MARY S. EASTON CENTER for Alzheimer's Research and Care at UCLA
DAVID GEFFEN SCHOOL OF MEDICINE AT UCLA

David Geffen School of Medicine

Spring 2025 Newsletter

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The Mary S. Easton Center for Alzheimer's Research and Care at UCLA has very active teams working on basic research, drug discovery, biomarkers for early diagnosis and clinical activity including clinical trials, cognitive testing, and patient care.

Advancing Hope Through Philanthropy

At the **Mary S. Easton Center for Alzheimer's Research and Care at UCLA**, advancing hope isn't just a phrase—it's a shared mission. In an era of growing challenges to public research funding, philanthropy has become more than supportive; it's essential. The generosity of our donor community is fueling the breakthroughs that bring renewed hope to individuals and families facing Alzheimer's disease—and sustaining our efforts to deliver care, discovery, and compassion at every step.

Pioneering Research Amidst Funding Challenges

The Easton Center remains at the forefront of Alzheimer's research, focusing on early diagnosis and the development of new therapeutic agents. Our multidisciplinary approach encompasses basic science studies, animal models, biomarker research, and clinical trials of novel medications. Despite the broader financial challenges impacting research institutions nationwide, our commitment to advancing the understanding and treatment of Alzheimer's disease remains unwavering.

Recent Milestones and Collaborative Efforts

In 2024, the Easton Center achieved significant milestones, including the launch of the UCLA Amyloid Immunotherapy Care (AIC) Program. This initiative has enabled the treatment of patients with groundbreaking therapies such as lecanemab and donanemab, marking a new era in Alzheimer's care. Our collaborative efforts with other UC Health campuses have established shared clinical guidelines, ensuring the safe and responsible use of these treatments.

Moreover, our Drug Discovery Laboratory continues to make strides in developing drug candidates for neurodegenerative diseases, focusing on Alzheimer's disease. The lab's multifaceted approach includes

phenotypic screens, target validation, and medicinal chemistry, contributing to the advancement of potential therapies.

Community Engagement and Inclusive Research

Understanding that Alzheimer's disease affects diverse populations, the Easton Center prioritizes outreach to underrepresented communities. Our efforts include educational presentations and partnerships with community organizations to bridge gaps in awareness and care. By fostering inclusivity in our research and care initiatives, we aim to address disparities and ensure that advancements benefit all individuals affected by Alzheimer's disease.

The Imperative of Philanthropic Support

In light of the current fiscal challenges facing scientific research, philanthropic contributions are more critical than ever. Your support enables us to sustain and expand our research endeavors, develop innovative treatments, and provide comprehensive care to patients and their families. Every donation, regardless of size, plays a pivotal role in our ongoing fight against Alzheimer's disease.

Join Us in Making a Difference

We extend our heartfelt gratitude to our donors whose generosity fuels our mission. Together, we can navigate these challenging times and continue to make meaningful progress in Alzheimer's research and care.

To contribute or learn more about supporting the Easton Center, please contact **Jessica Vrazilek**, Director of Development, at **(310) 869-8611** or jvrazilek@mednet.ucla.edu.

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Bridging Genetics and Alzheimer's: Unlocking the Role of APOE4 with the Support of Randy and Jan Kessler

By: Jessica Rexach, MD, PhD, and UCLA Health Sciences Development for Department of Neurology

One of the most well-known genetic risk factors for Alzheimer's disease is the APOE gene, particularly the APOE4 variant, which increases the risk of developing Alzheimer's by up to 15 times. If you're familiar with Alzheimer's research, this gene is likely well-known. However, despite decades of study, many fundamental questions remain about how exactly APOE4 influences Alzheimer's risk. Recent advances are shedding light on some of these mysteries. Scientists have identified a growing list of molecular and cellular changes that occur in cells and animal models carrying the APOE4 variant. Additionally, researchers are discovering that the impact of APOE4 on Alzheimer's risk can vary among individuals. Some of these differences can be traced to genetic variations near the APOE gene, influenced by our ancestral backgrounds.

To close this knowledge gap, we need specialized infrastructure that collects genetic data from large groups of individuals, along with detailed information about their disease status. This infrastructure must be able to directly link this data with human cellular models of APOE4's effects based on patient samples. By leveraging the innovative UCLA ATLAS Community Health Initiative, which integrates genetic and clinical data from patients across the healthcare system interested in participating in research, we are adding a pipeline to combine ATLAS with cell models. This will tie together genetic variation, clinical data, and experimental human cell models. This integrated resource will connect cutting-edge genomic research with real-world patient data, helping us better understand how APOE4 alters cellular function and drives Alzheimer's disease.

Our goal is not only to facilitate new discoveries about APOE4 but also to establish a robust research pipeline that links experimental neuroscience with real-world disease. In doing so, we aim to enhance our understanding of human biology, genetic variation, and disease mechanisms in Alzheimer's, ultimately paving the way for new therapeutic targets.

We are excited to apply philanthropic support from **Randy and Jan Kessler '75**, longstanding supporters and partners of the UCLA Department of Neurology, to advance this critical work. Their continued generosity reflects a shared commitment to research that bridges science and care. *"We are honored to support the kind of bold, translational research that connects genetics with real-world patient care,"* said Jan and Randy Kessler. *"It's deeply meaningful to know that our contribution is helping to drive innovation in Alzheimer's research at the Mary S. Easton Center for Alzheimer's Disease Research and Care within the UCLA Department of Neurology."*

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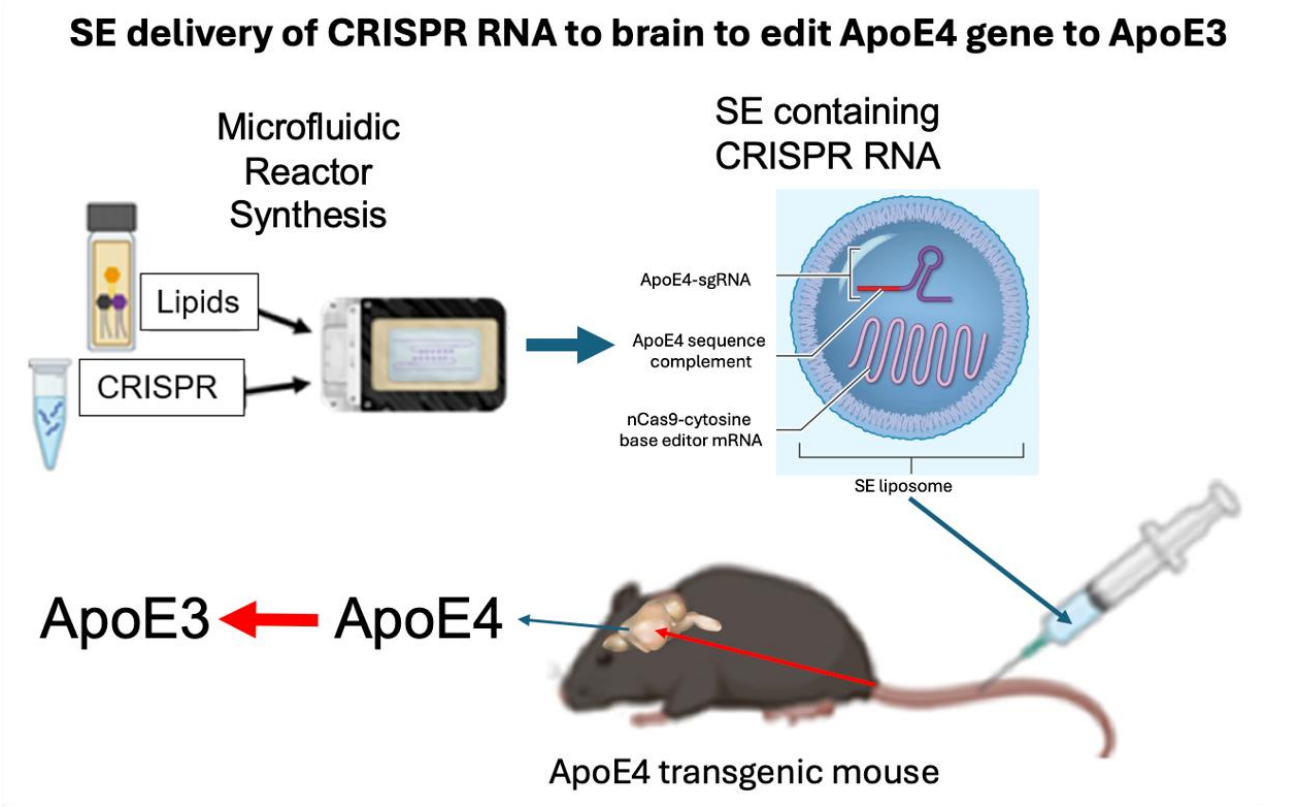
Targeting the Major Risk Factor for Alzheimer's Disease, Apolipoprotein E4 By SE-CRISPR Gene Editing in the Brain

By: *(left to right)* Bruce Teter, PhD, Jesus Campagna, MS, Chunni Zhu, PhD, Patricia Spilman, MA, Varghese John, PhD

Most cases of Alzheimer's disease (AD) are sporadic, which mean they are not due to a gene mutation that leads to familial AD. But different types of genes can increase the risk for AD, such as the gene for apolipoprotein E4 (or ApoE4). ApoE has many roles, but ApoE4 compared to another type, ApoE3, increases the risk for the development of AD. Compared to ApoE3, ApoE4 causes more amyloid production in the brain, that can accumulate and form plaques. These amyloid plaques are characteristic of AD brain tissue and are the target of FDA-approved antibody-based AD therapies such as lecanemab and aducanumab. While these therapies reduce amyloid load in the brain, they have only shown limited ability to induce clinical improvement or delay cognitive decline in AD patients. Most people, however, would agree it would be better to prevent amyloid plaques from forming than try to remove them after they have done damage to the neuronal circuits involved in cognition.

Interestingly, the gene sequence for ApoE4 only differs from ApoE3 by one single nucleotide and this one difference - a cytosine versus a thymine – leads to an amino acid called arginine appearing in ApoE4 where in ApoE3, it is cysteine. A simple change in the code for the amino acid from 'CGC' (cytosine-guanine-cytosine) to 'TGC' (thymine-guanine-cytosine) is all that is needed to change ApoE4 into ApoE3, and that is exactly what SE-CRISPR gene editing can do.



CRISPR editing, originally discovered as a way micro-organisms protect themselves from invader, uses components of CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) including 'guide RNA' specific for the codon to be edited, and the mRNA for the cytosine base editor (CBE) enzyme needed to make the edit.

With this knowledge, the Drug Discovery Lab (DDL) at UCLA, under the direction of Prof. Varghese John, is attempting to use CRISPR technology to edit ApoE4 to ApoE3 for the purpose of lowering the risk of AD. The main obstacle the lab faces in successfully inducing CRISPR editing in the brain is the delivery of SE-CRISPR across the 'blood-brain barrier' (BBB). Fortunately, using a UCLA Innovation grant, the DDL has developed a technology to bypass the BBB and deliver CRISPR components to the brain. The technology is a platform that involves the packaging of SE-CRISPR components in small nanoparticle particles called 'Synthetic Exosomes' (or SEs).

SEs are created by 'microfluidic synthesis' whereby the components for CRISPR editing and the components for SEs can be mixed to create vesicles that encapsulate CRISPR components, which not only increase brain delivery but can be stored for later use. SEs, like natural exosomes, can enter the brain by slipping past the protective cells of the BBB, delivering cargo to the brain.

In the SE-CRISPR project at the DDL led by Bruce Teter, Ph.D., the guide RNAs and CBEs were designed and tested in cells; then the best components underwent scaled-up SE-CRISPR production for testing in mice. The lab has an excellent mouse model for SE-CRISPR testing that is engineered to express human ApoE4. In the study, mice were injected with SE-CRISPR, and 5 days later, brain tissue was collected for analysis of ApoE4 to ApoE3 using Next Generation (DNA) Deep Sequencing.

The amount of gene editing, as well as the production of ApoE3 mRNA, was low but detectable and provides proof-of-concept of successful ApoE4 to ApoE3 editing in mouse brains. This has inspired the lab to continue onto the next steps, which will include trying different component designs to increase editing and new types of SEs and dosing methods to increase brain delivery, with the goal of achieving ~50% gene editing as part of an NIH R01 grant.

While in its early stages, if ApoE4 to ApoE3 gene editing in the brain is found to be possible, it would represent a new precision medicine therapy for the treatment of AD, and it may also open up possibilities for other types of gene editing in the brain.

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Clinical Research Opportunities

Help us learn more about Alzheimer's disease by joining a research study. If you're interested, simply scan the QR code and complete the short form. Our team will reach out to ask a few simple questions. When a study is a suitable fit for you, we will contact you with further information. For additional information, please reach out to us at ***(310) 794-6191.***

Below are the current recruiting trials. For a complete list of enrolling studies, visit our website at https://eastonad.ucla.edu/.

OBSERVATIONAL STUDIES:

- Alzheimer's Disease Neuroimaging Initiative 4 (ADNI4) Protocol

- Alzheimer's Disease Research Center - Biomarkers in Neurodegenerative Disease (ADRC-BIND)
- ARTFL-LEFFTDS Longitudinal Frontotemporal Lobar Degeneration (ALLFTD)
- Dementia Research, Education, and Advancement in Los Angeles (DREAM-LA)
- Dementia Research Focus Group
- Family History and Genetics Risk Factors for Dementia Focus Group
- Music Stimulation to Improve Cognition (MUSIC)
- National Institute on Aging Alzheimer's Disease Family Based Study (NIA-AD-FBS)

INTERVENTIONAL STUDIES:

- Brain Recovery and Individualized Neuromodulation (BRAIN Trial)
- Brain Tau PET Histopathological Study
- Microbiota Mediated Flavonoid Metabolites for Cognitive Health (MAEVE)
- Modulating Memory with Low-Intensity Focused Ultrasound (LIFUP-MCIAD)
- Protocol for Maintaining and Improving Mental Status in Alzheimer's Disease (PROMIS-AD)
- SUVEN Study

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For more information on our upcoming lectures and events, please visit the Easton Center Community Calendar.

ONEgeneration 16th Annual Senior Symposium

Date: Saturday, May 17, 2025
Time: 9:00 AM – 12:00 PM (PDT)
Location: ONEgeneration Senior Enrichment Center
17400 Victory Boulevard
Van Nuys, CA 91406

Join us for this free annual event with health screenings, community resources, raffles, and entertainment! A representative from the Easton Center will be on hand to share information about brain health, research, and clinical trials. No RSVP is required.

Alzheimer's Association Longest Day Ice Cream Fundraiser

Date: Wednesday, May 28, 2025
Time: 2:00 PM – 4:00 PM (PDT)
Location:
4215 Elenda Street
Culver City, CA 90230

The Easton Center will be supporting our long-time community partner at this annual event. Join us for education, community, and ice cream! No RSVP is required.

Men Who Care: Breaking Barriers and Building Bonds in Caregiving

Date: Thursday, May 29, 2025
Time: 3:00 PM – 4:30 PM (PDT)
Virtual Platform

Join the South Bay Dementia Education Consortium for a 1.5-hour workshop designed for male caregivers, including spouses, sons, brothers, and friends, caring for individuals with dementia or aging loved ones. Please register to receive your Zoom link.
https://us06web.zoom.us/meeting/register/_Vn7bUn1TzOLkhZ8LvtRsg?_x_zm_rtaid=J43NKZFiQb-hmgorkc47dA.1746633853512.54cbf0353d82ab4a1c023ad64a6d90e7&_x_zm_rhtaid=264#/registration

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Alzheimer's Los Angeles Caregiver Wellness Day #1

Date: Saturday, May 31, 2025
Time: 9:00 AM – 1:00 PM (PDT)
Location: Weingart Senior Center
5220 Oliva Avenue
Lakewood, CA 90712

The Mary S. Easton Center and the Equity for Latinx-Hispanic Healthy Aging (ELHA) lab are joining Alzheimer's LA's Caregiver Wellness Day. This free event offers wellness workshops, resources, continental breakfast and lunch, and raffles/giveaways.

Attendance is free, but registration is required. For registration help, questions, or disability accommodations, please contact **Yanet** at **(323) 930-6280** or email rsvp@alzla.org**.** Limited funds are available for respite care and ride-share costs. Please contact Yanet for more information.

Mind over Matter Mental Health & Wellness Festival

Date: Saturday, May 31, 2025
Time: 11:00 AM – 4:00 PM (PDT)
Location:
3rd Street Promenade
Santa Monica, CA 90401

Sponsored by the Santa Monica Black Empowerment Association. The Mary S. Easton Center will be in attendance, sharing information about brain health, dementia, research, and clinical care at UCLA
Open to the public - no RSVP is required.

Dementia Awareness Champion Summit (for providers/professionals)

Date: Monday, June 2, 2025
Time: 8:30 AM – 11:00 AM (PDT)
Location: Olive View-UCLA Medical Center
14445 Olive View Drive, Conference Room
Sylmar, CA 91342

Brain health awareness and early detection of dementia are key to supporting our aging population across Los Angeles County. This summit will focus on the importance of early detection, as well as best practices for operationalizing timely screening and diagnosis in primary care settings.
RSVP to https://www.eventbrite.com/e/dementia-awareness-champion-summit-tickets-1344912572709?utm-campaign=social&utm-content=attendeeshare&utm-medium=discovery&utm-term=listing&utm-source=cp&aff=ebdsshcopyurl

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Bet Tzedek's 9th Annual World's Elder Abuse Awareness Day (WEAAD) : A Focus on Dementia & Elder Abuse

Date: Wednesday, June 4, 2025
Time: 9:00 AM – 3:30 PM (PDT)
Location: California Endowment's Center for Healthy Communities
1000 North Alameda Street
Los Angeles, CA 90012

Dr. Díaz-Santos, Director of Equity for Latinx-Hispanic Healthy Aging (ELHA) Lab, will be the morning keynote speaker on this year's Bet Tzedek's 9th Annual World's Elder Abuse Awareness Day (WEAAD).

Bet Tzedek's WEADD annual event brings together leaders in aging across the fields of medicine, legal, social work, government, and non-profit sectors. There is no cost to attend. Light breakfast and lunch will be provided. For additional questions, email **Alisa Anderson** at aanderson@bettzedek.org
Registration: Bet Tzedek's 9th Annual WEAAD Registration

Alzheimer's Los Angeles Early Memory Loss Conference

Date: Saturday, June 7, 2025
Time: 9:00 AM – 1:00 PM (PDT)
Virtual Platform

This one-day conference offers support and education about early memory loss, mild cognitive impairment, early-stage Alzheimer's, or other dementias. Speakers will provide insights about financial and legal planning, brain health, the latest research, and current medications, as well as frequently asked questions about living with early memory loss.
Registration is required by **June 5th** at: AlzheimersLA.org/EMLC or call **(844) 435-7259.**

2025 Spring Lennox Health Fair

Date: Saturday, June 7, 2025
Time: 9:00 AM – 1:00 PM (PDT)
Location: Lennox Middle School
11033 Buford Avenue
Lennox, CA 90304

The Equity for Latinx-Hispanic Healthy Aging (ELHA) lab is joining DREW/UCLA LMSA's Annual Lennox Health Fair to provide brain health and early detection of dementia resources in Spanish and English. Since 1993, the Lennox Health Fair has been a vital community event dedicated to providing free medical services, wellness education, and critical resources to underserved and uninsured families.
No RSVP is required.

Alzheimer's Awareness Day

Date: Monday, June 16, 2025
Time: 1:00 PM – 3:00 PM (PDT)
Location: St. Barnabas Senior Center
675 South Carondelet Street
Los Angeles, CA 90057

This FREE multilingual event (in Korean, Spanish, and English), being sponsored by Alzheimer's Association and the Easton Center, will discuss early warning signs, detection, and diagnosis of dementia. RSVP to **Monica Moore** at mrmoore@mednet.ucla.edu

Alzheimer's Los Angeles Caregiver Wellness Day #2

Date: Saturday, June 28, 2025
Time: 9:00 AM – 1:00 PM (PDT)
Location: ONEgeneration Senior Enrichment Center
18255 Victory Boulevard
Reseda, CA 91335

The Mary S. Easton Center and the Equity for Latinx-Hispanic Healthy Aging (ELHA) Lab are joining Alzheimer's LA's Caregiver Wellness Day. This free event offers wellness workshops, resources, continental breakfast and lunch, and raffles/giveaways. Dr. Díaz-Santos, Director of ELHA, will be leading one of the Spanish workshops.

Registration is required at: June 28, 2025, AlzLA Caregiver Wellness Day 2
For registration help, questions, or disability accommodations, please contact **Yanet** at **(323) 930-6280** or email rsvp@alzla.org. Limited funds are available for respite care and ride-share costs.

Update on Alzheimer's Disease Research

Date: Friday, July 18, 2025
Time: 12:00 PM – 1:00 PM (PDT)
Location: Altadena Senior Center - Loma Alta Park
3330 North Lincoln Avenue
Altadena, CA 91001

Monica Moore, MSG, will present the latest findings related to the symptoms and causes of dementia and Alzheimer's disease. She will discuss the latest treatments and the current research being conducted to find a cure for this devastating disease. RSVP to **Monica Moore** at mrmoore@mednet.ucla.edu

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