A LEGACY OF SUPPORT—the Dr. Andrew G. Israel Memorial Lectures

In May we held the inaugural Dr. Andrew G. Israel Memorial Lecture to honor and remember our beloved friend and colleague Dr. Israel. Welcomed by 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 experiences of a person with dementia-related visual impairment and their loved 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 to the vision and generosity of Darlene and the late Dan 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
9100 Gilman Drive, #0937 | La Jolla, CA 92093

To make a gift online, please visit:
giveto.ucsd.edu (enter fund “72140” for the SMADRC)

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

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 navigate the engine of the center’s in-person programs and to (stil)levitate 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 one step closer to the scourge of Alzheimer’s disease and related neurodegenerative disorders seen in aging. We are delighted to highlight some of our key programs and outcomes that will bring us closer to the breakthroughs that will bring us the cure to the scourge of Alzheimer’s disease and related neurodegenerative disorders seen in aging.

This year, we were honored to welcome 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 experiences of a person with dementia-related visual impairment and their loved 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.

It’s 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. In good news from the University of California San Diego, visionary donors have funded a diverse community of teams who are exploring unexpected answers that can transform humanity for the better. Together, we must find cures, researchers, healers, entrepreneurs and creators. Because here, breaking new grounds is the norm — and people are the point.

Daniel Epstein
Chair, Department of Neurosciences
**Gene Therapy: A Potential Cure in One Shot**

The Roy Lab, led by Subhajit 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 affecting 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 pathological amyloidogenic pathway that gives rise to toxic products such as beta-amyloid. Instead of producing toxic fragments, the gene-edited APP—a lacking the extreme C-terminus—is redirected in an alternative non-amyloidogenic pathway, which generates neuroprotective and neuroregenerative fragments. Thus, overall, their strategy 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 alter this 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 optimize the delivery and 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 are more likely 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, which was initially funded by the California Department of Public Health along with the Alzheimer’s Association. They collect participant data via PET scans and brain donation, as well as conduct research to understand how inflammation may be driving this process.

From all this information, Sundermann and Banks hope to find potential biomarkers that can be targeted to slow progression of Alzheimer’s in women’s early stages. In the Roy Lab’s study, 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 alter this 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 optimize the delivery and 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 are more likely 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, which was initially funded by the California Department of Public Health along with the Alzheimer’s Association. They collect participant data via PET scans and brain donation, as well as conduct research to understand how inflammation may be driving this process.

From all this information, Sundermann and Banks hope to find potential biomarkers that can be targeted to slow progression of Alzheimer’s in women’s early stages. In the Roy Lab’s study, 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 alter this 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 optimize the delivery and test safety and efficacy in large nonhuman primates before human application.

**partners with our community**

The SMADRC has worked to enhance research involvement among various populations and has been recognized for its achievements, research, formal and informal partnerships with several organizations in San Diego County. They aim to support their efforts and hard work with a sustainable way to return their commitment.

**EMERGING SCHOLARS**

**THE FUTURE OF ALZHEIMER’S RESEARCH**

Virginia Commonwealth University

Study of Latinos—Investigation of as a place for gathering data to inform research. Dr. Morlett received reflecting the SMADRC’s role in a postdoctoral fellow in the Lab, led by Zvinka Zlatar, PhD, a bilingual and bicultural neuropsychologist and clinical scientist whose research focuses on cognitive and clinical outcomes of WITS participants increases. Learn more at www.wits.ucsd.org.