UCDAVIS

INSTITUTE FOR PSYCHEDELICS AND NEUROTHERAPEUTICS

Opening New Horizons in Research and Healing

WINTER 2023 | NEWSLETTER

A Note from Our Directors

Dear Friends and Supporters,



Welcome to the inaugural edition of the UC Davis Institute for Psychedelics and Neurotherapeutics (IPN) Newsletter. As we mark our first year, we are thrilled to share with you some of the groundbreaking discoveries and translational efforts that emphasize our enduring commitment to transform mental health.

Within these pages, you'll find stories of innovation, dedication, and hope, all driven by the relentless pursuit of understanding the human mind and unlocking its potential for healing. Together, we are shaping the future of mental health and neuroscience. Your support has been instrumental in reaching these milestones and as we look ahead, we see even more opportunities on the horizon to impact individuals, communities and beyond.



We hope that you enjoy reading about our successes in transcending traditional disciplinary boundaries on our way to discovering new pathways to wellness. Your partnership and generosity will help us realize our goal of understanding how psychedelics impact the brain and using this information to develop optimized therapeutics for a range of conditions.

Thank you for believing in our vision and joining us on this extraordinary journey.

Sincerely,

David E. Olson - Director

John A. Gray - Associate Director

UC Davis Institute for Psychedelics and Neurotherapeutics

David Olson John Gray

A VIEW INSIDE:

How Psychedelics Promote Neuroplasticity

Earlier this year, a team of researchers from the UC Davis Institute for Psychedelics and Neurotherapeutics revealed in <u>Science</u> that psychedelics spur cortical neuron growth by activating intracellular pools of 5-HT2A receptors. This neuroplasticity combats the withering dendritic spines characteristic of several neuropsychiatric disorders.

A neuron in isolation can be thought of like a tree. Protruding from its body are branch-like dendrites that reach out and connect to other neurons throughout the brain.

When a psychedelic compound encounters a cortical neuron, it induces a host of effects, including neuroplasticity, or the growth of dendrites and formation of synapses.

But what are the molecular steps that promote this process? And what neuronal receptors are activated by these psychedelic compounds? Are they located on the surface of the neuron facing outwards? Or are they somewhere within the neuron itself?

Through cell culture and experiments with mice, UC Davis alum Maxemiliano Vargas

('23 Ph.D. in neuroscience) and his colleagues discovered that 5-HT2A receptors are key to promoting the beneficial neuroplastic effects of psychedelics. The researchers found that activation of these receptors kickstarts a cascade of molecular events that ultimately promote neuronal growth.

But first, the psychedelic must slip through the neuron's cellular membrane.

"The ability of these psychedelics to activate intracellular receptors really comes down to their chemical composition and properties," Vargas said. "They tend to be small and lipophilic, and because of this, they can passively diffuse across membranes. Now they're in the intracellular environment and they can bind to a receptor, like 5-HT2A."

The researchers found that activation of intracellular 5-HT2A receptors, which are primarily located in an organelle called the Golgi body, leads to downstream activation of the mammalian target of rapamycin (mTOR) pathway.

"That leads to the synthesis of a bunch of different proteins, some of which are necessary to induce neuroplasticity," said Vargas. "That's the general biochemical pathway that we think is mediating the changes in neuroplasticity, enabling these neurons to form new connections with each other and strengthen already existing connections."



The UC Davis Institute for Psychedelics and Neurotherapeutics is harnessing this research to develop novel psychoplastogens that activate the same pathways. The hope is that these new neurotherapeutics could be used to treat various neuropsychiatric disorders.

CLINICAL TRIAL

Technology invented at the UC Davis Institute for Psychedelics and Neurotherapeutics (IPN) at the University of California, Davis has been further developed by Delix Therapeutics, leading to a groundbreaking clinical trial of DLX-001, the first non-hallucinogenic psychoplastogen to be approved for human trials. Delix's phase I clinical trial successfully completed dosing for the initial group of participants. The trial demonstrated the compound's predicted behavior in humans, without major safety concerns or hallucinogenic effects. Delix recently presented interim Phase I data at the American College of Neuropsychopharmacology annual meeting. The collaboration between Delix Therapeutics and the IPN brings hope for the development of transformative therapies for mental health disorders.

ANNOUNCEMENTS

BUILDING UPDATE:

The UC Davis Institute for Psychedelics and Neurotherapeutics is going to

have a physical home! Early next year, we will unveil our state-of-the-art facility in the new wing of the Chemistry Building, strategically located in the center of the UC Davis main campus in close proximity to the Department of Psychology, the College of Biological Sciences, the Center for Neuroscience and the Health Sciences District.





This cutting-edge space will house our proprietary central nervous systemfocused compound library and be used for pharmacological screenings. It is set to be a hub of innovation, fostering interdisciplinary research and collaboration related to neurotherapeutics. Stay tuned for more updates regarding our ribbon-cutting ceremony! To the right is an exclusive look at the building plans!







NEW HIRES:

Savannah Sanchez-Kauth

Savannah Sanchez-Kauth recently joined us as our Program Coordinator! Savannah is a United States Marine Corps veteran with a B.A. in psychology. She plays a crucial role in our operations, managing tasks such as social media, data analysis and event planning. Savannah is incredibly passionate about the mission of the UC Davis Institute for Psychedelics and Neurotherapeutics, especially given that psychedelics and related compounds are demonstrating enormous potential for improving the mental health of veterans.

Program Coordinator, UC Davis Institute for Psychedelics and Neurotherapeutics

NEW POSITION:

We are thrilled to announce that our very own Associate Director, **Dr. John A. Gray**, has taken on a new role as the Director of the Physician-Scientist Training Program at the UC Davis School of Medicine. This is a dual degree program where students complete both medical school (M.D.) and graduate school (Ph.D.) to become the next generation of physician-scientists advancing medical science from the bench to the bedside. This remarkable achievement highlights Dr. Gray's dedication to advancing education, mentorship, and the pursuit of scientific and clinical excellence. We congratulate Dr. Gray on this prestigious appointment and are confident that his passion for science will continue to inspire future leaders in the field of medicine and beyond.

YEAR-END REMINDER:

All gifts to the UC Davis Institute for Psychedelics and Neurotherapeutics are meaningful and appreciated. To qualify for a tax deduction in the 2023 calendar year, you can **make a secure online gift with your credit card until 11:59 P.M. on December 31, 2023**.

Alternatively, you can mail your gift, making it payable to the UC Davis Foundation, to the Institute for Psychedelics and Neurotherapeutics, ATTN: Charlene Mattison, One Shields Avenue, Davis CA 95616, USPS postmarked by December 31, 2023.

For inquiries or to explore our funding priorities, please contact Charlene Mattison, assistant dean of college relations and development, at (530) 754-2225 or cmattison@ucdavis.edu

EVENTS

UC DAVIS PSYCHEDELIC SUMMIT 2023: A RESOUNDING SUCCESS!

The recent UC Davis Psychedelic Summit was a monumental gathering that brought together a diverse panel of clinical and preclinical experts to delve into the rapidly evolving field of psychedelics and neurotherapeutics. The event was a resounding success and showcased the tremendous potential these novel treatments hold for a wide range of neuropsychiatric and neurodegenerative diseases.

The summit explored the profound impact that psychedelics may have on conditions such as anxiety, depression, substance use disorders, obsessive-compulsive disorders and post-traumatic stress disorders, among many others. It was an enlightening experience that sparked thought-provoking discussions and presented exciting possibilities for the future of mental health treatment.

Hosted collaboratively by the UC Davis Department of Psychiatry and Behavioral Sciences, the UC Davis Institute for Psychedelics and Neurotherapeutics and the UC Davis Behavioral Health Center for Excellence, the summit exemplified the power of interdisciplinary cooperation and the dedication of our institution to advance the frontiers of science and medicine.

We give special thanks to Dr. Helen Kales, the chair of the UC Davis Department of Psychiatry and Behavioral Sciences, for making the event a huge success. You can view all of the Psychedelic Summit lectures <u>here</u>.

Due to the overwhelming enthusiasm and interest in this transformative field, we're excited to announce that we are already planning the next Psychedelic Summit. Stay tuned for more groundbreaking insights, innovative research and collaborative discussions as we continue our journey to shape the future of mental health treatment.

HIGHLIGHTS

Celebrating a Year of Achievements at the IPN!

As we near the end of this remarkable year, we're thrilled to reflect on the incredible milestones and successes achieved by the UC Davis Institute for Psychedelics and Neurotherapeutics. As part of the first institute of its kind funded by a major public university, we are working hard to make sure that initial investments lead to tangible benefits for the public. Already, our groundbreaking research and innovative work have been featured in over 220 media articles (click here for selected articles). A true highlight of the year was our feature in a PBS KVIE special. This captivating program dives into the potential of psychedelic therapy, shedding light on how it might transform the landscape of mental health treatment.

These accomplishments, among many others, underscore the dedication, passion, and commitment of our team and partners to establish a new paradigm in mental health. We look forward to a year of continued growth and discovery in the field of psychedelics and neurotherapeutics. Thank you for your unwavering support of our mission!

Directors' Biographies



Dr. David E. Olson, Ph.D.

Director, UC Davis Institute for Psychedelics and Neurotherapeutics

Associate Professor of Chemistry, Associate Professor of Biochemistry and Molecular Medicine;

Affiliate Member, UC Davis Center for Neuroscience

Meet the person leading our mission to unlock the potential of psychedelics for both healing and elucidating the mysteries of how the brain functions. Dr. David E. Olson, a distinguished scientist, is not only the Founding Director of the UC Davis Institute for Psychedelics and Neurotherapeutics but also a co-founder and

the Chief Innovation Officer of Delix Therapeutics. With a strong academic background in chemistry and neuroscience from prestigious institutions such as Stanford University and the Broad Institute of MIT and Harvard, Dr. Olson's expertise spans medicinal chemistry, molecular/cellular neurobiology, and behavioral neuropharmacology. He is a UC Davis Chancellor's Fellow, and his numerous accolades include being listed as one of the 100 Most Influential People in Psychedelics by Psychedelic Invest. He has a passion for using chemistry to answer fundamental questions in neurobiology and solving problems in central nervous system drug discovery. Under his leadership, the Institute is charting new territories in the understanding of the human mind and pioneering the development of innovative neuroplasticity-promoting therapeutics for improving mental health.



Dr. John A. Gray, M.D., Ph.D.

Associate Director, UC Davis Institute for Psychedelics and Neurotherapeutics

Core Member, UC Davis Center for Neuroscience

Associate Professor of Neurology; Associate Professor of Psychiatry and **Behavioral Sciences**

Director, Physician-Scientist (MD/PhD) Training Program, UC Davis School of Medicine

Allow us to introduce Dr. John A. Gray, our accomplished Associate Director. With an impressive academic background that includes an M.D. and Ph.D. from Case

Western Reserve University, Dr. Gray has been studying the effects of psychedelics since he was in graduate school. He is an expert on the synaptic basis of neuropsychiatric disorders, and his work has delved into the cellular intricacies of serotonin 5-HT2A and NMDA receptors, the primary targets of classic psychedelics and dissociative anesthetics (e.g. ketamine), respectively. A board-certified psychiatrist and synaptic biologist, Dr. Gray leads groundbreaking research focused on understanding synapse formation and plasticity, with a special emphasis on the potential of psychedelics to promote long-lasting synaptic plasticity. His work exemplifies our commitment to understanding the pathophysiology of synaptopathies so that we may find new therapeutic approaches for reshaping the landscape of mental health.

SCIENTIFIC ADVISORY BOARD



Dr. Craig W. Lindsley, Ph.D.

University Distinguished Professor, Vanderbilt University; Executive Director, Warren Center for Neuroscience Drug Discovery; Editor-in-Chief, Journal of Medicinal Chemistry

Dr. Craig W. Lindsley is a prominent figure in medicinal chemistry and neuroscience, known for pioneering the development of allosteric ligands for G protein coupled receptors and leading the Warren Center for Neuroscience Drug Discovery at Vanderbilt University. With extensive experience in both industry and academia, he's provided a roadmap for doing central nervous system drug discovery in an academic setting. As the founding Editor-in-Chief of ACS Chemical Neuroscience and the current Editor-in-Chief of the Journal of Medicinal Chemistry, he has had a profound influence on the field of neurotherapeutic development.



Dr. Kimberley McAllister, Ph.D.

Director, UC Davis Center for Neuroscience; Professor of Neurology; Neurobiology, Physiology and Behavior; Director, NIMH Learning, Memory and Plasticity T32

Co-Director, UC Davis Conte Center; Co-Champion, Emerging Health Threats Grand Challenge

A. Kimberlev McAllister obtained her Ph.D. in neuroscience in the laboratory of Dr. Lawrence C. Katz at Duke University in 1996, followed by a postdoctoral fellowship at the Salk Institute with Dr. Charles F. Stevens. She has been a Professor of Neurology and Neurobiology, Physiology, and Behavior at UC Davis since 2000 and director of the Center for Neuroscience since 2016. Dr. McAllister's research focuses on understanding the cellular and molecular mechanisms of brain development and the role for neuralimmune interactions in brain development and disease. She is deeply committed to mentoring and promoting diversity, equity and inclusion at all levels. Her research has been continuously funded by the National Institutes of Health for over 20 years and she has received substantial support from private foundations through research grants and awards including the Basil O'Connor Research award from the March of Dimes, the Pew Scholars award, the Merck Scholars award and an Independent Investigator

award from National Alliance for Research on Schizophrenia & Depression (NARSAD). She also received the Young Investigator Award from the Society for Neuroscience. In addition to leading interdisciplinary neuroscience initiatives at UC Davis as co-champion of the Emerging Health Threats Grand Challenge, she directs a NIMH T32 focused on graduate training in learning, memory, and plasticity and is PI and co-director of the UC Davis NIMH Conte Center.



Dr. Mark Namchuk, Ph.D.

Puja and Samir Kaul Professor of the Practice of Biomedical Innovation and Translation in the Department of Biological Chemistry and Molecular Pharmacology; Executive Director, Therapeutics Translation, Harvard Medical School

Dr. Mark Namchuk leads drug discovery efforts at Harvard Medical School, focused across all therapeutic areas and drug modalities. With a rich background in the biotech and pharmaceutical industry, he guides the Harvard Medical School's Therapeutics Initiative, shaping an on-campus incubator and educational programs. Prior to joining Harvard Medical School, Dr. Namchuk held senior research and development positions at Alkermes and Vertex Pharmaceuticals. He has worked on drug discovery efforts across many indications including neurodegenerative and neuropsychiatric disorders, inflammatory diseases, orphan disease, infectious diseases, and oncology.



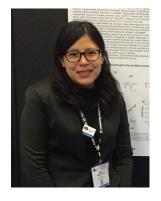
Dr. Katrin Preller, Ph.D.

Group Leader, University of Zurich; Principal Clinical Biomarker Lead Center for Neuroscience, Boehringer Ingelheim

Dr. Katrin Preller is a prominent researcher in neuropsychiatry with

a background in neuropsychology. Her academic work focuses on the clinical and mechanistic effects of novel therapies in neuropsychiatry, and she has co-authored some of the most impactful mechanistic studies of psychedelics in humans. In 2020, she joined F. Hoffmann La Roche as Biomarker and Experimental Medicine Leader and subsequently Boehringer-Ingelheim as Principal Clinical Biomarker Lead CNS.

SPATICITY



Dr. Mayra I Torres-Flores

TRAINEE

Postdoctoral Fellow

Dr. Mayra Torres, Ph.D., is a dedicated postdoctoral research fellow working in the Gray Lab, where she explores the synaptic plasticity changes induced by psychedelics and their potential therapeutic applications in neuropsychiatric disorders. She holds an B.S. in psychology, an M.S. in neuropharmacology and experimental therapeutics, and a Ph.D. in biomedical science from the Universidad Nacional Autónoma de México. In her current research, Dr. Torres is working to understand the synaptic, cellular, and circuit effects of psychedelics on the claustrum, an enigmatic brain region associated with consciousness. Previously, she

studied the chronic effects of inhalant abuse, a common problem among low-income populations in Mexico, on synaptic transmission in the prefrontal cortex. In addition, she has studied the synaptic and behavioral changes associated with the prefrontal-hippocampus circuit in animal models for Alzheimer's disease.

Dr. Torres is passionate about teaching and science communication, saying "I enjoy teaching complex topics in a fun and digestible way that allows people from different backgrounds to engage with science." Her advice to prospective students is to be gracious to yourself and develop perseverance as research and learning takes time and patience.



Dr. Lindsay Cameron, Ph.D.

ALUMNI

Postdoctoral Fellow

Since completing her Ph.D. in neuroscience while working in the Olson Lab, Dr. Lindsay Cameron has been performing postdoctoral research related to neuroplasticity at Stanford University under the mentorship of Drs. Robert Malenka and Karl Deisseroth. Her interest in psychedelics stemmed from her pharmacology background and the work she did in the Olson Lab, where she discovered the potential for these substances to positively impact mental health. Some of her key achievements

include contributing to pivotal research, such as an influential 2018 Cell Reports paper on psychedelic-induced neuroplasticity, and exploring whether hallucinations are necessary for producing therapeutic effects. Her investigations into microdosing and non-hallucinogenic analogues of psychedelics revealed that hallucinations may not be essential to achieve therapeutic benefits, potentially widening treatment accessibility. Dr. Cameron's education in the Olson Lab and the Neuroscience Graduate Program fueled a passion for establishing her own independent lab and sustained her dedication to academia, despite challenges in executing difficult experiments and facing gender biases in a male-dominated field. For her research efforts, she has won numerous awards including the highly competitive Young Investigator Travel Award from the International Society for Serotonin Research, the Harold M. Weintraub Graduate Student Award and the NIH Outstanding Scholars in Neuroscience Award Program (OSNAP). Her vision for the future of psychedelic science involves efforts to obtain a full understanding of their broad-scale, circuit-level effects. She hopes to launch her own lab to use systems neuroscience to optimize therapeutic outcomes. Her advice for aspiring professionals: "Immerse yourself in your intrigue, understanding that failure in science is part of the process. Cultivate resilience, a support network and explore diverse avenues within the field."

STUDENT AWARDS



Samuel Carter

AMPAC Undergraduate Poster Award - April 2023.

College of Biological Sciences
Distinguished Scholar Award
- April 2023.

Ronald and Lydia Baskin Research Award - May 2023.

Hanson Family Undergraduate Research Publication Award - May 2023.

Honorable Mention - Chancellor's Award for Excellence in Undergraduate Research - May 2023.

Best Presentation in Chemical Biology- Richard Larock Conference - May 2023.



Adam Clapp

Molecular and Cellular Biology T32 - June 2023.



Rishab lyer Keefer Fellowship - June 2023.



Arabo Avanes Professors for the Future Fellowship, 2023–2024.



Anna VernierChemical Biology T32 Fellowship



Dear Friends and Supporters,

As we wrap up this edition of our newsletter, we want to take a moment to express our deepest gratitude to all of you who have been with us on this incredible journey. It's your support, enthusiasm and unwavering commitment that make our work at the UC Davis Institute for Psychedelics and Neurotherapeutics (IPN) not only possible but truly impactful. We are deeply grateful for your contributions to our community and mission. The road ahead will be challenging, but hopefully, it will be filled with many new discoveries. We're committed to keeping you informed and engaged as we embark on this exciting journey together.

Once again, thank you for being an integral part of the IPN community and for standing by us as we work to improve the lives of countless people worldwide. We truly appreciate your support and look forward to what we'll achieve together in the future.

With warm regards,

David E. Olson - Director

John A. Gray - Associate Director

UC Davis Institute for Psychedelics and Neurotherapeutics

David Olson John Gray





