THE EPSTEIN FAMILY ALZHEIMER'S RESEARCH COLLABORATION

AN EXTRAORDINARY COMMITMENT TO ENDING ALZHEIMER'S DISEASE

Daniel and Phyllis Epstein

With a transformational gift, the Epstein Family Foundation has even further propelled our decades-long hunt for a cure for Alzheimer's disease. In 2022 they launched the Epstein Family Alzheimer's Research Collaboration, a powerhouse that unites UC San Diego Alzheimer's experts with their esteemed peers at USC. Beyond their initial $50 million investment, the Epsteins have challenged USC and UC San Diego to raise $25 million each to support Alzheimer's research.

The gulf between the widespread impact of Alzheimer's disease and the lack of solutions inspired the Epsteins to establish this collaboration to speed the way toward meaningful therapies. To extend the impact of this extraordinary infusion of funding, the Shiley-Marcos Alzheimer's Disease Research Center (SMADRC) continues to partner with our broader programs in Alzheimer's disease within and beyond UC San Diego. Specifically, the SMADRC supports the achievement of two research initiatives with exceptional potential for achieving significant advancements in Alzheimer's treatment in the near future: gene therapy, which has found success in definitively treating several neurological diseases and the "Powder for Pennies" collaborative program, a rapid evaluation of existing drugs that show potential for relieving the debilitating symptoms of Alzheimer's disease.

"It is just a matter of time before most people will have someone in their families develop dementia or Alzheimer's, yet there are no viable treatments beyond temporary measures to delay the onset. If, together, we can double our initial investment, imagine the impact we can have in creating real solutions for this condition."

– DANIEL EPSTEIN

A LEGACY OF SUPPORT
THE DR. ANDREW G. ISRAEL MEMORIAL LECTURES

Andrew Glenn Israel, MD 1951–2020

In May we held the inaugural Dr. Andrew G. Israel Memorial Lecture to honor and remember our beloved friend and colleague Dr. Israel. We welcomed Dr. Israel's colleagues, friends and family to an informative discussion on posterior cortical atrophy led by guest speaker Sebastian Crutch, PhD, from the Dementia Research Centre at the University College London Institute of Neurology. This event provided a window into the experience of a person with dementia-related visual impairment and their care partners. It drew multidisciplinary scholars invited by Dr. Brewer to submit project proposals and explore collaborations to utilize the rich resources now available to advance science in this understudied disease area.

THANK YOU

Thanks to the vision and generosity of Darlene and the late Don Shiley, 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:
UC San Diego Health Sciences Advancement
Attn: Shiley-Marcos ADRC
9500 Gilman Drive, #0937 | La Jolla, CA 92093

To make a gift online, please visit:
giveto.ucsd.edu *(enter fund "E2140" for the SMADRC)*

To learn about estate giving, memorial gifts or volunteering, contact:
Kim Wenrick | (858) 735-5137 | kwenrick@ucsd.edu

UC San Diego
Health Sciences

At the University of California San Diego, visionary donors help us unleash a diverse community of doers: those who imagine unexpected answers that can transform humanity for the better. Together, we foster bold scholars, researchers, healers, entrepreneurs and creators. Because here, breaking new ground is the norm — and people are the point.

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Health Sciences

SHILEY-MARCOS ALZHEIMER'S DISEASE RESEARCH CENTER

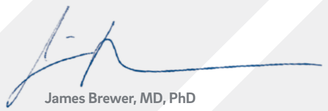
THE IMPACT OF YOUR GIVING | 2022

MESSAGE FROM THE DIRECTOR

It is wonderful to get this chance to send a heartfelt thanks to you, our steadfast partners who have contributed so generously to our groundbreaking programs at the Shiley-Marcos Alzheimer's Disease Research Center. As another year passes, it is truly inspiring to see how the teams have pulled together to reignite the engine of the center's in-person programs and to feel the energy of this flourishing and one-of-a-kind partnership between scientists, clinicians, staff, participants, caretakers, families and donors. The ecosystem was challenged during the pandemic, but we emerged stronger than ever.

This robust partnership and your support are key to advancing the science that will bring us the cure to the scourge of Alzheimer's disease and related neurodegenerative disorders seen in aging. We are delighted to highlight some of our exciting new developments and to welcome the broad set of new donors who showed their generosity and commitment to the Andrew Israel Memorial Fund, which honors the legacy of a truly remarkable man and his beautiful and loving family. We also are energized by the new programs that will be enabled through the transformative Epstein Family Foundation gift to UC San Diego and the University of Southern California. The synergies it permits lend promise that "one plus one equals three (or more)" in this fight against Alzheimer's.

It is my privilege to ensure that your support is put to optimal use in this fight. I hope this report gives you a sense of our tremendous passion in putting these new funds to their best use in bringing us a cure. I thank you sincerely, on behalf of the Center and its teams, for your generous contributions and ongoing partnership with us.



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

EMERGING SCHOLARS

THE FUTURE OF ALZHEIMER'S RESEARCH

Alejandra Morlett Paredes, PhD

Alejandra Morlett Paredes, PhD, a native of Tijuana, Baja California, is a postdoctoral fellow in the Study of Latinos-Investigation of Neurocognitive Aging (SOL-INCA) lab. Her work focuses on understanding the attitudes of older Latinos toward participating in aging research, specifically research that requires invasive procedures such as lumbar puncture, as well as brain donation for research. Dr. Morlett received her PhD in health psychology from Virginia Commonwealth University and completed a two-year research fellowship in geriatric mental health at UC San Diego. She has been involved in various efforts to develop normative data for several neuropsychological tests in Spanish-speaking adults living in the U.S. and Latin America.

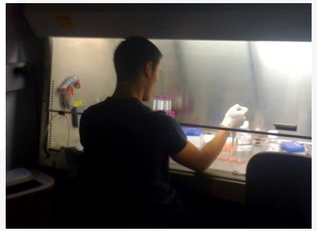
Dr. Paredes is currently working on a pilot project entitled Maximizing and Improving Latino Participation for Aging Studies (MILPAS). Latinos are the fastest-growing segment of the older adult population and are significantly more likely to develop Alzheimer's disease and related dementias (ADRD) than the general population but are greatly underrepresented in research participation. Specifically, there is a dearth of brain tissue that is essential for confirming clinical ADRD diagnoses. Better understanding the attitudes and perceptions of brain donation for research can facilitate targeted, culturally relevant approaches for increasing autopsy consent that will have a significant and enduring impact on eliminating critical barriers in ADRD treatment for Latinos.

The study's title was inspired by the term "milpa," a traditional crop-growing system in Mexico, reflecting the SMADRC's role as a place for gathering data to inform research.

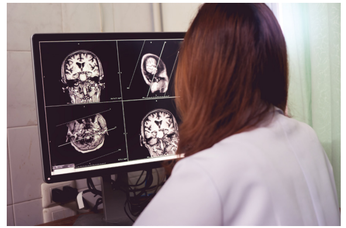
GENE THERAPY: A POTENTIAL CURE IN ONE SHOT

The Roy Lab, led by Subhojit Roy, MD PhD, is developing a single-dose gene therapy to treat Alzheimer's disease. The alteration of key disease genes using CRISPR, a revolutionary gene editing technology, is emerging as a powerful therapeutic tool. Several recent clinical trials for treating blood disorders and other diseases have reported unprecedented success — nearly 100% — in alleviating symptoms. Translating these successes to diseases afflicting the brain and spinal cord could have a transformative impact on a broad range of diseases for which there are currently no cures.

The Roy Lab is targeting the APP gene, which has an established role in Alzheimer's disease. Their approach essentially cuts out a small segment at the extreme C-terminus of the APP protein, which is known to trigger the pathologic amyloidogenic pathway that gives rise to neurotoxic products such as beta-amyloid. Instead of producing toxic fragments, the gene-edited APP — lacking the extreme C-terminus — is redirected into an alternative non-amyloidogenic pathway, which generates neuroprotective and neuroregenerative fragments. Thus overall, their approach alters the amyloid pathway from a pathologic state to a physiologic state, which is expected to reduce Alzheimer's pathology and symptoms. The CRISPRs will be delivered using viral vectors — which have a long history of safety and use in humans. A one-time injection is expected to permanently edit the APP gene and lead to a lasting therapeutic effect. Using a similar viral delivery approach, the Roy Lab has already tested their strategy in animal models of Alzheimer's disease. The next step is to perform a battery of FDA-relevant tests to determine the optimal CRISPR (guide-RNA) for use in humans; package the best one into viral vectors that are in human use; and finally, test safety and efficacy in large nonhuman primates before human application.



WOMEN: INFLAMMATION AND TAU STUDY



Women account for two-thirds of all cases of Alzheimer's disease, and research shows that women tend to be diagnosed later and decline more quickly than men. Why these differences exist is unknown, but Erin Sundermann, PhD, and Sarah Banks, PhD, think inflammation may be key, and that it may be driving an important pathological process in Alzheimer's disease that involves the aggregation of tangles in the brain composed of abnormal tau protein. The team developed a study, dubbed the Women: Inflammation and Tau Study, or WITS, which was initially funded by the California Department of Public Health along with the Alzheimer's Association. They collect participant data via PET scans, lumbar punctures, blood samples, memory and thinking tests, home sleep studies and wearable activity trackers.

From all this information, Sundermann and Banks hope to find potential factors that can be targeted to slow progression of Alzheimer's in women. Early results were shared at the Alzheimer's Association International Conference this summer. Along with graduate student Kitty Lui, they found that a large majority of women in the study had some level of sleep apnea, and its severity correlated with tau in their brains. As sleep apnea is a treatable condition, recognizing and treating it could slow the progression of Alzheimer's disease. Another analysis, led by project coordinator Alyx Shepherd, pointed to the importance of studying memory for shapes versus words. Memory for shapes was sensitive to early tau tangles in WITS, but memory for words was not, a finding that could help refine how we diagnose and track memory decline in women, which is likely different from men. We expect more exciting findings as the number of WITS participants increases. Learn more at www.witsucsd.org.

PARTNERING WITH OUR COMMUNITY

THE PROMOTORA INITIATIVE

Latinos are grossly underrepresented in Alzheimer's research despite the fact that they are disproportionately impacted by the disease. To help reduce barriers to enrolling in studies, the SMADRC partners with promotores — those who serve their communities by acting as liaisons with health and social service providers. Promotores build trust with their communities and are well positioned to promote health education, services and clinical research because they share the same language, culture, ethnicity, status and experiences as the individuals they serve.

The SMADRC has a tradition of working with promotores embedded in the Latino community. We have informal partnerships with several promotora groups in San Diego County and have benefited from their insights and recommendations. In response to their requests and our desire for a more formalized partnership, a group of eight engaged promotoras recently completed a series of four training events hosted by the SMADRC covering research ethics and privacy requirements, the facts about Alzheimer's disease and related dementias, commonly used research procedures, and the methodology for enrolling and participating in studies at UC San Diego. This endeavor was led by Zvinka Zlatar, PhD, a bilingual and bicultural neuropsychologist and clinical scientist whose research focuses on lifestyle interventions to promote healthy brain and cognitive aging among diverse populations and improving our understanding of early risk markers of Alzheimer's disease and related disorders in Hispanic older adults. The promotoras will be recognized for their achievements, receive formal certification and badging from UC San Diego and be poised to represent the SMADRC in the communities we serve to provide accurate information and direct referrals for research enrollment. We aim to support their efforts and hard work in a sustainable way to retain their commitment and engagement.

Newly certified Promotores with SMARDC team members at the first-ever promotion event on September 30. 2022.