



APRIL 2021



Special Edition CACPR Newsletter:

Honoring Joel D. Greenspan,
former CACPR Co-Director

Our dear colleague, mentor, and friend Joel Daniel Greenspan passed away on the morning of February 8, 2021 in the comfort of his home with his wife of over 40 years by his side.

Joel grew up in Florida where he obtained a bachelor's degree in Behavioral Sciences at Rollins College in 1974. Joel then obtained his PhD in Neuroscience at Florida State University in 1980 under the mentorship of Dan Kenshalo, Sr. With Kenshalo his dissertation was "The Effects of Skin Compressibility Upon Psychophysical Functions of Tactile Intensity: A Comparison of Force and Depth of Skin Indentation as Stimulus Dimensions". During this time, Joel would work at Disney World to fund his education when the lab did not have funding for his stipend. After receiving his PhD, Joel worked in a research fellowship under the mentorship of Ed Perl at University of North Carolina-Chapel Hill, where he continued his work with non-human primates to study the psychophysics associated with electrophysiological activity in cutaneous primary afferent nociceptors. From 1987 to 1995, Joel was an assistant

professor at SUNY Health Sciences Center at Syracuse, where he contributed fundamental work towards our understanding of the neural encoding of nociceptive mechanical stimuli and the perception of sharpness and pain.

He moved his lab to the University of Maryland, Baltimore in 1996, recruited by Ron Dubner, where he continued researching the neural mechanisms underlying the perception of pain. At UMB, Joel added functional neuroimaging of nociceptive processing in the human central nervous system to his portfolio. He also maintained a faculty affiliation with the Johns Hopkins University School of Medicine, and was a member of the Johns Hopkins Center for Mind-Body Research. Joel worked with friend and colleague Rich Traub and other distinguished researchers to lead the IASP “Consensus Conference to Establish Guidelines for Research on Sex Differences in Pain” in 2006, which led to a highly impactful publication that continues to guide the field. Joel provided his expertise in psychophysics to the Orofacial Pain Prospective Evaluation and Risk Assessment Study from 2006 until 2016 and managed the study site at the University of Maryland, Baltimore. Joel was the co-founder and co-director of the University of Maryland Center to Advance Chronic Pain Research with Susan Dorsey from 2014 until 2020. Joel was chair of the department of Neural and Pain Sciences from 2008 until 2020. He was primary mentor for PhD recipients Eleni Sarlani, Eric Moulton, Raimi Quiton, and Timothy Meeker and postdoctoral fellows David Andrew, Elizabeth Roy Felix, D. S. ‘Judy’ Veldhuijzen, Anne-Christine Schmid and Yiming Liu. He contributed to the publication of more than 125 research articles and numerous book chapters. These book chapters included *Gender Differences in Pain and Its Relief* in Melzack and Wall’s Textbook of Pain authored with Rich Traub.

Joel was a cerebral and inquisitive scientist, a patient and supportive mentor, and a kind and gentle soul to all who knew him. He is survived by his wife Deborah Greenspan, his son, Robert Crews, Sr. and two grandchildren Roberts Crews, Jr. and Candice Crews.



Dr. Greenspan was a leader in the field of translational pain research focusing on the orofacial region and widely regarded as a pioneer in exploring sex and gender differences in pain and analgesia. His extensive multidisciplinary research was central to advancing our understanding of orofacial pain disorders. Dr. Greenspan was ideally suited to serve, together with Dr.

Susan Dorsey, as a founding co-director of the Center to Advance Chronic Pain Research.

-Mark A. Reynolds, DDS, PhD, MA, Dean of the School of Dentistry

Dr. Joel Greenspan, along with Dr. Susan Dorsey, created the vision for the University's first joint Research Center and was instrumental in marking the Center to Advance Chronic Pain Research a reality. The Center provides an environment for researchers from across the University of Maryland, Baltimore to come together to advance our understanding of chronic pain which was one of Dr. Greenspan's professional legacies.



-Jane M. Kirschling, PhD, RN, FAAN, Dean of the School of Nursing



I am deeply saddened by the passing of my dear friend, Joel D. Greenspan. Dr. Greenspan was instrumental in the vision, creation, and growth of the Center to Advance Chronic Pain Research (CACPR). We worked alongside one another as Co-Directors of the CACPR for six years and the Center would not be where it is today without his exceptional guidance and leadership. His extensive research and significant contributions within the neuroscience and pain fields will leave a lasting impact, and his absence will be felt within the CACPR and larger UMB communities.

-Susan G. Dorsey, PhD, RN, FAAN

Not only as a man of "sex difference in pain" and the eminent leader of our pain group, but Joel has also been a generous boss and gentle colleague. He often patted my back for encouragement, which is unforgettable. Whenever I was in disappointment, he shared his experiences to comfort me and added "It is not the end of the world". As Joel asked everyone, we will do our best to continue to make NPS and CACPR as a source of pride.



-Man- Kyo Chung, DMD, PhD



Joel was my PhD mentor from 2010 until 2017. During that time, we collected extensive psychophysical and neuroimaging data on participants exposed to a

capsaicin-heat pain model. He was always enthusiastic about my ideas and supportive through several failures that I learned more from than the successes. His sage advice always improved my thinking about how the peripheral and central nervous system likely processed painful stimulation in pathology and health. He supported me when my mother's disability required me to move her in with me and attend numerous doctor's appointments in attempts to improve her spinal disability. He supported me six years later when she died. Joel was a compassionate, supportive, and constructively critical mentor. Every project he worked on, whether it was his own idea, or someone else's, received his full contemplative thought and attention. He was never dismissive and always remained curious. To say that my best experiences in my 30s were spent discussing science with Joel would be too modest. He enthusiastically and patiently helped me develop into a scientist. His absence will leave a great void in my life.

-Tim Meeker, Ph.D.

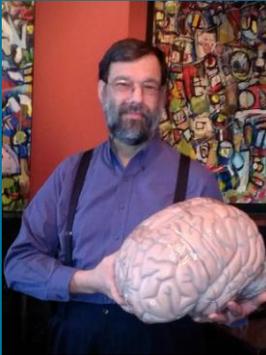
I knew Joel for 25 years. He was my colleague, but more importantly he was my friend. We started at Maryland a few months apart, so we helped each other along the promotion ladder. We both were interested in sex differences in pain and developed the Research Center for Neuroendocrine Influences in Pain along with Mike



Gold and Anne Murphy. We funded the center with an NIH SCOR grant, did some good science, and since Joel was the center/grant director, he used his contacts to get us shirts & bags. Along with the IASP SIG on Sex, Gender and Pain, I was co-chair at the time, we put together the consensus conference on sex and pain. What an extraordinary meeting with an international cast and some of the best minds in the field of sex differences research. Joel

spearheaded writing the consensus report, a herculean effort once described as herding cats. It is still one of the most highly cited articles in the field. Working with Joel, having Joel as the department chair, our families spending time together, enriched my life in innumerable ways. He will be missed more than I can express.

-Richard Traub, Ph.D.



As a mentor and a boss, you couldn't ask for anyone better. Joel led with passion, openness, and empathy and created within our department and CACPR a sense of community as close as a family. He was brilliant as a mentor and he pushed me to always strive to do better and for that I owe him a lot of credit for my successes. I will miss our discussions on pain science, his stories, his sense of humor. Joel was a good scientist and a good friend and I will forever cherish the fun times we had in and outside of the lab.

-David Seminowicz, Ph.D.

If you would like to make a donation to UM CACPR in honor of Dr. Joel Greenspan, please visit: <https://dental-umaryland.networkforgood.com/causes/12792-center-to-advance-chronic-pain-research>.

From there, you will see an option to donate in memory or honor of someone. We at the University of Maryland, Baltimore (UMB) are incredibly grateful for your generosity that will honor the legacy of Dr. Greenspan by equipping our dental and nursing students, faculty, and the wider UMB community with transformative resources to alleviate the challenges of chronic pain.

Please visit Joel Greenspan's Memoriam to view wonderful photos of Joel and his dear colleagues from over the years.

CACPR Member Laurels

Highlights of recent grant awards, publications, and presentations.

Luana Colloca, MD, PhD, MS

Pain Med. 2021 Mar 1

doi: 10.1093/pm/pnaa454

Patient and Provider Acceptability of a Patient Preauthorized Concealed Opioid Reduction

Theresa Bedford, Timileyin Adediran, Nathaniel R Haycock, C Daniel Mullins, Michelle Medeiros, Thelma Wright, Michele Curatolo, Lynette Hamlin, **Luana Colloca**

Patients and providers appear to understand the benefits of a concealed opioid reduction. Our findings support future randomized controlled trials that compare concealed and overt opioid tapering in patients with chronic pain. More research is needed to understand the difference in attitudes between research and clinical practice and to test the acceptability of a concealed reduction following a participation in an active clinical trial.

Junfang Wu, BM, PhD

1. Dutta D, Khan N, **Wu J** #, Jay SM #. Extracellular Vesicles as an Emerging Frontier in Spinal Cord Injury Pathobiology and Therapy. Trends Neurosci. 2021 Feb 10: S0166-2236(21)00016-3. doi: 10.1016/j.tins.2021.01.003. Online ahead of print. PMID: 33581883. (**# correspondent**)

Highlight: Extracellular vesicles (EVs) have functional roles in neuron–glia and CNS–periphery communication following neurotrauma by regulating neuronal function, axonal regeneration and remyelination, metabolic activity, and the inflammatory milieu. Understanding EV signaling following spinal cord injury (SCI) is limited, but recent studies have identified differences in circulating EV counts and miRNA cargoes that may contribute to remote inflammatory changes. The therapeutic potential of EVs for SCI treatment depends on the phenotype of the source cell and is linked to the repertoire of the EV-associated cargo. New bioengineering approaches such as 3D printing demonstrate improved control over the production microenvironment of EVs and the cellular phenotype that can accelerate the development of high-potency therapeutic EVs for applications in neurotrauma, including SCI, in a reproducible and scalable fashion.

2. He J, Ritzel RM, **Wu J**. Function and Mechanisms of the Voltage-Gated Proton Channel Hv1 in Brain and Spinal Cord Injury. Frontiers Cellular Neuroscience, 2021, April, in press.

Highlight: The voltage-gated proton channel Hv1 is a newly discovered ion channel that is highly conserved among species. It is known that Hv1 is not only expressed in peripheral immune cells but also one of the major ion channels expressed in tissue-resident microglia of the CNS. One key role for Hv1 is its interaction with NOX2 to regulate ROS and cytosolic pH. Emerging data suggest that excessive ROS production increases and requires proton currents through Hv1 in the injured CNS, and manipulations that ablate Hv1 expression or induce loss of function may provide neuroprotection in the CNS injury models including stroke, traumatic brain injury, and spinal cord injury. Recent data demonstrating microglial Hv1-mediated signaling in the pathophysiology of CNS injury further supports the idea that Hv1 channel may function as a key mechanism in posttraumatic neuroinflammation and neurodegeneration. In this review, we summarize the main findings of Hv1, including its expression pattern, cellular mechanism, role in aging, and animal models of CNS injury and disease pathology. We also discuss the potential of Hv1 as a therapeutic target for CNS injury.

Upcoming Event



The 3rd International conference of The Society for Interdisciplinary Placebo Studies (SIPS): Harnessing placebo mechanisms for optimal pain management and treatment of alcohol and other drug use disorders.

When: May 26-28, 2021

Where: University of Maryland, Baltimore U.S. A.

Program Overview

The 3-day conference is designed to provide an unparalleled platform for integrating current knowledge on placebo research in pain, alcohol use disorders, and other substance use disorders. Pain and alcohol use disorders are inter-related conditions with large and individually variable placebo effects on disease progression and response to treatments. The ultimate goal of this conference is to develop holistic and adequate strategies for better management and treatment of these conditions. Specifically, the conference will:

- provide a collaborative platform to present and share innovative research findings and theoretical ideas on placebo research to a national and an international audience of researchers;

- promote training and education of trainees, academic junior researchers, healthcare professionals, agencies, stakeholders and the public; and
- advocate for the participation of minorities and women while expanding the U.S. research in the global network of placebo research.

Features of this program include:

- Seven Plenary sessions
- Three special Sessions on COVID-19, Placebo methodology, and Virtual Reality
- Over twenty workshops
- Peer reviewed short oral presentations
- Peer reviewed poster sessions
- Inclusion of both basic-science and clinician researchers
- Networking forums

In-depth discussions that will:

- expand the knowledge of placebo responsiveness,
 - facilitate collaborations and synthesize new approaches in research and treatment
 - enhance the empirical, conceptual and ethical understanding of the placebo effect among academic researchers, health care professionals, as well as external stakeholders.
- Continuing education (CE) credit will be available for physicians, nurses and pharmacists.

For detailed information and to register, visit <https://sips-conference.com/registration/detailed-information-and-link-to-online-registration>

Attendees will participate via laptop, tablet, or mobile device. Upon registration and before the meeting, attendees will be able to use the Apps below:

Web App for Society for Interdisciplinary Placebo Studies 3rd International Conference

Accolades



Change in Leadership, Department of Neural & Pain Sciences

Effective February 1, 2021 following the retirement of Joel D. Greenspan, Dr. Richard Traub will become the interim chair of the Department of Neural and Pain Sciences in the School of Dentistry. NPS has 17 faculty, 10 with a focus on pain

research spanning basic, translational, and clinical science. The department is also home to the Brotman Facial Pain Clinic. Dr. Traub was vice-chair of the department for 7 years which helped prepare him to lead the department moving forward. NPS has a research portfolio exceeding \$15 million and is strongly situated as a leader in pain research. Dr. Traub is looking forward to helping the faculty to develop new ideas and collaborative opportunities within the department, university and beyond.



Dr. Marcela Romero-Reyes was appointed to the role of American Academy of Orofacial Pain (AAOP) Liaison to the American Headache Society (AHS). This is in addition to her leadership role that has been mentioned previously serving as the chair of the special section of TMD, Cervical Spine and Orofacial Pain of AHS.

Dr. Romero-Reyes' leadership role as the liaison is as a bridge of communication and support between these two organizations who have the common goal to improve the care and lives of patients with headache and orofacial pain disorders.

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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