UCI MOND Institute for Memory Impairments and Neurological Disorders

MIND Matters

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SPECIAL FEATURE

IN THIS ISSUE

Dr. Ira Lott receives prestigious Montserrat Trueta Award

Progress toward blood tests for Alzheimer's disease detection

Early findings on LATE

Cortical thickness: a predictor of cognitive performance

Welcome Cherry Justice

The UCI MIND training pipeline

UCI MIND DuPont-Carlson Award & 2021 UCI MIND Award

Dr. Ira Lott receives prestigious Montserrat Trueta Award

On Monday February 7th, the General Secretary of the Trisomy 21 Research Society (T21RS) announced that UCI MIND's Dr. Ira Lott has been awarded with the T21RS Montserrat Trueta Award for his outstanding career in Down syndrome research.

This endowed award is named for one of the founders of the European Down Syndrome Association, who spent her life fighting for the rights of people with Down syndrome. This makes the award a fitting tribute to Dr. Lott, who has spent his entire career conducting critical research on this topic and serving as a leading voice in the field.

Among many career highlights, Dr. Lott has led the field in research to understand the clinical presentation of Alzheimer's disease in people with Down syndrome and performed several clinical trials of compounds to treat Alzheimer's disease in this important population. Furthermore, he has published numerous papers elucidating the biological changes in the brains of people with Down syndrome and Alzheimer's disease. As the awardee, Dr. Lott will be the plenary speaker in the next T21RS International Conference to be held in June in Long Beach.



Dear Friends of UCI MIND,

The COVID-19 surge caused by the Omicron variant has produced unwanted challenges for our research. Yet, our investigators remain unrelenting and highly successful in their work. Dr. Ira Lott received the international Trisomy 21 Research Society Montserrat Trueta Award (p. 1). Dr. Claudia Kawas received the UCI Senate Better World Award (p. 5). We honored Bob and Virginia Naeve with our UCI MIND Award, though we were unable to hold our A December to Remember Gala, to deliver it with the pomp and circumstance they deserve (p. 7). Cherry Justice has joined UCI MIND (p. 5) to lead efforts on the 2022 Gala and all other fundraising. With the philanthropic support of Jacque DuPont and Marc Carlson, we have established a new award to allow UCI MIND trainees to travel to scientific conferences (p. 7). Training the next generation of clinicians and scientists remains key to our mission (p. 6). The work of UCI MIND and the work of the field continues to advance. Page 3 highlights progress in blood biomarkers. We are excited about the opportunities to engage in innovative work in this area, due to new technologies

For the latest news, stories, and resources, visit www.mind.uci.edu/blog

brought to campus under the leadership of Drs. Elizabeth Head and Ed Monuki. Combined with our large catalog of clinical data and our remarkable brain bank, these tools could yield new insights into the earliest signs of Alzheimer's disease, as well as other brain conditions such as LATE (p. 4).

Finally, since our last newsletter, the Centers for Medicare & Medicaid Services (CMS) announced their decision to cover monoclonal antibodies against the beta amyloid protein, such as Aduhelm, only in the setting of randomized controlled trials. This was the latest in the series of controversies surrounding this drug. Our UCI MIND Blog will be used to continue to provide updates as these and other important events unfold in the mission to discover solutions for Alzheimer's disease and related dementias.



Joshua D. Grill, PhD Director, UCI MIND

Faculty members

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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

Xiaoyu Shi, PhD

Developmental & Cell Biology

Edwin Monuki, MD, PhD Ali Mortazavi, PhD Diane O'Dowd, PhD Xiaoyu Shi, PhD

Epidemiology

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

Medicine

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Microbiology & Molecular Genetics Emiliana Borrelli, PhD Alan Goldin, MD, PhD

Molecular Biology & Biochemistry Charles Glabe, PhD Andrea Tenner, PhD

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Pathology & Laboratory Medicine

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Pediatrics

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Physical Medicine & Rehabilitation Aileen Anderson, PhD Brian Cummings, PhD

Physiology & Biophysics Kevin Beier, PhD Alan Goldin, MD, PhD

Psychiatry & Human Behavior

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Psychological Science Daniel Nation, PhD

Radiation Oncology Charles Limoli, PhD

Statistics Daniel Gillen, PhD, Chair Bin Nan, PhD

Progress toward blood tests for Alzheimer's disease detection

What is a biomarker? A biomarker is a clinical characteristic indicating a normal or abnormal biological process. Biomarkers may measure health and risk for disease (cholesterol and blood pressure), presence of disease (e.g., some genetic tests), or response to treatment (e.g., tumor size in cancer or viral loads in HIV).

The diagnosis of definite Alzheimer's disease (AD) is made when autopsy confirms the pathology of plaques and tangles. Major research advances in the field of biomarker discovery have given rise to new methods for detecting whether a person has plaques and tangles in their brain while they are still alive. Positron Emission Tomography (PET) scans can measure amyloid plaques or tau neurofibrillary tangles in the brain. Measuring proteins associated with plaques and tangles in the cerebrospinal fluid (CSF) can also give strong evidence to support AD as the cause of cognitive problems.

While CSF and PET biomarkers play important roles in research and can be valuable tools in the clinical setting, the holy grail of biomarker research would be to have a blood test for AD. Blood biomarkers have developed quickly in the past few years with one test, called PrecivityAD[™] made by C2N Diagnostics, now available for clinical use. The test measures the ratio of two amyloid proteins in the blood and relies on additional information related to age and APOE status to come up with a risk value to help doctors determine the likelihood that amyloid plagues are present in the brain. The test is also being used to accelerate recruitment to a large clinical trial called the AHEAD Study (aheadstudy.org), which is happening now at UCI MIND. In this trial, the test is used differently, mainly to rule out people who are unlikely to qualify based on screening amyloid PET scans. PrecivityAD[™] is undoubtedly a huge step forward in the development of diagnostic blood tests, but it isn't perfect. PrecivityAD[™] should be used only by expert clinicians in the evaluation of patients with cognitive impairment and dementia—it is a tool for their use, not a replacement for the diagnostic work up. On its own, the test cannot be used to determine whether AD pathology is present as it can produce uncertain results and has a relatively high false positive rate. It also has costs (\$1250) and is not currently covered by insurance. Finally, it has not been studied in diverse populations, so our understanding of what the results mean in Hispanics and non-White races is limited.



Work at UCI MIND aims to develop research in blood further. Under the leadership of Drs. Elizabeth Head and Ed Monuki, UCI MIND has brought new state of the art systems to campus to analyze blood and CSF samples provided by participants in the longitudinal study performed in the Alzheimer's Disease Research Center. Dr. Mark Mapstone, Professor and Vice Chair of Research in the Department of Neurology and a UCI MIND faculty member, has spent several years researching blood-based biomarkers. Dr. Mapstone uses an 'omics' approach to biomarker discovery, where he and his colleagues look for patterns of molecules that he hypothesizes are involved in the early changes associated with AD. His promising work is ongoing and has recently yielded interesting results in studies of Alzheimer's disease in people with Down syndrome.

To read about their research, visit: mind.uci.edu/cortex

Cortical thickness: a predictor of cognitive performance

Two graduate students in Dr. Craig Stark's lab, Elena Dominguez (Neurobiology and Behavior) and Yueqi Ren (Mathematical, Computational and Systems Biology) in collaboration with Drs. Claudia Kawas and Maria Corrada recently published a paper in *Frontiers in Aging Neuroscience* examining the relationship between regional and whole brain cortical thickness and superior thinking skills in older adults. Using magnetic resonance imaging (MRI) data from the 90+ Study and the National Alzheimer's Coordinating Center, to which the UCI MIND Alzheimer's Disease Research Center contributes data, the team found that greater whole brain cortical thickness was associated with better "top cognitive performance" (individuals performing significantly better than



expected for their age) in adults ages 70 years and older. These results challenge previous assumptions that the thickness of one brain region, the cingulate cortex, a portion of the cerebral cortex responsible for linking emotional and analytic processes, is most strongly related to "top" cognition. This paper exemplifies the innovative and collaborative spirit of UCI MIND and highlights the utilization of data provided by our invaluable research participants across multiple studies.

Did you know? The cerebral cortex is an outermost layer of the brain that is broadly responsible for our higher-level thinking and is characterized by a dense concentration of neurons.

Early findings on LATE



Limbic-Predominant Age-related TDP-43 Encephalopathy, or LATE, as it is more commonly known, is a recently described brain disease that affects people primarily in their 80's and 90's and has a clinical presentation similar to Alzheimer's

disease. LATE pathology, which currently can only be identified at autopsy, is estimated to be present in the brains of up to 25% of people over the age of 80 years and is often accompanied by other deleterious brain changes. Unlike Alzheimer's disease, LATE does not show the hallmark features of amyloid plaques or tau neurofibrillary tangles in their brain. The clinical symptoms caused by LATE are thought to result from

misfolding of another type of protein called TDP-43, which is also involved in some Frontotemporal Lobar Dementias and other neurodegenerative diseases like ALS. LATE was first described in 2019 so research on the disease is still very limited. UCI MIND faculty member and Assistant Professor of Neurology, Ahmad Sajjadi, MD, PhD, studies LATE in his laboratory and is learning more about this enigmatic disease. Dr. Sajjadi's research involves identifying fluid biomarkers in plasma and CSF, of which there are currently none for LATE, and understanding how symptoms of LATE differ from other forms of dementia. His lab's research relies heavily on clinical data and brain tissue collected from participants enrolled in the ADRC longitudinal cohort and the 90+ Study.

Welcome Cherry Justice

We are delighted to welcome Ms. Cherry Justice to the UCI MIND team as Executive Director of Development. Cherry is an experienced fundraiser who has been leading local, regional, and national campaigns for over 12 years, raising critical funds to support research, program growth, and capital expansions.

Prior to joining UCI, Cherry was a leader at Verity Health System, Autism Speaks, and Grady Health System. At Grady she served as a lead fundraiser and worked to complete their \$325M capital campaign that reached its goal 12 months ahead of schedule.



She has also served as a consultant, working to support specific projects focused on reducing health disparities in communities of color.

Cherry's non-profit commitment extends to her work with other organizations, where she has been a Primary and Secondary Education mentor for National Cares Mentoring Movement, a member of Healthcare Businesswomen's Association and a proud member of Alpha Kappa Alpha Sorority Inc. Cherry is a North Carolina native, where she received her bachelor's and master's degrees from Winston-Salem State University.



Dr. Claudia Kawas, a Professor of Neurology and co-principal investigator for the 90+ Study, was recently recognized with the **2021-2022 UCI Distinguished Faculty, Academic Senate Better World Award** for her efforts to improve the human condition through research.

Thank you to our donors

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The UCI MIND training pipeline

As the nation grapples with an aging population and the knowledge that Alzheimer's disease and other dementias will skyrocket in prevalence and burden over the coming years, training the next generation of dementia scientists and clinicians is a critical mission for UCI MIND. Partnering with donors like Dr. Lorna Carlin and the Beall and Harris families and organizations like HFC and the Brethren Community Foundation, and aligning this support with highly competitive NIH grants, UCI MIND has built a pipeline of training programs that reach high school and college students, graduate and post-doctoral trainees, and junior faculty and other early career investigators. Each of these programs pairs trainees with world renowned researchers to deliver essential skills and inspire them to become leaders in geriatric health care and neuroscience research.



- The Beall Scholar Program is a summer research experience for rising 12th graders from local high schools. The program consists of neuroscience lectures by faculty, lab tours & handson brain demonstrations, & panel discussions on UCI admissions & future career options.
- 2. Anteater's Against Alzheimer's is an undergraduate course that exposes UCI undergraduates to the public health impact of Alzheimer's Disease & Related Disorders (ADRD) & enlists them in efforts to increase public awareness of ADRD research needs & opportunities.

To learn more about research education at UCI MIND, visit mind.uci.edu/REC

- 3. Research and Education in Memory Impairments and Neurological Disorders (REMIND) is a campus organization led by UCI MIND predoctoral & postdoctoral trainees. It aims to encourage collaboration among the next generation of scientists & clinicians & promote community outreach & education on neurodegenerative diseases.
- Two National Institute on Agingfunded T32 grants support pre & postdoctoral students to study ADRD basic, translational, & clinical research.
- 5. Research and Mentoring Program (RAMP) matches UCI medical students with UCI MIND faculty to conduct novel ADRD research. The program is supported by Dr. Lorna Carlin & HFC, an organization led by Seth Rogen & Lauren Rogen Miller.

6. The Brethren Community Foundation Fellowship

> supports the research of new postdoctoral fellows in clinical research, including neurologists, psychiatrists, neuropsychologists, & neuropathologists.

- 7. The Research and Education Component (REC) of the ADRC is led by Dr. Elizabeth Head & provides foundational training in ADRD research & career nurturing to UCI early career investigators.
- 8. Institute on Methods and Protocols for Advancement of Clinical Trials in ADRD (IMPACT-AD) is

a comprehensive training program for early stage investigators across the nation to gain knowledge about clinical trials for ADRD.

UCI MIND DuPont-Carlson Award



Jacqueline Lehn DuPont, PhD and her husband Mr. Marc Carlson generously donated \$50,000 to support a unique funding opportunity at UC Irvine.

The newly minted UCI MIND DuPont-Carlson Award has been matched by the university to provide a \$100,000 endowment to give UCI MIND predoctoral students the opportunity to attend national and international research conferences. Doing so is an integral part of graduate student training, giving them the chance to present their work and network with colleagues.

Dr. DuPont is an accomplished gerontologist and longtime supporter of UCI MIND. She serves on our Leadership Council, co-chaired the first Gala in 2010 with her husband Marc, and both have contributed to every gala since. They have supported many endeavors including a campaign to recruit faculty members like Dr. Vivek Swarup. UCI MIND is grateful to these champions for their recent and sustained generosity.

2021 UCI MIND Award

Each year UCI MIND identifies an individual or individuals whose actions particularly exemplify our mission to improve the lives of people with Alzheimer's disease.

In December, we recognized Bob and Virginia Naeve with the 2021 UCI MIND Award. Virginia first became aware of UCI MIND in 2011 as a result of caring for her mother who had Alzheimer's disease. In the years since, she and Bob have partnered with UCI MIND time and time again to support our cause.

Aside from their consistent philanthropic contributions, they have hosted the Wine for the MIND event at their beautiful home. In addition, Virginia serves as a vital member of our Leadership Council and has planned several of our annual *A December to Remember* Galas, which she and Bob co-chaired in 2017. She is also one of the co-hosts and producers of Spotlight on Care, UCI MIND's successful podcast on dementia caregiving. The Naeve's are tireless advocates for the cause of Alzheimer's research and worthy recipients of the 2021 UCI MIND Award.



UCI MOND

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National Institute on Aging Designated Alzheimer's Disease Research Center

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Giving Opportunities 949.824.3251 Lscheck@uci.edu **Research Participation** 949.824.0008 research@mind.uci.edu



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UPCOMING EVENTS

Save the date! Dementia across the lifespan

33rd Annual SoCal Alzheimer's Research Conference Friday, September 9, 2022 | conference.mind.uci.edu

Save the date!

A December to Remember 12th Annual UCI MIND Gala

Saturday, December 3, 2022 | gala.mind.uci.edu

Ask the Doc Video Series Guest Experts from UCI MIND

New Episodes Monthly UCI MINDcast | mind.uci.edu/mindcast

Spotlight on Care Podcast Series Steve O'Leary, Virginia Naeve, & Guests

New Episodes Regularly UCI MINDcast | mind.uci.edu/mindcast

Past education sessions are archived on UCI MINDcast and youtube.com/ucimind