PHILANTHROPY IN ACTION

LATATTORE FOUNDATION HELPS EXPAND ACCESS TO CLINICAL RESEARCH

Thanks to support from the Latattore Foundation, the SMADRC is leading a new effort to improve access to clinical trials among the Latino population, which is disproportionately impacted by Alzheimer's disease yet underrepresented in clinical research.

This funding is paving the way for a new cohort of clinical trial participants within the Study of Latinos-Investigation of Neurocognitive Aging (SOL-INCA), the largest study of cognitive aging, impairment and disorders among Latinos. It is supported by the NIA and led by Hector M. González, PhD, professor of neurosciences at UC San Diego School of Medicine and co-director of the Latino Core of the SMADRC.

This nationwide longitudinal study looks for biomarkers of risk and resilience related to cognitive aging among Latinos of varied heritages. It aims to inform more effective approaches to prevention, diagnosis, care and therapy for Alzheimer's disease and related dementias (ADRD) for an aging and increasingly diverse population of patients. It focuses on targeted, more inclusive team-based research that addresses the needs of understudied populations, as well as complexities related to the heterogeneity of ADRD. The SMADRC has a local Latino cohort that also fosters this science, engages the research community and broader communities, and educates an emerging cadre of Latino/a researchers.

From left: SMADRC Director and Professor of Neurosciences James Brewer, Latattore Foundation CEO Lorenza Fabre Vega, Assistant Professor Olivia Kim McManus, and Professor of Neurosciences Hector González.

THANK YOU

Thanks to the vision and generosity of the Shileys, the Shiley-Marcos Alzheimer's Disease Research Center has led the way in scientific learning, exploration and discovery that can transform lives. Philanthropic support is critical to achieving our mission, and gifts of all sizes play an important role in sustaining our momentum.

To make a gift by check, mail to:

Betsy Collins | UC San Diego Health Sciences Advancement
Attn: Shiley-Marcos ADRC | Fund E2140
9500 Gilman Drive, # 0937 | La Jolla, CA 92093

To make a gift online, please visit:

giveto.ucsd.edu *(enter fund "E2140" for the SMADRC)*

For more information about how you can support the SMADRC, contact:

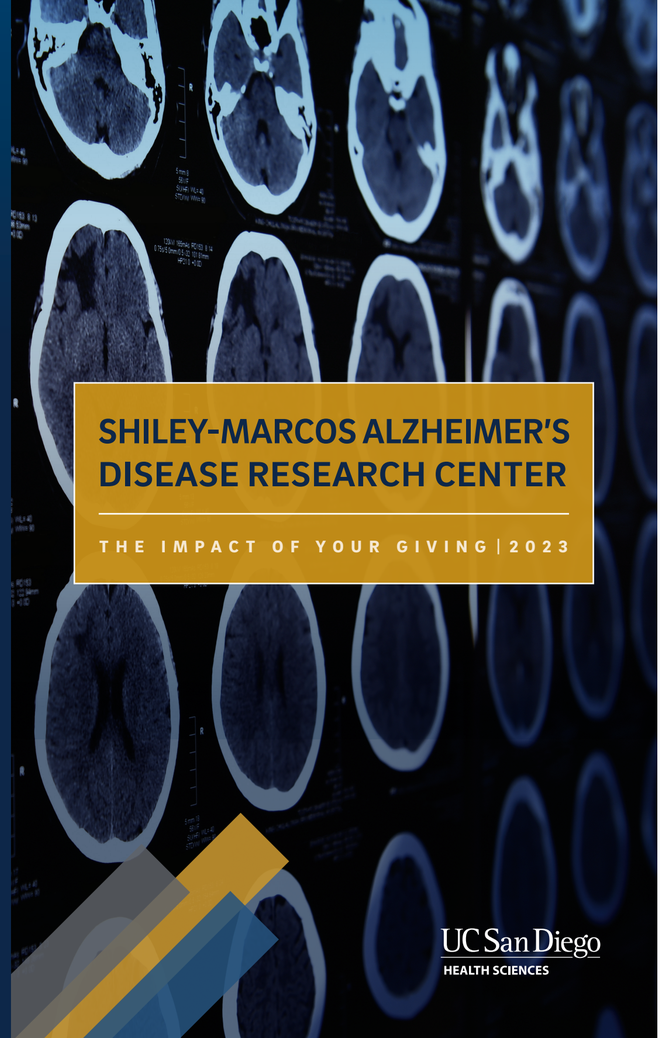
Betsy Collins | (858) 349-0034 | e3collins@ucsd.edu

We can offer several planned gift options that allow you the flexibility to add to a current gift or create a new one, now or later. For information on supporting the SMADRC through estate giving — including donating real estate, transferring appreciated securities, or designating a contribution in a living trust — please contact:

Kim Wenrick | (858) 735-5137 | kwenrick@ucsd.edu

At UC San Diego, we believe that what we don't know today will forever change our tomorrows. Empowered by generosity and fueled by curiosity, we are unafraid to chase the unknown — to ask the questions no one has asked before and to push the boundaries of possibility. Together with your support for the Shiley-Marcos Alzheimer's Disease Research Center, we will unite diverse people and unconventional perspectives to propel limitless impact. Because we know that when we come together, nothing is beyond us.

UC San Diego
HEALTH SCIENCES



SHILEY-MARCOS ALZHEIMER'S DISEASE RESEARCH CENTER

THE IMPACT OF YOUR GIVING | 2023

UC San Diego
HEALTH SCIENCES

MESSAGE FROM THE DIRECTOR

This is a landmark year for the Shiley-Marcos Alzheimer's Disease Research Center (SMADRC). We are celebrating the 40th year of continuous grant funding from the National Institute on Aging (NIA) at the National Institutes of Health and the 20th year since Darlene and the late Donald Shiley named the center in honor of Darlene Shiley's mother, Dee Marcos. The Shileys' partnership has facilitated incredible advancements in the understanding of the disease, its causes and strategies for improving the quality of life for the patient as well as the caregiver. The continued commitment of donors like you has made the SMADRC a world-renowned leader in Alzheimer's disease (AD) research.

Philanthropy is the catalyst that allows us to lay the groundwork necessary to obtain major research awards. Donors provide funding for early-stage research that has repeatedly led to millions in federal grants and potentially life-changing advancements in treatment. Your support gives us the flexibility to quickly pivot to focus on the most promising research areas and to attract the very best Alzheimer's disease experts to lead our efforts. As part of UC San Diego, we leverage the exceptional neurosciences environment and diversity of our region to support and accelerate multidisciplinary research. With rapidly expanding access to biomarker-assisted clinical characterization and the emerging availability of anti-amyloid therapeutics, our center is adapting and contributing to an evolving scientific and care environment. I am grateful for this opportunity to share with you some of our achievements from the past year.

I hope that this report helps to illustrate the ripple effect of your giving. I look forward to reporting on the SMARC's next chapter, which you are helping us to write. Thank you very much for partnering with us to improve the lives of our patients and their families — and ultimately, to make Alzheimer's disease a thing of the past.

Sincerely,

James Brewer, MD, PhD
Director, Shiley-Marcos Alzheimer's Disease Research Center
Chair, Department of Neurosciences

EMERGING SCHOLARS

THE FUTURE OF ALZHEIMER'S RESEARCH

Neurologist Johannes Schlachetzki, MD, and molecular biologist Jeff Jones, PhD, are two SMADRC scientists pursuing research that aims to advance our understanding of the mechanisms behind the development of ADRD, potentially leading to new approaches to treatment.

Dr. Schlachetzki is seeking to understand the contribution of genomic instability to the pathogenesis of ADRD. He focuses on identifying somatic mutations in neurons and glial cells and the mechanisms that lead to the accumulation of somatic mutations and eventually genomic instability during aging and in AD. He also aims to decipher the underlying transcription factor network that drives gene expression profiles of microglia, neurons and oligodendrocytes in neurodegenerative disorders. He has developed advanced methods to isolate and deeply profile distinct brain cell types and states.

Johannes Schlachetzki, MD

Jeff Jones, PhD

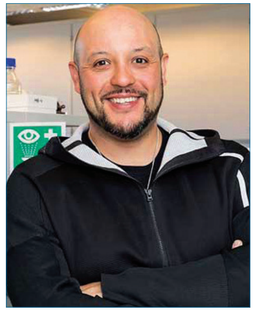
Dr. Jones, a researcher at the Salk Institute for Biological Studies, aims to determine what cellular mechanisms drive neuronal dysfunction and susceptibility to ADRD.

Decades of evidence indicate that increased DNA damage coupled with reduced repair capacity results in genomic instability and sterile inflammation. Dr. Jones utilizes induced pluripotent stem cells (iPSCs) to characterize how age and disease alter genome integrity and understand how age-dependent changes in neuronal nucleotide metabolism are dealt with in aging and ADRD. Using leading-edge sequencing techniques and an in vitro model that reflects human neuronal aging and AD, this research hopes to define the frequency and location of genomic repair as well as the cellular machinery involved in genomic maintenance in aging and ADRD, providing fundamentally important data on aging as well as new long-term targets for therapeutics. This work received an SMADRC Developmental Project grant, a program funded by the center and philanthropic giving.

WELCOMING THE NEURAL AGING LABORATORY

Jerome Mertens, PhD, joined UC San Diego this fall and became the inaugural holder of the Florence Riford Chair for Neurodegenerative Disease and Dementia. In his Neural Aging Laboratory, he and his team reprogram human skin cells into brain cells to better understand age-related diseases. They apply both directly induced neurons (iNs) and iPSC technologies to develop and learn from the next generation of human disease models. By combining a patient-centric approach with cellular neuroscience techniques and a passion for big data biology, the goal of the lab is to identify the key molecular players of human biological aging to point toward new treatment strategies for neurological age-related neurodegenerative diseases.

A forthcoming study led by Dr. Mertens aims to identify the distinct disease pathways in an ethnic and genetic subgroup of AD patients. Although people of Latin American heritage are 1.5 times more likely to develop the disease, research on the involved mechanisms is underrepresented. He aims to decipher the underlying features of the molecularly and clinically atypical Jalisco PSEN1 variant, which is the second most common genetic mutation for familial AD in Latin Americans, by leveraging patient-derived iNs.



Jerome Mertens, PhD
Associate Professor of Neurosciences
Florence Riford Chair for Neurodegenerative Disease and Dementia
UC San Diego School of Medicine

"Patient-derived models for the human brain are centered around the actual patient and can teach us about the development of — and potential therapeutic targets for — diseases of the brain."

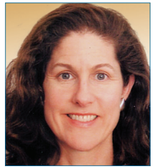
Jerome Mertens, PhD

REVEALING THE ROLE OF TAU

Xu Chen, PhD
Assistant Professor
UC San Diego Department of Neurosciences

Neuroscientist Xu Chen, PhD, joined UC San Diego in 2020 and leads a lab dedicated to understanding the pathophysiology of tau, a protein that proliferates in the brain and is a strong indicator of ADRD — the most prevalent neurodegenerative diseases in the U.S. and worldwide. This toxic protein accumulates in neurons and spreads from one to the other, which correlates with progressive cognitive decline and neurodegeneration. Thanks to pilot funding from the SMADRC that led to additional grant funding from the NIA, Dr. Chen and her team are seeking answers to three fundamental questions in their quest for a greater understanding of the causes of these debilitating diseases: What makes tau a toxic protein in the diseased brain? How does pathogenic tau form and accumulate in neurons? How does tau spread from neurons to neurons? The answers could point to new targets for therapeutic treatment.

UNDERSTANDING COGNITION IN AGING



Diane Jacobs, PhD
Associate Adjunct Professor
UC San Diego Department of Neurosciences

Neuropsychologist Diane Jacobs, PhD, studies the assessment of cognition in aging and dementia, with an emphasis on early detection and differential diagnosis of ADRD. Previously at Columbia University, she conducted research on clinical, neuropsychological and epidemiological aspects of AD. At UC San Diego, she obtained a pilot grant from the SMADRC to develop novel cognitive measures for detection of subtle cognitive changes in preclinical AD in collaboration with colleagues at Brown University and Heriot-Watt University, Edinburgh. Her initial findings led to funding from the NIA to develop and validate neurocognitive measures that are sensitive to preclinical AD. Since standard neuropsychological tests typically are not sensitive to the earliest phases of AD pathology, there is a critical need for novel measures that can detect subtle cognitive changes and track progression over time. The development of such measures will result in improved clinical care and outcomes research, including clinical trials.

PARTNERING WITH OUR COMMUNITY

OPTIMIZING THE QUALITY OF LIFE OF BOTH PATIENTS AND CAREGIVERS

As part of our comprehensive approach to care, we offer educational and outreach programs for Alzheimer's patients and their caregivers across the region. These offerings have returned to an in-person format. Between July 2022 and June 2023, the SMADRC team provided:

8.5 HOURS OF CAREGIVER TRAINING, reaching over 100 participants

158.5 HOURS OF SUPPORT GROUP GATHERINGS offered to people experiencing memory loss and their care partners, including seven unique groups for participants and their care partners, two of which meet weekly and five of which meet monthly, spanning 286 unique individuals who have benefited from these programs

37 COMMUNITY EVENTS reaching approximately 1,000 individuals

Funding for these programs is provided through philanthropic support from donors like you and governmental agencies like the California Department of Public Health and the County of San Diego's Health and Human Services Agency.

For more information or to participate in our programs, visit **neurosciences.ucsd.edu/centers-programs/adrc**.

DONOR SUPPORT OPENS ACCESS TO PET IMAGING

Several years ago, an anonymous donor stepped in to fund personnel costs to implement a grant that covered the costs for 30 participants' screenings for amyloid and another 45 for tau. Without philanthropic support, the SMADRC would not have been able to fund recruitment, consent and coordination of participant visits.

This project eventually helped prove the SMADRC's capacity to complete PET (positron-emission tomography) imaging for amyloid biomarkers in the brain, leading to further funding to conduct imaging on all three major AD-related biomarkers in the brain (amyloid, tau and neurodegeneration) on approximately 50 people per year for the next five years. This is just one example of the snowball effect that your contributions can have when we partner to work toward shared goals.