following nerve injury via the binding of IgG to Fcγ receptors (FcγR).

Methods
Subjects are adult male and female muMT mice (lacking mature B cells), *Fcer1g*$^{-/-}$ mice (lacking activating FcγRs), and wildtype (WT) C57BL/6J mice. Allodynia was established via unilateral chronic constriction injury (CCI) of the sciatic nerve and was quantified via paw withdrawal to innocuous stimuli. B cells were depleted in WT mice via administration of anti-CD20 monoclonal antibody (mAb) at the time of injury. Splenic B cells from WT mice were transferred to muMT mice. IgG was isolated from WT serum and transferred to muMT and *Fcer1g*$^{-/-}$ mice two weeks after CCI. Patch clamp electrophysiology was performed on cultured mouse L4-5 DRGs.

Results
B cell depletion with anti-CD20 mAb prevented the development of allodynia in mice of both sexes. B cell-deficient muMT mice were also protected from CCI-induced allodynia, but reconstituting muMT mice with B cells prior to injury was sufficient to reinstate allodynia after CCI. Passive transfer of IgG from injured WT mice to injured muMT mice resulted in development of allodynia, and the pro-nociceptive qualities of IgG relied on the contribution of FcγRs. Finally, CCI resulted in increased spontaneous activity in DRGs from WT mice, but not *Fcer1g*$^{-/-}$ mice.

Conclusions
These data reveal a pro-nociceptive role for B cells in CCI-induced neuropathic pain in both male and female mice via an IgG-FcγR-mediated mechanism.

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Poster 29

Accumulation of Immunoglobulin G in Dorsal Root Ganglia and Spinal Cord After Nerve Injury

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Background
Neuropathic pain is a debilitating condition caused by damage to the somatosensory system. Because many existing pain medications do not effectively treat neuropathic pain, and those that do often cause adverse side effects, there is a high demand for new therapeutic targets. Previous unbiased transcriptomic analysis revealed upregulation of B cell associated genes in the spinal cord following peripheral nerve injury. Evidence from rheumatoid arthritis and fibromyalgia studies suggest that B cell-derived immunoglobulin G (IgG) can bind sensory neurons and induce pain. However, the involvement of IgG following nerve injury has not yet been characterized.

Hypothesis/Goals
Here, we investigate if IgG deposition increases in the dorsal root ganglia (DRG) and spinal cord after peripheral nerve injury.

Methods
The subjects were adult male and female C57BL/6J mice, B-cell deficient muMT mice, and mice lacking activating Fc gamma receptor ($FcR\gamma^{-/-}$). Neuropathic pain was unilaterally induced using chronic constriction injury (CCI) of the sciatic nerve. Subjects were euthanized at days 3, 7, and 21 post-surgery, and lumbar spinal cord and L4-5 DRGs were collected for cryosectioning. The tissues were stained using immunohistochemistry and IgG deposition was imaged with fluorescent confocal microscopy. Human DRGs were immunostained for IgG.

Results
IgG deposition was significantly increased in the ipsilateral spinal cord in WT mice at days 7 and 21 following CCI compared to sham controls. Further analysis of IgG deposition was performed for contralateral spinal cord and DRGs. DRGs from human chronic pain patients revealed increased deposition of IgG compared to healthy patients.

Conclusion
These data suggest that CCI results in increased IgG accumulation at DRG and spinal cord. Future studies will examine if IgG accumulation drives allodynia, which could provide insight into the mechanisms of neuropathic pain after nerve injury.

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