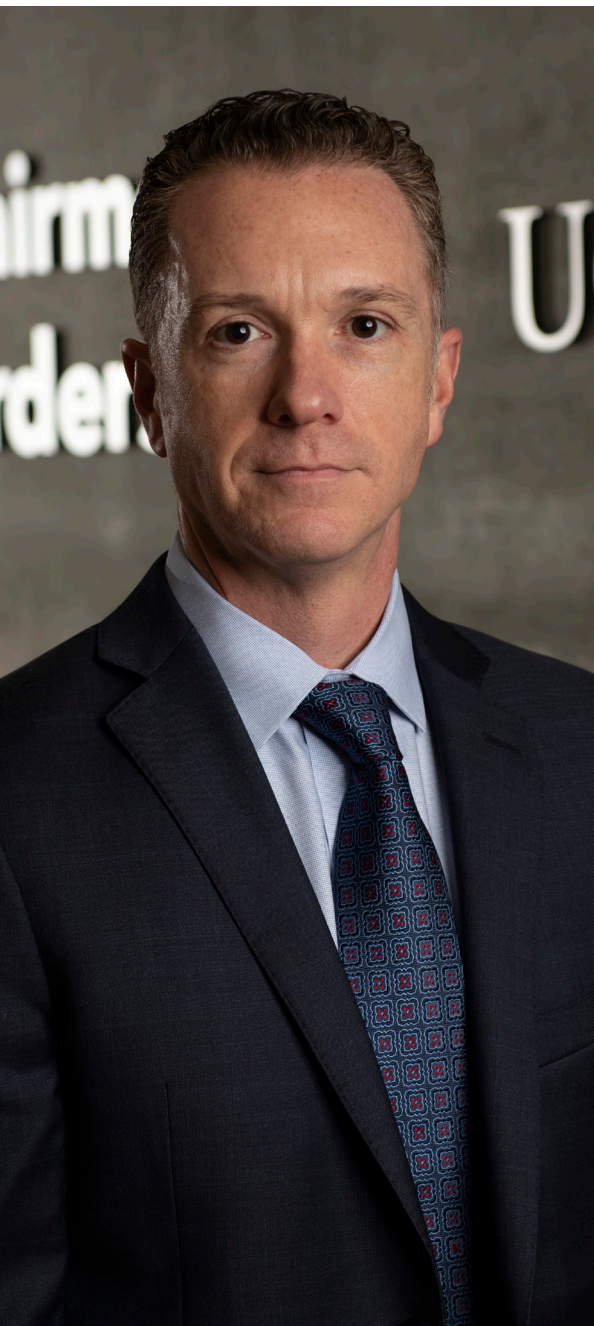




2020: Excellence through Adversity

UCI MIND Annual Report



Dear Friend of UCI MIND,

The COVID-19 pandemic has impacted every facet of life, especially for families enduring Alzheimer's disease and related dementias. In 2020 alone, deaths due to Alzheimer's increased 16% in the United States. Caregivers were forced to adapt how they manage care and cope with burden, while many endured painful separation from loved ones. Researchers faced delays and challenges in continuing our work. Yet, the past year has further ignited in us an urgency to discover solutions for Alzheimer's disease and related dementias and improve the lives of those affected.

In response to the pandemic, UCI MIND adapted to meet the needs of our community and to continue our critical research and education mission, while prioritizing the safety of our participants and their families. We launched virtual cognitive assessments for our hallmark Longitudinal Study, as well as a new dedicated webpage to communicate updates to research participants and family members. We developed caregiver-focused educational resources in multiple languages to help guide families through this unprecedented journey. And our annual events, including our research conference and gala, shifted to virtual formats for the first time in their decades-long histories.

Despite the challenges that came, 2020 also marked a year of achievements for UCI MIND. We reached our silver anniversary as an Organized Research Unit, founded by Carl Cotman, PhD in 1995. We were awarded a \$14.4 million grant from the National Institute on Aging to sustain our federally designated Alzheimer's Disease Research Center, led by Dean Frank LaFerla, PhD. Our investigators continued to make key discoveries in the areas of animal models, cellular changes, and human biomarkers of Alzheimer's disease, the oldest old, and Down syndrome. NIH grant funding to UCI MIND investigators has never been higher in the Institute's illustrious history.

Philanthropic support has also played a critical role in our 2020 successes:

- Our Women's Initiative, in partnership with Maria Shriver's Women's Alzheimer's Movement, awarded two new grants to UCI investigators to study sex and gender disparities in Alzheimer's disease.
- Our Innovative Research Initiative supported three novel projects investigating the role of hearing loss in Alzheimer's disease, the potential therapeutic qualities of a parasitic infectious agent, and a systems biology approach to investigating disease mechanisms in Down syndrome brain tissue.
- We launched the UCI MIND Research and Mentorship Program (RAMP) that pairs medical students with faculty mentors to inspire future careers in dementia research and care with support from our philanthropic partners Dr. Lorna Carlin and the nonprofit HFC led by Seth Rogen and Lauren Miller Rogen.

For UCI MIND, 2020 was a year of adaptations and adversity, but also great progress thanks to our strong community partnerships and dedicated research team. In recognition of our shared mission, and with gratitude for our community of advocates, philanthropists and research participants, we thank you for your support.


Joshua D. Grill, PhD,
Director, UCI MIND

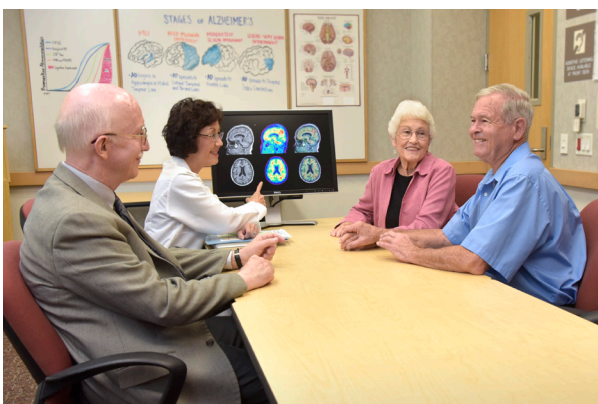


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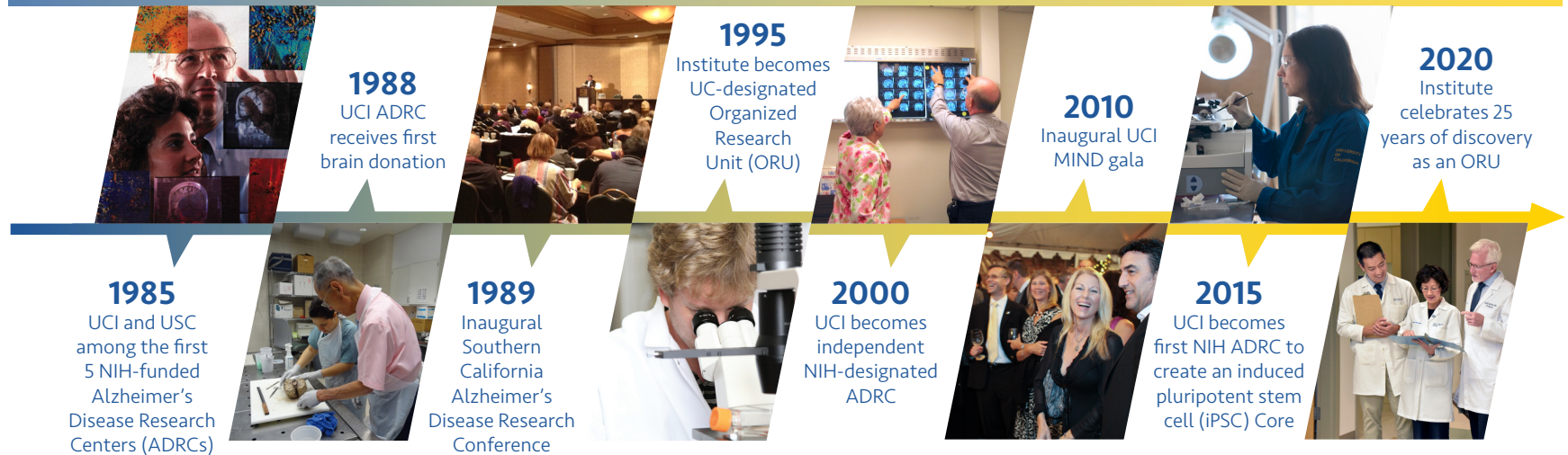
Excellence through Leadership

Leadership is part of the fabric of UCI MIND. Since its inception, UCI MIND has been a leader in the field of Alzheimer's disease and related disorders.

UCI MIND Leadership Council

Gil Aranowitz	Steve O'Leary
Sydney Balalis	Ken Pao
Kim Butrum	Mark Phillips, PharmD
Shirley Cameron	Randy Platt
Barbara DeMar	Ann Quilter
Jacqueline DuPont, PhD	Susan Reese
William Edwards	Barbara Reiland
Janet Gianulias	Heather Sahargun
Joe Gonzalez	Fred Salter
Harriet Harris	Wendy Salter
Fumiko Ishii	Jennifer Simpson
Karen Kamel	Keith Swayne
Sara Kelly	Meg Treat
Rosalyn Laudati, PhD	Jonathan Varenchik
Roger Lisabeth	Bobbitt Williams
Diane Mondini	Kitty Woodworth
Rita Moreira	Susan Yedor
Virginia Naeve	Boon Ja Yoo
Beverly Newton	Burton Young
Marla Noel	

25 Years of Discovery



Leadership:

1995-2009

Carl Cotman, PhD

2009-2014

Frank LaFerla, PhD

2014-2016

Andrea J. Tenner, PhD

2016-2018

Frank LaFerla, PhD/
Joshua Grill, PhD

2018-present

Joshua Grill, PhD



\$150+ million
in NIH grants awarded to
UCI MIND investigators



1,000+
brains donated by UCI MIND
research participants



1,500+
publications of UCI MIND's
research discoveries



300+
new scientists trained
by UCI MIND faculty

Orange County's Only NIH-Funded Alzheimer's Disease Research Center



Led by Frank LaFerla, PhD, dean of the UCI School of Biological Sciences and director of the UCI Alzheimer's Disease Research Center, a multidisciplinary team of UCI MIND investigators were awarded a five-year, \$14.4 million grant from the National Institutes of Health (NIH) to sustain critical research and education as Orange County's only Alzheimer's Disease Research Center (ADRC). The NIH funds only 32 of these centers at major medical institutions across the United States.

This marks the eighth time that UCI MIND has earned the competitive five-year award

from the NIH. UCI was one of the original five centers funded by the NIH, initially in a combined center with USC. Founding director Carl Cotman, PhD led the effort at UCI, including its transition to an independent center in 2000. Dr. LaFerla took the reins in 2009 and has overseen major growth of the ADRC in the past 10 years. This growth includes the recent award. The new NIH grant funds 10 collaborative "cores", each with a unique focus and led by a different UCI MIND faculty member (above). Three new cores were added in the current cycle, a biomarker core and two special populations cores, reinforcing UCI's longstanding leadership in

research with people with Down syndrome and people age 90 years and older. The new grant will also signal the start of a new research education component, which aims to train the next generation of researchers and clinicians through novel programs.

"Our research team brings passionate and novel cross-disciplinary approaches to try to solve this insidious disease. We collaborate with colleagues across the nation, and we provide critical resources to the community," said Dean LaFerla.

UCI MIND Faculty Members

Anatomy & Neurobiology

Aileen Anderson, PhD
Tallie Baram, MD, PhD
Christine Gall, PhD, Chair
Alan Goldin, MD, PhD
Kei Igarashi, PhD
Gary Lynch, PhD
Steven Schreiber, MD
John Weiss, MD, PhD
Xiangmin Xu, PhD

Biomedical Engineering

Gregory Brewer, PhD

Chemistry

James Nowick, PhD

Developmental & Cell Biology

Ali Mortazavi, PhD
Diane O'Dowd, PhD

Epidemiology

Maria Corrada, ScD
Karen Edwards, PhD, Chair
Daniel Gillen, PhD

Medicine

Masashi Kitazawa, PhD
Steven Tam, MD

Microbiology & Molecular Genetics

Emiliana Borrelli, PhD
Alan Goldin, MD, PhD

Molecular Biology & Biochemistry

Charles Glabe, PhD
Andrea Tenner, PhD

Neurobiology & Behavior

Mathew Blurton-Jones, PhD
Jorge Busciglio, PhD
Carl Cotman, PhD
Christine Gall, PhD
Kim Green, PhD
Joshua Grill, PhD
Claudia Kawas, MD
Frank LaFerla, PhD, Dean
Michael Leon, PhD
Craig Stark, PhD
Vivek Swarup, PhD
Leslie Thompson, PhD
Marcelo Wood, PhD, Chair
Michael Yassa, PhD

Neurology

Tallie Baram, MD, PhD
Maria Corrada, ScD
Carl Cotman, PhD
David Cribbs, PhD
Mark Fisher, MD
Lisa Flanagan, PhD

Neurology (continued)

Claire Henchcliffe, MD, DPhil, Chair
Claudia Kawas, MD
Albert La Spada, MD, PhD
Ira Lott, MD
Mark Mapstone, PhD
Tahseen Mozaffar, MD
S. Ahmad Sajjadi, MD, PhD
Steven Schreiber, MD
Gaby Thai, MD
John Weiss, MD, PhD
Michael Yassa, PhD

Pathology & Laboratory Medicine

Elizabeth Head, PhD
Ronald Kim, MD
Albert La Spada, MD, PhD
Edwin Monuki, MD, PhD, Chair
Mari Perez-Rosendahl, MD

Pediatrics

Tallie Baram, MD, PhD
Virginia Kimonis, MD
Ira Lott, MD
Andre Obenaus, PhD

Pharmaceutical Sciences

Emiliana Borrelli, PhD

Physical Medicine & Rehabilitation

Aileen Anderson, PhD
Brian Cummings, PhD

Physiology & Biophysics

Kevin Beier, PhD
Alan Goldin, MD, PhD

Psychiatry & Human Behavior

Ruth Benca, MD, PhD, Chair
Joshua Grill, PhD
Gary Lynch, PhD
Bryce Mander, PhD
Joan Steffan, PhD
David Sultzer, MD
Leslie Thompson, PhD
Michael Yassa, PhD

Psychological Science

Daniel Nation, PhD

Radiation Oncology

Charles Limoli, PhD

Statistics

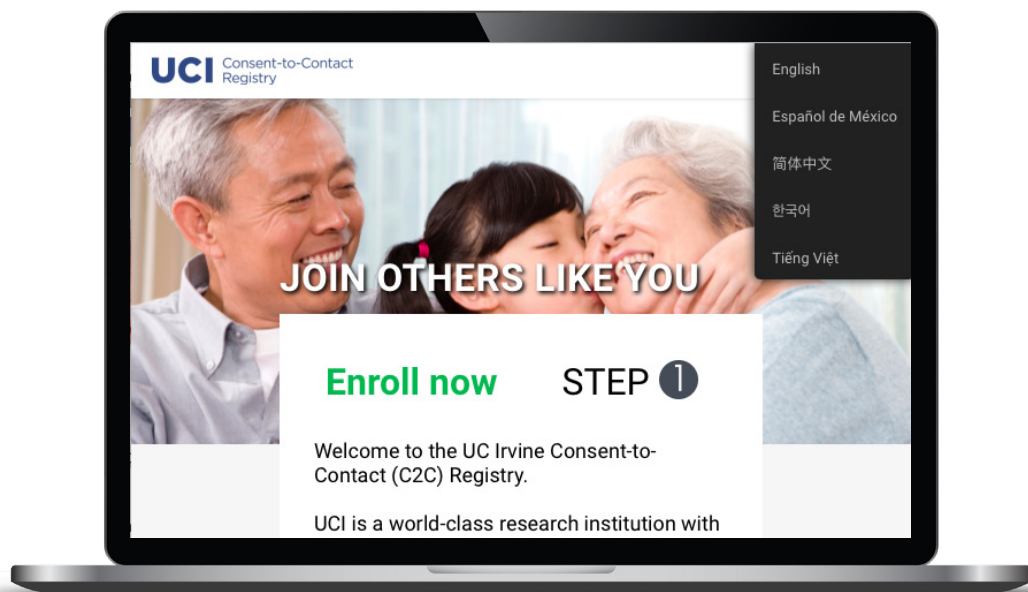
Daniel Gillen, PhD, Chair
Bin Nan, PhD



Excellence through Research

Built on a legacy of scientific excellence, UCI MIND continues its innovative and cutting-edge research to find solutions for Alzheimer's disease and related disorders.

Diversity in Research Participation



The UCI C2C Registry (left) and the new statewide registry, CARE (right), are now live in multiple languages.

UCI MIND is dedicated to increasing diversity in research studies to better represent all people affected by Alzheimer's disease and related dementias (ADRD), and Orange County's diverse community creates an opportunity to do so.

In 2016, UCI MIND launched a local recruitment registry – the UCI Consent-to-Contact (C2C) Registry – to raise awareness of research participation opportunities at UCI (c2c.uci.edu). In fall 2020, the UCI C2C went live in Spanish, Korean, Mandarin, and Vietnamese to allow more people to

access this online tool. Additionally, in partnership with UCSF, UC Davis and Asian Americans and Pacific Islanders (AAPI) advocacy organizations, UCI MIND is now participating in a new statewide registry – the Collaborative Approach for AAPI Research and Education (CARE) – to support representation of AAPI in aging research (careregistry.ucsf.edu).

Also in partnership with UC Davis and the Northern California Kaiser Division of Research, UCI investigators are helping establish a one-of-a-kind multi-ethnic cohort

of individuals age 90 and older, called Life After 90, which will redefine our knowledge of dementia and brain pathology in the oldest-old.

UCI MIND continues to partner with the Korean-American community organization Somang Society, an Asian American Community Advisory Board to increase participation in our longitudinal cohort study, and our newly-formed Hispanic Advisory Board is seeking new members.

New Global Multicenter Clinical Trial

AHEAD STUDY

Worldwide, nearly 50 million people have dementia and the cases are expected to triple in the coming decades unless researchers discover effective preventions or disease-delaying therapies. With this backdrop, UCI MIND, as a member of the NIH-funded Alzheimer's Clinical Trials Consortium (ACTC), is launching a new trial in preclinical Alzheimer's disease—a proposed stage of disease that comes before memory problems begin.

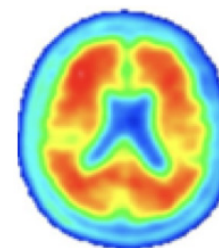
The AHEAD 3-45 Study is a global multicenter clinical trial aimed at preventing memory loss due to Alzheimer's disease. The study, designed and conducted by ACTC, is funded through a public-private partnership with the National Institute on Aging, Eisai, and several philanthropic organizations. As one of approximately 100 sites worldwide

selected to conduct the study, UCI MIND will enroll cognitively healthy adults ages 55-80 who have evidence of brain beta amyloid to test whether an investigational drug called BAN2401 can prevent the onset of memory problems due to Alzheimer's disease. This four-year clinical trial is unique in its design in that it will enroll two types of participants: those with elevated levels of amyloid and those with slightly lower intermediate levels of amyloid as evidenced by a positron emission tomography (PET) scan.

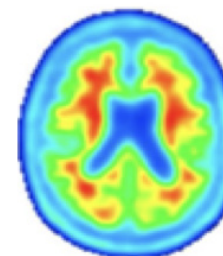
Volunteer participation in these trials is critical. A major emphasis in the AHEAD Study is to enroll a diverse population that is representative of the nation and of Alzheimer's disease—which affects every racial and ethnic group.

Amyloid PET scans measure the levels of amyloid plaque in the brain. The top image is taken before the participant has started the investigational treatment. The image on the bottom is taken after 18 months of investigational treatment, indicating a reduction of amyloid plaque burden in the brain.

Pre-Investigational Treatment



Post-Investigational Treatment



Alzheimer's Biomarker Consortium for Down Syndrome



(from left) Elizabeth Head, PhD, research participant Jeremy Throckmorton, Ira Lott, MD, and Eric Doran, MS

People with Down syndrome are at very high risk for Alzheimer's disease as their extra copy of chromosome 21 leads to accelerated amyloid buildup with aging.

Though many people with Down syndrome do develop symptoms of dementia by mid-life, some avoid the devastating consequences despite having plaques in their brains.

To learn more about the Down syndrome and Alzheimer's disease connection, UCI MIND researchers Elizabeth Head, PhD, and Mark Mapstone, PhD, are leading a major international research effort to follow

hundreds of adults with the syndrome (ages 25+) and their siblings over the next five years.

Funded by a \$109 million grant from the National Institutes of Health, the multisite Alzheimer's Biomarkers Consortium — Down Syndrome (ABC-DS) will focus on identifying biomarkers of Alzheimer's disease. The project will build on the groundbreaking work of Ira T. Lott, MD, and Eric Doran, who had the foresight to include people with Down syndrome in our Alzheimer's Disease Research Center decades ago.

Although ABC-DS focuses on people with Down syndrome, Head believes the study will have broader implications:

"The goal is to come up with a set of biomarkers to not only diagnose and help families prepare for the future, but also to develop outcome measures that could be used in clinical trials of potential new treatments," Head said.

This article was excerpted from the winter 2021 issue of the UCI Health magazine, Live Well. View the full article at ucihealth.org/abc-ds

UCI MIND WAM Women's Initiative



(from left) Alisha Ballard, Mathew Blurton-Jones, PhD, Anshu Agrawal, PhD, Maria Shriver, Sunil Gandhi, PhD, and Joshua Grill, PhD

In 2017, Maria Shriver's Women's Alzheimer's Movement (WAM), which is committed to helping researchers discover why two out of every three people with Alzheimer's disease are women, and UCI MIND announced a funding initiative to encourage top UCI scientists from multi-disciplinary areas to study sex and gender disparities in Alzheimer's disease. The goal of the Initiative, supported and sustained through philanthropy, is to fund at least one grant each year to accelerate this critical area of research at UCI MIND.

Since launch:

- The inaugural \$100,000 grant awarded to Mathew Blurton-Jones, PhD and Sunil Gandhi, PhD from the UCI School of Biological Sciences, resulted in \$1.9 million funding from the National Institutes of Health to continue their exploration of sex differences in the brain's immune cells.
- A second \$100,000 grant was awarded to Anshu Agrawal, PhD from the UCI School of Medicine to examine how sex affects inflammation and immunity in Alzheimer's disease.
- The Living Legacy Foundation, led by Vice President and Executive Director Alisha Ballard, committed \$250,000 to help sustain the Initiative.
- The Living Legacy donation supported two grants in 2020 awarded to Liz Chrastil, PhD from the UCI School of Biological Sciences, and Sara Mednick, PhD from the UCI School of Social Sciences. Dr. Chrastil will investigate the role of sex and hormones in age-related brain changes using novel imaging tools, and Dr. Mednick will investigate the role of sex and hormones in the brain's ability to facilitate memory consolidation during sleep.



Excellence through Education

UCI MIND serves as an expert source for community education and training of future scientists and clinicians.

The Power of Partnership



Brethren Community Foundation Board of Directors with Harriet Harris (center)

The Brethren Community Foundation supports youth education and senior health through philanthropic grants to non-profit organizations and individuals of all backgrounds in need of financial assistance.

As a non-profit organization seeking to improve senior health through research and education, Foundation board member Harriet Harris identified UCI MIND as a natural partner. Since Harriet facilitated the partnership in 2018, the Brethren Community Foundation has contributed \$500,000 to research and training at UCI MIND. With its dual focus on education, the Foundation took a special interest in supporting fellowships for new clinician investigators focused on senior health.

So far, the partnership has resulted in the recruitment of two neuropsychologist fellows, Jean Ho, PhD and Jung Jang, PhD to train with renowned UCI MIND investigator, Daniel Nation, PhD from the UCI School of Social Ecology. Dr. Ho's research focuses on the link between blood pressure medication use in older adults and potential cognitive benefits, which may have implications to future dementia prevention. As a UCI MIND fellow, Dr. Jang's research aims to improve understanding of how vascular damage to the brain may contribute to the understudied emotional and behavioral symptoms associated with dementia, hopefully providing insights to potential new assessments and treatments for dementia.

Together, community leaders and UCI MIND can and will solve Alzheimer's disease and related dementias and improve circumstances for future generations.



Mentored by Dr. Daniel Nation (center), Drs. Jean Ho (left) and Jung Jang (right) were awarded UCI MIND Fellowships supported by the Brethren Community Foundation.

Promoting Diverse Leadership in Clinical Trials



The inaugural IMPACT-AD class attended a week-long training course via Zoom in September 2020

UCI MIND, along with experts from across the country, launched a unique and comprehensive course last fall to educate and diversify the next generation of leaders in clinical trials for Alzheimer's disease and related dementias. The program, called IMPACT-AD, is co-directed by UCI MIND director Joshua Grill, PhD and Rema Raman, PhD, director of biostatistics at the USC Alzheimer's Therapeutic Research Institute. The purpose of the course, Dr. Raman said, "is to make the clinical trials' workforce as

diverse and representative as the participants we hope to recruit for our studies." Out of more than 100 applicants, 35 were selected for the inaugural course, held virtually this past September. The group included medical doctors, nurses, public health professionals, study coordinators and other scientists as well as postdoctoral researchers and research fellows from universities and health care systems across the country. Seventy percent were women and 40% self-identified as persons of color; one-fifth of the cohort were

the first in their families to earn advanced degrees.

Said Dr. Grill, "With this new program, we really want to invigorate the field by engaging trainees at many levels, from many backgrounds, with different personal experiences and demographics as well, because we wholeheartedly believe in team science and the diversity of ideas will move the field forward."

RAMP-ing Up Alzheimer's Training for Medical Students



HFC founders, Lauren Miller Rogen and Seth Rogen virtually congratulated UCI MIND RAMP inaugural trainees

In partnership with UCI School of Medicine, UCI MIND launched a new Research And Mentorship Program (RAMP) for medical students in summer of 2020.

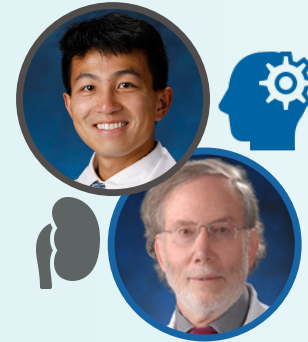
The program, made possible by support from community philanthropist Dr. Lorna Carlin and the nonprofit HFC led by Seth Rogen and Lauren Miller Rogen, pairs medical students with UCI MIND faculty mentors to inspire scientific ideas and future careers in dementia research and care.

As the field presently grapples with a serious shortage of geriatric healthcare professionals, this

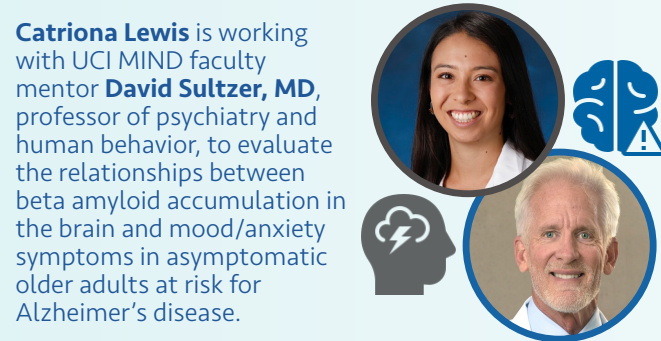
program aims to create a pipeline of enthusiastic trainees who, motivated by their experiences and mentorship, choose medical careers to advance knowledge and care for older adults.

Three talented students were selected for the inaugural summer program and projects are underway.

The students will present their projects to colleagues at the conclusion of the program and have the opportunity to publish results in peer-reviewed journals to be shared with Alzheimer's and dementia researchers worldwide.



Eric Han is working with UCI MIND faculty mentor **Mark Fisher, MD**, professor of neurology, to study the relationship between cognitive decline, cerebral microvascular disease, and uremic toxins (compounds usually filtered and excreted by the kidneys) among patients with chronic kidney disease.



Catriona Lewis is working with UCI MIND faculty mentor **David Sultzer, MD**, professor of psychiatry and human behavior, to evaluate the relationships between beta amyloid accumulation in the brain and mood/anxiety symptoms in asymptomatic older adults at risk for Alzheimer's disease.



Raumin Neville is working with UCI MIND faculty mentor **Claudia Kawas, MD**, professor of neurology and neurobiology and behavior, to study the relationship between cognitive functioning and neuropathology among people aged 100 and older, or centenarians.

First-Ever Virtual Community Research Conference

September 10, 2020

8 AM - 12 PM

FREE Virtual Event

31st Annual SoCal Alzheimer's
Disease Research Conference

tackling **DEMENTIA**
with **TECHNOLOGY**

UCI MIND

Alzheimer's
ORANGE COUNTY

Smart homes. Video games. Artificial intelligence.

The conference theme for 2020, "Tackling Dementia with Technology," became all the more appropriate as COVID-19 transformed the landscape of educational events. UCI MIND, in partnership with Alzheimer's Orange County, was ready to adapt and transitioned the 31st annual event to a free and accessible online format.

The online presentations reached over 1,000 healthcare providers, senior/ social service providers, researchers, students, patients and families around the world via Facebook and YouTube LIVE.

Viewers learned how new technologies are being used to accelerate science and care for Alzheimer's disease and related dementias. International experts each spoke on innovative technologies for 30 minutes, followed by 10 minutes of live Q&A.

Those who may have faced barriers with in-person events due to cost or location were now able to attend from the comfort of their home on their own schedule. In a year where so many faced financial hardships, this first-ever virtual no-cost event was made possible with support from sponsoring organizations and generous donors.

SLEEP GADGETS



RUTH BENCA, MD, PHD
University of California, Irvine

COMPUTERIZED COGNITIVE TESTING



DORENE RENTZ, PSYD
Harvard Medical School

GAMING FOR BRAIN TRAINING



CRAIG STARK, PHD
University of California, Irvine

AI @ AUTOPSY



EDWIN MONUKI, MD, PHD
University of California, Irvine

SMART TECH FOR IN-HOME CARE



ALEX MIHAILIDIS, PHD, PENG
University of Toronto, Canada

A December to Remember Gala Goes Virtual



Music, magic, and memories **FOR ALZHEIMER'S RESEARCH** **SATURDAY, DECEMBER 5, 2020**

UCI MIND's *A December to Remember Gala* on December 5, 2020, exceeded expectations in every way. The event took place virtually for the very first time amid the COVID-19 pandemic, reaching over 850 viewers.

Motivated by personal stories, world-class entertainers, and enticing auction items, donors gave over \$300,000 toward UCI MIND's vision to rid the world of Alzheimer's disease and related dementias.

"Not only did viewers offer UCI MIND an overwhelming amount of support through their donations, they also offered rave reviews of the broadcast," said Chair of the Gala Committee, Virginia Naeve. "It was an honor to work with such dedicated committee members who helped produce a powerful virtual event benefiting such an important cause."

Honoring the Retirement of Dr. Malcolm Dick



Dr. Malcolm Dick with a research participant

After 36 years of research, mentorship, and service, UCI MIND bids a grateful farewell to senior neuropsychologist, Malcolm Dick, PhD, who entered retirement in summer 2020. During his tenure with UCI MIND, Dr. Dick conducted neuropsychological and cognitive assessments with over 10,000 participants as part of the Alzheimer's Disease Research Center longitudinal study and the California Alzheimer's Disease Center program. Patients and families have long revered Dr. Dick for his professional, compassionate nature when delivering challenging diagnoses.

His colleagues and over 80 psychology trainees have equally admired his mentorship in providing unparalleled attention and care to each participant with whom he interacted.

Although he began retirement, Dr. Dick has selflessly volunteered to see UCI MIND through the current challenges associated with the COVID-19 pandemic, and to aid the transition to two new neuropsychologists, Maria Corona, PhD and Michelle McDonnell, PhD, who started with UCI MIND in the early fall.

Dr. Dick's dedication to participants, families, and trainees has contributed significantly to the continued success of UCI MIND over the past three decades.



Maria Corona, PhD (left) and Michelle McDonnell, PhD (right)



Thank You

**On behalf of the entire UCI MIND team,
thank you for this opportunity to share our work with you.**

For questions or more information, please contact:



Danny Harper
Senior Director of Development, UCI MIND
2656 Biological Sciences III
Irvine, CA 92697-4545

949.824.3793 office
714.369.7283 cell
ddharper@uci.edu
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