HMRI | Huntington Medical Research Institutes
SCIENTIFIC DISCOVERY, MADE IN PASADENA

Insights

WINTER 2025

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HMRI Huntington Medical Research Institutes
Insights
WINTER 2025

A MESSAGE FROM OUR PRESIDENT & CEO

To all our dear friends in Pasadena, Altadena, and surrounding areas, we recognize the challenges many of you are facing in the wake of the tragic Eaton Canyon Fire, which will linger for the weeks and months ahead. I especially want to acknowledge the Altadena Guild members, who have ardently supported HMRI for more than 70 years. Many of you have lost your homes, businesses, or both. All of us at HMRI will continue to be here for you, just as you have been for us over the years. The tumultuous uncertainty of the past weeks has brought us together with encouragement and inspiration, and I am confident we will rebuild our beloved community stronger than ever.

Thanks to our incredible facilities team, I'm pleased to share that HMRI laboratories and operations have been fully restored. Preparations are now underway to welcome the 2025 cohort of students to our campus in June, and student recruitment efforts are in full swing. On January 30, we resumed our public programs with the panel discussion, "Critical Conversations on Artificial Intelligence in Biotechnology and Medicine," moderated by Chief Science Officer and Director of Cardiovascular Research Robert A. Kloner, MD, PhD.

Our dedicated scientists continue to advance their research. In the Cardiovascular Research Laboratory, James G. Boswell Fellow Rashid Alavi, PhD, is using Artificial Intelligence to predict the long-term risk of cardiovascular damage from e-cigarettes through an innovative method of blood flow dynamics based on intrinsic frequency. Astrid Suchy-Dicey, PhD, Chair of Clinical and Translational Neurosciences, recently published a paper in Communications Psychology titled "Cognitive Reserve is Associated with Education, Social Determinants, and Cognitive Outcomes Among Older American Indians in the Strong Heart Study." In the Angiogenesis and Brain Development Laboratory (ABDL), researchers are currently conducting basic research to understand vascular GABA and its receptor signaling mechanisms during postnatal brain development, which can enhance the fundamental understanding of the origins of psychiatric diseases. In the ABDL's translational research, they are generating human embryonic forebrain-like endothelial cells that may be used for repair and regeneration in the adult brain in various disease scenarios.

As we continue to move forward together, advancing research that improves health outcomes, our thoughts are with you. From all of us in the HMRI family, we wish you and your loved ones the very best for your safety and well-being.

With gratitude and care,

Julia E. Bradsher, PhD, MBA
President and Chief Executive Officer

HMRI Welcomes New Biostatistician to Clinical and Translational Neurosciences

Aishwaryah Ravisankar joins the Clinical and Translational Neurosciences Team as a biostatistician. Her training in advanced biostatistics and experience in clinical research provide expert analysis for the Brain Aging Study. She conducts extensive retrospective analyses, examining the longitudinal effects of aging. Her work tracks changes in cognitively healthy individuals who experience decline due to aging, as evidenced by neuropsychological assessments, biomarkers, and changes in specific areas of the brain. Additionally, Aishwaryah leverages her expertise in data visualization to communicate research conclusions concisely. Her insights, skill set, and collaborative approach have contributed to meaningful conclusions and data preparation for publication. ❖

Aishwaryah "Aish" Ravisankar, biostatistician, pictured with President and CEO Julia E. Bradsher, PhD, MBA

The Heart of the Clinical Experience

A decade ago, David Buennagel, clinical coordinator for HMRI's Brain Aging Study, became the heart of the clinical experience. He is the first point of contact for most study participants, beginning with recruitment and enrollment process, and he continues to be the most visible individual throughout their experience.

David guides study participants through each stage of their clinical visits. Over three months, participants are initially scheduled for three to five visits, each lasting about one to four hours, at HMRI's facility in Pasadena. Buennagel schedules each appointment, coordinates necessary tests, explains the study and process to new participants, and gathers data, including family and clinical histories.

However, on a deeper level, the most rewarding part of his job is building rapport with the study participants. "I enjoy working with participants and getting to know people," said Buennagel. "After the initial set of appointments, participants return for follow-up visits every two years. It's a privilege to spend time with our participants and learn about the enriching experiences of their lives." Study participants appreciate David's caring and thoughtful demeanor. Those who have been in the Study for a long time look forward to seeing him regularly and describe him as an old friend.

"David is instrumental to the conduct of the Brain Aging Study. His kindness and generosity, as well as humbleness, are appreciated by all, but also important is his work ethic," said Astrid Suchy-Dicey, Principal Investigator of the Brain Aging Study. "He is tireless, often working on nights and weekends, to ensure everything is handled in a timely manner and prepared for participants' appointments in the study offices. His contributions are critical to our success, and we could not do it without him!"

"HMRI is a great environment," said Buennagel. "I've developed professionally and broadened my knowledge of clinical neuropsychology; I'm grateful to contribute positively to the Brain Aging Study through this rewarding experience." ❖

Moving Forward Together: Advancing Pre-Alzheimer's Disease Biomarkers

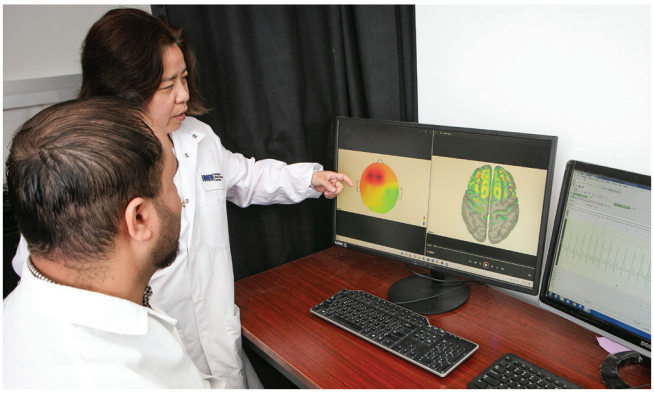
Alzheimer's disease is a global epidemic, with about 47 million diagnosed cases worldwide. However, current Alzheimer's diagnoses typically identify patients who are in the later stages of the disease, after clinical symptoms have emerged. Consequently, an estimated 315 million people worldwide remain undiagnosed with pre-Alzheimer's, before symptoms appear, missing a critical window of opportunity for prevention or to delay onset.

HMRI's dedicated Clinical and Translational Neuroscientists aim to tackle these challenges by advancing studies to discover pre-Alzheimer's disease biomarkers as part of the Brain Aging Study under the direction of Principal Investigator Astrid M. Suchy-Dicey, PhD. Pre-Alzheimer's biomarkers can begin to surface 20 to 30 years before clinical symptoms manifest. With a better understanding and identification of these biomarkers, opportunities arise to create new diagnostic tools to detect the disease and changes in cognition well before clinical symptoms are evident.

The Biomarker and Neuro-disease Mechanism Laboratory (BNML), led by Alfred Fonteh, PhD, has finished refining the assays for measuring urine short-, branched, and long-chain fatty acids as potential biomarkers for neurodegenerative injury. The new assay using ultra high-performance liquid chromatography tandem mass spectrometry (UHPLC-LM/MS) is more than a thousand times more sensitive than our previous gas chromatography mass spectrometry (GC-MS) and thus detects a wider range of biomarkers.

The BNML has also completed the analyses of cerebrospinal fluid proteins and metabolites that change when the same cognitively unimpaired person declines cognitively. These studies show changes in a group of proteins called extracellular matrix protein (ECM) and in metabolites that control sleep and neuronal function. These studies suggest that preventing the breakdown of ECMs or a decrease in the levels of sleep hormones can be useful strategies to prevent cognitive decline in older adults

Dr. Xianghong Arakaki, MD, PhD, funded by the National Institute on Aging, leads the Cognition and Brain Integration Laboratory (CBIL) to advance neurocognitive studies through a neurophysiological approach. Her team and collaborators are investigating brain wave (EEG) and heart wave (ECG) signatures during cognitive challenge testing. Study participants are cognitively healthy, in resting states, and may or may not have the pathology for Alzheimer's disease and related dementias (AD/ADRD). Researchers have identified specific neurophysiological signatures in the early stages of AD/ADRD. For example, cognitively healthy participants (without mild cognitive impairment) who have AD/ADRD pathology display neurophysiological profiles characterized by autonomic dysfunction and changes in brain activation and connectivity during testing. These variations depend on the specific tasks and the different brain regions involved. These neurophysiological signatures have the potential to become low-cost, noninvasive biomarkers for the early detection of the disease.



The Brain Aging Study team continues to work in collaboration with the Doheny Eye Institute to link Alzheimer's disease plasma biomarker levels to optical coherence tomography, a simple noninvasive imaging technique for mapping the retina. In the future, this technique may also be used as a noninvasive test to identify pre-Alzheimer's disease biomarkers.

The Brain Aging Study administrative and data teams are diligently working to collect and clean data for use by study partners and other investigators from UCLA, Caltech, and Fuller Theological Seminary to advance research and support future publications. This data provides a comprehensive snapshot of each participant as they complete visits throughout the Study, analyzing a broad spectrum of modalities, including MRI, EEG, biomarkers, and neuropsychological assessments. The diversity of modalities and the large volume of data confer high value on HMRI's

Brain Aging Study data among researchers. Once the data is integrated into the Brain Aging Study, the data team will use statistical and analytical methods to extract insights about the progression of aging within the Study.

The team hopes to further advance this vital work by continuing to investigate preclinical and early-stage cognitive change and novel facets of cognitive decline. As the Brain Aging Study advances and continues to collaborate with Study partners, plans are underway to develop new scientific hypotheses. Long-term, their goal is to help more people detect pre-symptomatic biomarkers to improve treatment options and outcomes for Alzheimer's disease.

The success of the Brain Aging Study and future advances in biomarkers for the early detection of Alzheimer's disease relies on the dedication of our study participants, along with support from the HMRI operations team, the Pasadena community, and our donors. Your ongoing commitment to the Study enhances our understanding of neurodegeneration and progresses us toward the early detection of Alzheimer's and other dementias. ❖

Local Foundation Champions Veterans Study

In 2018, with local foundation support, HMRI scientists expanded the Brain Aging Study to serve the Veterans community of Southern California. Veterans who spend time in training and military service, are especially at high risk of head injury, concussion, and traumatic brain injury. This exposure can lead to a higher risk of chronic traumatic encephalopathy, Alzheimer's disease, or other neurodegenerative pathology along with related cognitive symptoms such as dementia.

Veterans are also at high risk of post-traumatic stress disorder, which can be exacerbated by repeated blast exposures. These exposures may cause undetectable brain injuries that can have cumulative effects on brain structure and function. It remains unclear whether such exposures can result in chronic or cumulative post-traumatic stress.

At HMRI, Study investigators aim to examine undetected changes related to head injury, changes in stress and psychological health, and functional cognitive connectivity. Brain connectivity studies can provide insights into brain functioning and health that are non-invasive and psychologically non-damaging to study participants. The results are combined with evaluations that assess the history of exposure to blasts in training and service, as well as psychological health and stress.

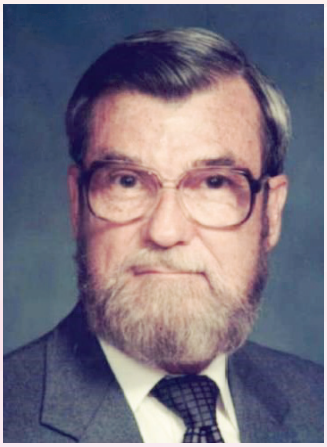
This Foundation continues to support research at HMRI on the specific impacts of military service. Now in its fifth year, the Veterans Study ensures that scientific data characterizing the lived experiences of our Veterans Community is collected and studied. "I am grateful for the Foundation's generosity and shared commitment to the Study," said Astrid Suchy-Dicey, PhD, chair and scientific director, Clinical and Translational Neurosciences and principal investigator, Brain Aging Study. "Their support allows our scientists to develop pilot data to support new hypotheses and larger studies examining Veteran health, risk, and brain aging. We are hopeful that our insights will ultimately help to reduce health disparities among Veterans as they age." ❖

For additional information on HMRI's Veterans Study, email brainaging@hmri.org.

Supporting The Altadena Guild

For more than 70 years, the Altadena Guild has been part of the heart and soul of HMRI, lifting us up and standing by our side. Now, as nearly 30 Guild members face the unimaginable loss of their homes in the Eaton Fire — and so many more deal with displacement, smoke, and ash — we want you to know: we are here for you. In good times and in hard times, we stand together. Just as you've always been there for us, we'll be with you every step of the way as you rebuild and heal. If you need help with insurance claims or FEMA applications, we're here to support you. And if you need internet access, Guild members are welcome to stop by HMRI during the lunch hour to use our Wi-Fi. We're in this together. ❖

THE ALTADENA GUILD OF HUNTINGTON MEMORIAL HOSPITAL



George Coulter's Legacy

At the end of 2024, HMRI received a transformational bequest from the late George Prothro Coulter, a longtime Pasadena resident whose generosity continues to strengthen the nonprofits that serve the community he loved. Born on June 8, 1930, in El Dorado, Arkansas, George lived a life defined by intellect, service, and philanthropy. He was a proud graduate of UCLA and earned his law degree from George Washington University. George was married to two remarkable women in his lifetime: his first wife, Gloria "Corky" Cohn Coulter, and later, Margaret "Meg" Quinn Coulter. He built a distinguished career as both a lawyer and also served his country: he was a veteran of the U.S. Navy and briefly served in the NSA, demonstrating the same sense of duty and dedication that shaped his professional and philanthropic endeavors. George passed on December 12, 2023.

Tragically, George's Altadena home, where he resided since 1962, was among the many homes lost during the devastating Eaton Fire. While the physical embodiment of his memories has been reduced to ashes, his enduring legacy persists through the generosity he extended to the causes he cherished. Our hearts go out to his family and friends as they mourn his passing, and we are honored to celebrate the impact he continues to have on our community.

"George's commitment to research will have a profound and lasting impact," said Dr. Julia Bradsher, HMRI President and CEO. " His gift is a testament to the power of philanthropy in driving scientific progress, and we are honored to carry his legacy forward."

George's story is a powerful reminder that a well-planned legacy can shape the future of a community and the lives of those who come after us. His generosity will continue to fuel innovation, providing hope for patients and families who look to medical research for answers. ❖

Please contact Paul Roach, Senior Director of Development at 909.210.6226 or email paul.roach@hmri.org for any support needs.

Community Comfort Zone

HMRI proudly partnered with Jones Coffee and the Pasadena Community Foundation (PCF) to create the Community Comfort Zone, a creative space for healing, connection and comfort. For two weeks after the fires, local musicians, artists, therapists, and HMRI team members volunteered their time, gathering at Jones daily to support the community. A substantial portion of all sales were donated to PCF's Eaton Fire Relief and Recovery Fund. ❖

Jennifer DeVoll and Jeannine Bogaard of PCF, Larry, Mireya and Chuck Jones, founders of Jones Coffee, and Regina Grice and Paul Roach of HMRI.

Giving Tuesday Fuels the Future Generation

Giving Tuesday, a global movement inspiring radical generosity, unleashes change and fuels causes people care most about. The people in the Pasadena community directed their generosity toward HMRI's "Give the Gift of Education" campaign on Giving Tuesday, December 3, 2024. Nicole Purcell, PhD, scientific director of Education programs, kicked off the day with a personal commitment to match all donations, dollar for dollar up to $3000, showing her leadership and dedication to the students and the institutes' education initiatives. "I chose to give this amount to ensure our students would receive CPR training as part of their education at HMRI," said Purcell.

> "A number of our students come from populations at high risk for cardiovascular disease. This practical skill can have a real life-saving impact in the community."
>
> —Nicole Purcell, PhD

"A number of our students come from populations at high risk for cardiovascular disease. This practical skill can have a real life-saving impact in the community." Collectively, supporters joined Purcell to raise a total of $7,365.58 for the 2025 cohort of aspiring scientists. The remainder of Giving Tuesday gifts will support students with laboratory supplies, stipends, and transportation support. We're grateful to everyone who participated in Giving Tuesday! Your kindness and generosity will directly impact the talented students. ❖

Do You Know a Student Looking for a Summer Biomedical Research Experience?

HMRI Student Undergraduate Research Fellowship (HMRI SURF), June 16 – August 8

Undergraduate students accepted into the program will collaborate with HMRI scientists, participate in professional development seminars, and learn safety protocols. The program offers a range of laboratory-based opportunities in biomedical research, including studies on Alzheimer's disease, neurovascular research, migraines, vaping, e-cigarette cardiac toxicity, and cardiovascular signaling.

Scan the QR Code to learn more and apply.

American Heart Association Supporting Undergraduate Research Experiences (AHA SURE), June 16 – August 8

AHA selected HMRI as a partner in the AHA SURE program, providing experiences in cardiovascular research for three exceptional students pursuing STEMM careers — science, technology, engineering, mathematics, and medicine.

Scan the QR Code to learn more, review eligibility criteria, and apply.

Student Spotlight

Sofia Stellar, Brain Aging Study Intern

Sofia Stellar, a Pasadena native, attended Chandler School before moving on to Flintridge Preparatory for high school. She graduated from the University of Southern California with a Bachelor of Science in Human Biology and a minor in Philosophy. In preparation for medical school, which is set to begin in July 2025, Sofia worked as an EMT, completed a phlebotomy course, and participated in various research projects. To expand her research experience, her grandfather, Jay Berger, suggested that Sofia consider exploring HMRI. "As soon as I learned more about HMRI's work and Dr. Suchy-Dicey's team in particular, I was immediately intrigued by the opportunity to gain a more comprehensive, hands-on experience in research," said Stellar.

Her project concentrated on standardizing questions to reduce ambiguity and enhance data accuracy in REDCap for HMRI's Brain Aging Study. "My goal was to leverage my insights and develop skills to improve the study's approach to data collection, reducing human error," said Stellar.

"Sofia was a hardworking self-starter, and easy to guide," said Suchy-Dicey. "We developed her project question together; I provided the guidance on background, direction, and field knowledge; but she learned the details independently." Suchy-Dicey's approach to mentorship is "guide-and-direct," providing mentees with resources to succeed.

> "Sofia was a hardworking self-starter, and easy to guide," said Suchy-Dicey. "We developed her project question together; I provided the guidance on background, direction, and field knowledge; but she learned the details independently."
>
> —Astrid Suchy-Dicey, PhD

Stellar included questions regarding the frequency and amount of alcohol and tobacco use, enabling participants to give clear, specific answers, such as "yes" or "no" responses or numerical values. This standardization not only streamlined data entry but also reduced bias when analyzing patterns of alcohol and tobacco use among participants.

"My experience significantly strengthened my collaboration skills. We engaged in open communication, asked questions, and learned from each other's expertise," expressed Stellar. "This collaborative environment not only helped me develop a deeper understanding of the research process but also reinforced the importance of teamwork in achieving shared goals, which will be crucial in my chosen profession of medicine." ❖

Applications to all programs are due by Friday, March 14, at 11:59 pm PST.

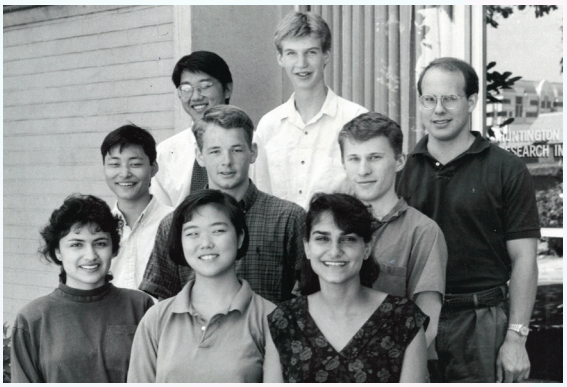
High School STEM Program June 16 – July 25

A six-week STEM education opportunity for 24 Pasadena Unified School District high school students. Rising juniors and seniors can apply to either the morning or afternoon session. Each week, students will explore new topics under the guidance of mentors and science teachers and conduct independent research projects.

Scan the QR Code to learn more and apply.

For additional information, email education@hmri.org or visit hmri.org/education.

HMRI Alumni History Project



In 2025, HMRI will celebrate 70 years of educating and inspiring the next generation of scientists and physicians. To commemorate this milestone, we want to reconnect with everyone who has contributed to HMRI's rich educational history, including students, faculty, mentors, and more.

Through this project, we will update your alumni information and gather your personal stories to commemorate the history of the HMRI educational experience.

To update your information and help us tell your story, please contact Wendy Welch-Keller at wendy.welch-keller@hmri.org or 626.389.3433.

Critical Conversations:

Understanding Your Risk for Vascular Dementia and Stroke

Stroke and vascular dementia are among the leading causes of death and disability worldwide, including in our local Pasadena community. Experts gathered to shed light on the complex relationship between vascular dementia and stroke, exploring various risk factors during a panel discussion last fall, moderated by HMRI's President and CEO Julia Bradsher, PhD, MBA.

Notable panelists included Robert A. Kloner, MD, PhD, chief science officer and director of Cardiovascular Research at HMRI; Astrid M. Suchy-Dicey, PhD, chair of Clinical and Translational Neurosciences and principal investigator of the Brain Aging Study at HMRI; Lawrence W. Jones, MD, board-certified urologist (ret.) and member of the HMRI Board of Directors; Helena Chui, MD, chair and professor of Neurology, Raymond and Betty McCarron Chair in Neurology at USC; and Arbi Ohanian, MD, board-certified neurologist and medical director of the Stroke Program at Huntington Hospital.

Although stroke is highly preventable, there has been a rapid increase in the global stroke burden from 1990 to 2021. While stroke can be linked to vascular dementia, it is not a stand-alone cause. Individuals can take preventive measures and make lifestyle changes to lower their risk for both, including a heart-healthy diet, regular physical activity, managing underlying health conditions, maintaining strong social connections, and increasing mental activity.

The next President's Event is scheduled for Thursday, April 24. Additional details are coming soon! ❖

BRAIN AGING STUDY

Helping Researchers Advance Science in Retirement

Janet, a clinical participant in the HMRI Brain Aging Study, is pictured with David Buennagel, the senior clinical coordinator of the Study.

HMRI researchers began investigating brain aging, Alzheimer's disease, and other dementias more than twenty years ago. The Brain Aging Study depends on clinical participants willing to contribute their time to help scientists uncover the causes of Alzheimer's disease and pioneer early detection tests.

Janet, a new retiree and resident of Pasadena, originally from the United Kingdom, joined the Brain Aging Study in 2012. One night over dinner in December, her friends, who were also study participants at the time, asked if she wanted to join them as a volunteer for brain aging research. Janet was searching for new ways to spend her time, and she agreed to look into the study.

Janet expressed excitement about joining the Study. "I wanted to know about how my brain operates and how it's aging; how to make my memory better." She continued, "Some of the tests can be tiring, but that's okay. Participating in the Study helps me worry less about my health and aging; I've learned so much about my body and overall well-being."

She enjoys spending time with the Brain Aging Study team, who are friendly and easily relatable. "I've known David the longest," said Janet. He has a warmth about him and always remembers little details about events in my life."

Janet attributes her health to a busy life and a positive outlook. She is a docent at Huntington Gardens and spends time with her friends and family. "Looking back on my life, I've survived everything I was confronted with. I've had a good life, I'm comfortable, and I have good friends."

Her advice to other people interested in joining the Brain Aging Study is, "Join in a minute. You'll learn about your strengths and weaknesses, help science, and gain new spheres of knowledge. And what else are you doing anyway?"

60 OR OVER?
VOLUNTEER FOR HMRI'S BRAIN AGING STUDY

What's the goal?
Today our neuroscientists are working to identify new tests to make early diagnosis of Alzheimer's possible, allowing for more effective treatment. These tests aim to detect changes in the brain caused by Alzheimer's and related diseases before the onset of cognitive symptoms, predicting individuals who do not yet show symptoms of the disease, the risk of future memory and fuctional decline.

What do volunteers do?
You will be interviewed about your medical history, and asked to undergo voluntary non-invasive and minimally-invasive tests. These may include physical exam, cognitive testing, magnetic resonance imaging (MRI), lumbar puncture, blood draw, electroencephalography (EEG, retina scan, and other examinations related to brain aging.

Who can take part?
You can potentially volunteer if you're at least 60 years old, live in the Pasadena area, and cognitively healthy.

How much time does it take?
You'll make three to five visits, each about one to four hours long, over the course of three months — all at our facility in Pasadena, California. These visits will be repeated every two years. You'll be compensated for your time.

INTERESTED? PLEASE CONTACT:
HMRI Brain Aging Study
brainaging@hmri.org or 626.389.3421

Neurocardiovascular Seminar Series

2025 Guest Speakers

WEDNESDAY, MARCH 26

Sarkis Mazmanian, PhD

Luis and Nelly Soux Professor of Microbiology
Merkin Institute Professor

Caltech

WEDNESDAY, APRIL 23

Young Cha, PhD

Assistant Neuroscientist
Basic Neuroscience Division
Assistant Professor of Psychiatry

Harvard Medical School

Dr. Cha's Seminar will be via Zoom

WEDNESDAY, MAY 7

Shin Shimojo, PhD

Gertrude Baltimore Professor of Experimental Psychology

Caltech

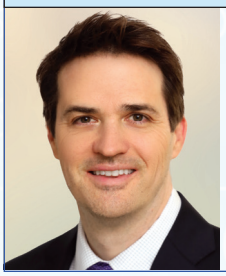
WEDNESDAY, JUNE 4

E. Dale Abel, MD, PhD

William S. Adams Distinguished Professor of Medicine
Chair and Executive Medical Director
Department of Medicine

David Geffen School of Medicine UCLA

WEDNESDAY, OCTOBER 1



Keith Vossel, MD, MSc

Michael M. Minchin, Jr., President
J.D. French Alzheimer's Foundation
Endowed Chair and Professor of Neurology

David Geffen School of Medicine UCLA

OPEN TO THE PUBLIC!

The seminar series will be held from 3 – 4 pm.

HUNTINGTON MEDICAL RESEARCH INSTITUTES*
686 S. Fair Oaks Avenue, Pasadena, CA 91105

For additional information, email education@hmri.org

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AND INSPIRE THE NEXT GENERATION OF SCIENTISTS
Thank you for supporting our vital research!

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Jessica West

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