UNIVERSITY of MARYLAND
CENTER TO ADVANCE CHRONIC PAIN RESEARCH

RELIEVING PAIN IN AMERICA

Publications

Highlights of recent grant awards, authorships, and other CACPR member news.

Vinita Agarwal, PhD

Agarwal, V. (April 21, 2020). Patient assessment and chronic pain self-management in ethnomedicine: Seasonal and ecosystemic embodiment in Ayurvedic patient-centered care. *International Journal of Environmental Research and Public Health, 17* (8), 2842. https://doi.org/10.3390/ijerph17082842 . Published in the special issue: Beyond Conventional Medicine: Ethnomedical Approaches for Health Promotion and Disease Prevention

This qualitative case study of Ayurvedic physicians from India explicates how Ayurveda describes the integration of the individual and the ecological in chronic pain management. It provides recommendations for tailoring patient-centered care in integrative chronic pain management through employing a *dosha* -based communication framework that relates the individual and the ecological in the patient's life-context and supports the co-creation of a collaborative plan of care using an ethnomedical framework

David A. Seminowicz, PhD

Psilocybin Acutely Alters the Functional Connectivity of the Claustrum With Brain Networks That Support Perception, Memory, and Attention
Frederick S Barrett [1], Samuel R Krimmel [2], Roland Griffiths [3], **David A Seminowicz** [2], Brian N Mathur [4]
PMID: 32454209
DOI: 10.1016/j.neuroimage.2020.116980

https://pubmed.ncbi.nlm.nih.gov/32454209/

This study uses a pharmacological intervention to provide the first empirical evidence in any species for a significant role of 5-HT2A receptor signaling in claustrum functioning, and supports a possible role of the claustrum in the subjective and therapeutic effects of psilocybin.

Joyce Teixeira Da Silva, PhD

Rocha P, Ferreira A, **Da Silva JT** , Alves A, Martins D, Britto L, Chacur M. Effects of selective inhibition of nNOS and iNOS on neuropathic pain in rats. Molecular and Cellular Neuroscience, 2020. PMID: 32353527.

Our most recent article investigated the effects of nitric oxide synthases (neuronal and inducible NOS) inhibition on chronic pain in rats. We found that drugs specifically targeting neuronal NOS represent a potential therapeutic strategy to manage chronic pain.

Richard Traub, PhD

Down-regulation of spinal 5-HT $_{2A}$ and 5-HT $_{2C}$ receptors contributes to somatic hyperalgesia induced by orofacial inflammation combined with stress.
Xue Y, Wei SQ, Wang PX, Wang WY, Liu EQ, **Traub RJ** , Cao DY. Neuroscience. 2020 Jun 1:S0306-4522(20)30346-8. doi: 10.1016/j.neuroscience.2020.05.044. Online ahead of print. PMID: 32497757

The two main findings from this paper are that in the presence of orofacial inflammation, the duration and type of stress affect the duration of somatic hypersensitivity, and the hypersensitivity is partly modulated by 5-HT2A and 2C receptors.

JunFang Wu, B.M., PhD

1. Ritzel RM, Li Y, He J, Khan N, Doran S, Faden AI, and **Wu J.** Sustained neuronal and microglial alterations are associated with diverse neurobehavioral dysfunction long after experimental brain injury. Neurobiology of Disease, 2020; 136:104713. PMID: 31843705

This paper provides evidence that a single moderate-level traumatic brain injury (TBI) has a profound and long-lasting impact on neurological outcome, coincided with TBI-associated changes in neuronal count, synaptic proteins, oxidative stress level, decreased phagocytic activity of microglia, as well as pathological alterations in the peripheral immune system. Together, these findings reinforce the idea that TBI alters the trajectory of normal aging, further compounding age-related neurological decline and immune pathology.

2. Henry RJ, Rodney RM, Barrett JP, Doran SJ, Jiao Y, Leach JB, Szeto GL, **Wu J** , Stoica BA, Faden AI, and Loane DJ. Microglial depletion with CSF1R inhibitor during chronic phase of experimental traumatic brain injury reduces neurodegeneration and neurological deficits. Journal of Neuroscience, 2020, 40(14): 2960-2974. PMID: 32094203.

The study demonstrates that short-term elimination of microglia during the chronic phase of traumatic brain injury followed by repopulation results in long-term improvements in neurological function, suppression of neuroinflammatory and oxidative stress pathways, and a reduction in persistent neurodegenerative processes.

3. Cao T, Matyas JJ, Renn CL, Faden AI, Dorsey SG, **Wu J.** Function and mechanisms of truncated BDNF receptor trkB.T1 in neuropathic pain. Cells, 2020, 9(5), 1194. PMID: 32403409

This review summaries the current research on the function and mechanisms of TrkB.T1 in neuropathic pain, including spinal cord injury-pain. Potential mechanism studies addressing the role of TrkB.T1 in neuropathic pain are highlighted. In addition, we explore the cellular mechanisms involved, such as the role of TrkB.T1 in astrocytes and post-injury reactive astrogliosis; as well as altered transcriptional programming that controls cellular movement and immune function in relation to injury-induced neuropathic pain.

Grants

Ke Ren, PhD / Feng Wei, PhD

R01 DE029946 (Ren/Wei, MPI)
NIH/NIDCR
07/01/2020-6/30/2025
Amount: $3,030,104 (Total direct and indirect)
"Disruption of Homeostatic Neuroimmune Interactions in Descending Circuitry in the Development of Pain Chronicity"

Project summary: Millions of people suffer from chronic or persistent pain, which is a major medical problem. The current treatment for chronic pain conditions is unsatisfactory. In recent years, ample evidence has documented the role of glia and their interactions with neurons in the development of persistent pain. Despite overwhelming evidence from preclinical studies, clinical trials for the treatment of chronic pain with glial modulators have not been successful, which is related to our incomplete understanding of the mechanisms. While a majority of studies show the pain-facilitating aspect of the injury-related glial activity, *a potential inhibitory/protective role of neuron-glial interactions in the development of persistent pain has been largely overlooked* . This project will analyze inhibitory/beneficial neuroglial interactions in the descending pain modulatory circuitry and test the hypothesis that disrupted inhibitory glial activity contributes to the emergence of chronic pain. Exploring the beneficial effect of glial activity will fill the gap in our understanding and lead to a transformative shift in the search for improved management for chronic pain.

JunFang Wu, B.M., PhD

PI Name: Junfang Wu; Long-Jun Wu (Mayo Clinic)

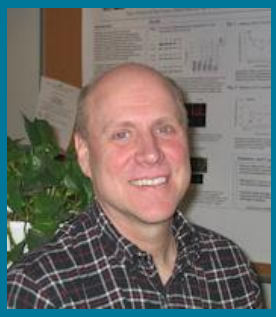
Project Title: The Function and Mechanisms of Voltage-Gated Proton Channel Hv1 in Spinal Cord Injury
Application ID: 1 R01 NS110825
Funding Period: 05/15/2020-04/30/2025
Funding Amount: $2,392,596 (direct and indirect)

Project Summary: The voltage-gated proton channel Hv1 is a newly discovered ion channel, highly expressed in resting microglia of the brain. Under pathological conditions, microglial Hv1 is required for NOX-dependent generation of ROS by providing charge compensation for exported electrons and relieving intracellular acidosis. Thus, Hv1 is a unique target for controlling multiple NOX activities and ROS production. In the present study, we will use systemic or microglial Hv1 KO, microglial NOX2 KO mice and in vivo and in vitro innovatively technologies to determine the mechanisms of SCI-triggered Hv1 elevation on post-injury neuroinflammation. Our study will be the first to implicate microglial Hv1/NOX2/ROS/IFN-g signaling in the pathophysiology of SCI, leading to novel treatment approaches for SCI. Given the proposed roles for Hv1 in other inflammatory models, Hv1 signaling represents a generic mechanism relevant to other neuroinflammatory states.

Presentations

Vinita Agarwal, PhD

Agarwal, V. (May 21, 2020). *Nature, Cycles, and Balance in Ethnomedicine: Ayurvedic Protocols in the Treatment of Chronic Pain.* 70th International Communication Association Virtual Conference.



Remembering
Dean Dessem, PhD

It is with great sadness that we inform you of the passing of **Dean Dessem, PhD, CACPR member** and Associate Professor in the Department of Neural and Pain Sciences, on Tuesday, June 2. Dean was a faculty member at the University of Maryland School of Dentistry for three decades. He conducted many fundamental studies of the neural mechanisms of trigeminal system sensory-motor integration and muscle pain. He was most recently collaborating with Richard Traub and Susan Dorsey on a comorbid pain model in rodents, investigating the mechanisms underlying the links among orofacial pain, visceral pain, and stress. He is remembered as a great person and colleague among the many faculty and staff that he worked with over the years and he will be sorely missed.

Accolades

Susan G. Dorsey, PhD, RN, FAAN appointed chair of National Institute of Nursing Research Initial Review Group. To read more, please click here .

Joyce Teixeira Da Silva, PhD received an award to participate in the Neuroscience Scholars Program of the Society for Neuroscience (SfN).

Underrepresented graduate or postdoctoral researchers have the opportunity to join this award-winning program to enhance their career and build community. To learn more, please click here .

Marcela Romero-Reyes, DDS, PhD was invited by Dr. Mario Rodriguez Tiscareño to give an online/virtual lecture at the National University of Mexico (UNAM), Mexico city. School of Dentistry, postgraduate and research division on May 5th, 2020, entitled: *"Perspectives in Orofacial Neuropathic Pains"*

Trigeminal neuropathic pains are non-odontogenic pains that are devastating for the quality of life of the patient and required multidisciplinary management. Not all trigeminal pains are equal and the differential diagnosis and care should be provided by a skillful trained clinician in the diverse orofacial pain disorders. The lecture discussed the difference between neuropathic, musculoskeletal and neurovascular pain disorders that can be present in the craniofacial and cervical structures as well as a discussion of different clinical cases illustrating episodic and continuous (peripheral and central) trigeminal neuropathies that may appear in the dental practice in addition to their possible prevention and management.

Announcements

Those of you with interests in Complementary and Integrative Health should be aware that the NCCIH is in the process of developing its strategic plan for 2021-2026. They are asking for comments from the public as they develop their plan. They held a town hall for this purpose in May and have another one scheduled for July 1. Independent of these town halls, they are soliciting ideas through email from all interested parties. As a member of the National Advisory Council for Complementary and Integrative Health, I can tell you that NCCIH is keenly interested in hearing from the research community, along with members of the general public. Pain research is a major component of NCCIH's portfolio, both intramurally and extramurally. We should all show support for that commitment and offer ideas of how their research portfolio should develop. Please go to this link and learn more about what you can do.

https://www.nccih.nih.gov/nccih-strategic-plan-2021-2026

Joel D. Greenspan ,
CACPR Co-Director

The UM Center to Advance Chronic Pain Research (CACPR) is a multidisciplinary center composed of nationally and internationally renowned clinical and preclinical translational scientists whose principle research focus is on the physiological, genetic, and psychosocial underpinnings of the development and persistence of debilitating chronic pain conditions.

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