

MIND Matters



SPECIAL TRIBUTE: CARL COTMAN

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On August 5th, the founding Director of UCI MIND, Carl Cotman, PhD, passed away. An absolute giant in the fields of aging and age-related brain disease research, Professor Cotman wrote or co-wrote eleven books and authored nearly 800 articles on multiple facets of neuroscience. He established the UCI Alzheimer's Disease Research Center (ADRC). Initially funded as a partnership between UCI and USC, Dr. Cotman and Dr. Tuck Finch of USC were awarded one of the 5 initial centers funded by the National Institute on Aging. The UCI ADRC has now been continuously funded for 40 years, built on the foundation laid by Dr. Cotman.

Professor Cotman's body of work resulted in numerous honors. He was the recipient of the Alzheimer's Association International Conference's Lifetime Achievement Award in Alzheimer's Disease Research and the National Institute on Aging Leadership and Excellence in Alzheimer's Disease Award. Other recognitions included the Council on Aging and Adult Development's Herbert deVries Research Award; ISI Highly Cited Researchers; and Co-Recipient, Reeve-Irvine Research Medal.

He received the 2004 UCI Medal for dedication in research, teaching and community service.

In 2003, three and a half decades into his storied career, the journal *Neurochemical Research* dedicated an entire edition to Dr. Cotman and his work. It was filled with articles by his peers, including former students. One author observed that "[his] enthusiasm for science and his ability to transfer this enthusiasm to his co-workers, his willingness to take risks, openness to fresh ideas, and that he was ahead of the curve: a distinguished basic neuroscientist pushing the translational envelope before doing so became popular".



Dr. Cotman (left) with Carla Liggett (middle) and Boyd Steele

Dr. Cotman's legacy will reverberate for generations. His scientific impact on the field is unquestioned. Through strategic vision, creativity, and remarkable mentorship

and leadership, he also built a world class organization at UCI. ■

Dear Friends of **UCI MIND**,

This summer, we lost our founder, Dr. Carl Cotman. Under Dr. Cotman's leadership, UCI became an independent ADRC in 2000. He recruited many of UCI's most prominent researchers and leaders, such as David Cribbs, Claudia Kawas, and Frank LaFerla. He also lured UCI researchers into collaborative work on dementia, such as Andrea Tenner, Ira Lott, and Marcelo Wood. He launched the Southern California Alzheimer's Disease Research Conference, now in its 35th year; secured the Neurobiology of Aging NIH training grant, now in its 41st year; and established the UCI ADRC brain bank, which now includes more than 1500 donated brains.

When Dr. Cotman's passing was announced to the ADRC network, the outpouring of respect, fond memories, and reverence was nothing short of astounding. We received nearly 100 public messages honoring his memory, leadership, and impact on the field and many more privately.

Dr. Cotman's legacy at UCI will live on in UCI MIND. We already have one annual award, given to an outstanding trainee—the Carl Cotman Scholar Award. We will look to create other mechanisms to honor Carl in the coming year. His family has asked that those interested to honor his legacy [make a donation](#) to UCI MIND.

All of us at UCI MIND send Carl's family our deepest condolences. His research family is saddened but committed to ensuring Carl's legacy lives on in our important work at UCI MIND.



Joshua D. Grill, PhD
Director, UCI MIND

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EVENT SPOTLIGHT

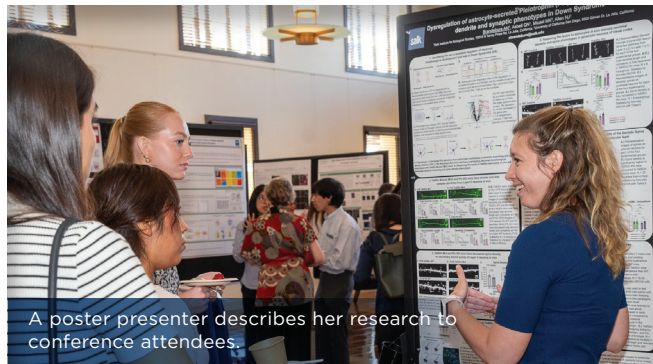


ACCELERATION THROUGH COLLABORATION

Lindsay Hohsfield, PhD, explains the mission of non-profit Youngtimers.

Collaboration propels scientific advancement and the progress we've seen over the past few years in Alzheimer's disease research is a result of decades of collaboration and synergy. Southern California is home to several highly regarded dementia research institutes and every year we gather for the Alzheimer's Disease Centers Collaborative Conference to share what we've learned and build partnerships for future work.

On Friday, June 28th, 2024, our center along with USC, Cedars Sinai, UCLA, and UCSD met at the Beckman Center near UCI for an afternoon symposium consisting of oral and poster presentations, networking opportunities and dinner. One basic scientist and one clinical scientist from each institution delivered talks on their research.



A poster presenter describes her research to conference attendees.

The esteemed, Frank LaFerla, PhD, Dean of the Charlie Dunlop School of Biological Sciences and the co-director of the UCI ADRC presented updates from MODEL-AD, the NIH funded project to create better mouse models of Alzheimer's disease.

The second speaker from UCI, Lindsay Hohsfield, PhD, a research scientist in the Green Lab, spoke about

Youngtimers, a non-profit organization she started to support families affected by Early Onset Familial Alzheimer's Disease.

In addition, 42 early career scientists presented posters from their research during an afternoon break and evening reception. The evening culminated with a networking dinner on the patio of the Beckman Center. ■



Attendees listen intently to a presentation by Dean Frank LaFerla on MODEL-AD.

STAFF SPOTLIGHT

ANDREA WASSERMAN RETIRES



Andrea Wasserman

On June 18th, UCI MIND hosted a retirement celebration for Chief Administrative Officer (CAO) Andrea Wasserman. On the sun filled, second floor terrace of UCI's Susan & Henry Samueli College of Health Sciences, faculty, staff, friends and family gathered to pay tribute to Andrea's amazing 36-year career at UCI MIND.

Andrea joined UCI in 1988 as a lab technician under the supervision of Dr. Carl Cotman. From there, she ascended to Lab Manager and then overseeing tissue procurement at the UCI MIND brain bank. She reluctantly took on the role of

CAO fourteen years ago, but quickly became the heart and soul of the entire organization.

During the celebration, numerous faculty and staff alike spoke about Andrea's unwavering commitment to UCI MIND. Dr. Joshua Grill offered that, "no single person deserves more credit for the success of UCI MIND than does Andrea Wasserman."

Frank LaFerla, PhD, the Dr. Lionel and Fay Ng Dean and Distinguished Professor, Charlie Dunlop School of Biological Sciences, who has worked with Andrea for decades says, "Andrea is an extraordinary individual whose dedication, exceptional work ethic, and kindness have made her truly irreplaceable. Her hard work and warmth have brightened every day, and her presence will be greatly missed. UCI MIND and the entire university are profoundly better for having had her contributions over the past three decades."

Andrea Wasserman's tenacity, intelligence, humor, and passionate commitment to the advancement of UCI MIND's important work will be greatly missed. We wish her well on her new adventures and endeavors; they are sure to be successful!

UCI SERVICE AWARDS

On June 18th, at the Bren Events Center, three of UCI MIND's key members, **Dan Hoang**, **Shirley Sirivong**, and **Andrea Wasserman**, along with 2501 other UCI employees, were honored with Service Awards for their longtime commitment to our institution. Andrea was awarded for 35 years of service; Dan and Shirley were given awards for 25 years of service.



Andrea Wasserman (left), Dan Hoang (middle), and Shirley Sirivong

Dan began working at UCI in 1997, as a student assistant to Suzanne Flynn, executive assistant to then UCI ADRC Director Carl Cotman. After completing his bachelor's degrees in English and Biological Sciences, he transitioned to full-time computer resource specialist in 1999 in the UCI ADRC. Since August 2022, he has been the IT Director for UCI MIND. When asked what he enjoys about working at UCI MIND, he said, "I enjoy being a part of a group that is dedicated to finding solutions

for Alzheimer's disease and other neurodegenerative disorders. I like working with researchers from different disciplines, backgrounds, and learning from their expertise and perspectives. I also like being the center of all the data workflows because it gives me a sense of responsibility and challenge. I have to ensure that the data is collected, processed, stored, and analyzed in an efficient and accurate way, and that it meets the needs for current and future scientific research."

Shirley was hired as a part-time student administrative assistant in 1994. In 1999 she was hired full-time as a data analyst and patient care coordinator in the ADRC. In 2001, she became the clinic manager, in addition to also serving as education coordinator, later becoming the community outreach manager. Since 2015, she has been the ADRC Manager of Clinical Research Operations.

In Shirley's words, her favorite part of working for UCI MIND is "interacting with research participants and their loved ones who entrust us to partner with them to learn more about themselves and to contribute to critical research studies. It is also immensely gratifying to work with dedicated, committed, hard-working, and like-minded individuals at UCI MIND who want to help make a difference."

EVENT SPOTLIGHT



Drs. Liz Chrastil (4th from left back row) and Liz Head (2nd from right back row) stands with other prominent Alzheimer's researchers and First Lady, Dr. Jill Biden (front left) and Maria Shriver (front right).

UCI MIND HEADS TO WASHINGTON D.C. FOR WOMEN'S HEALTH

On April 24, UCI MIND faculty Drs. Liz Head and Liz Chrastil were invited by Maria Shriver and the Women's Alzheimer's Movement (WAM) at Cleveland Clinic to attend a unique event at the Willard Hotel in Washington, DC. The event featured influential policymakers, health advocates, national media, and a special guest of honor, First Lady Dr. Jill Biden. The event celebrated research funded by WAM toward advancing women's brain health and Alzheimer's

prevention. Drs. Head and Chrastil were funded as part of the innovative UCI MIND WAM Women's Initiative, which is now in its 7th year and will soon fund it's 8th \$100,000 pilot award in this important area of research.



Jonathan and Kim Varenchik stand with Josh Grill at Cinco de MINDo.

CINCO DE MINDO- AN INTERVIEW WITH JONATHAN VARENCHIK

On Saturday, May 4th, at the home of Jonathan and Kim Varenchik, the first Cinco de MINDo event was held. Friends and family gathered for tacos, margaritas, and an informative and inspirational Q&A with Dr. Joshua Grill.

We spoke with Jonathan about his experience with UCI MIND, and his reasons for hosting this event.

What made you decide to start Cinco de MINDo?

My wife and I were trying to come up with ideas on how to donate more family resources to help raise money for Alzheimer's research, so I came up with the idea of coordinating a birthday fundraiser where

family/friends donate money instead of bringing gifts. My birthday is the same week as Cinco de Mayo, and with the assistance of a best friend, we came up with the perfect name of Cinco de MINDo, where all the money raised would be donated to UCI MIND.

Why did you choose UCI MIND over any other organization to donate the money raised for your birthday? What makes UCI MIND so special to you?

We were introduced to UCI MIND about seven years ago, and I immediately connected with the vision and values of Dr. Josh Grill and the mission of the whole UCI MIND organization focusing on Alzheimer's research. I immediately jumped in to volunteer, helped to lead the community outreach committee and have attended most of the annual December Galas. It's just a great group of people with a common mission and I'm always learning something every time I'm around them.

What is the vision for Cinco de MINDo in years to come?

My vision for Cinco de MINDo is to increase participation every year and thus increase our fundraising and education across the Orange County community while supporting our mission at UCI MIND. Eventually, I would love my birthday to take a backseat and have this become a marquee annual UCI MIND fundraising event until we find a cure! ■



On July 2nd, the US Food and Drug Administration granted full clinical [approval](#) to Eli Lilly to market donanemab, brand name Kisunla, for the treatment of early Alzheimer’s disease, including Mild Cognitive Impairment (MCI) or mild dementia. Donanemab is a monoclonal antibody against the beta-amyloid protein that accumulates in the brain of people with Alzheimer’s disease. This represents the second ever full approval for a drug that directly targets the biology of Alzheimer’s disease.

Donanemab was shown in a Phase 2 and then in a Phase 3 trial to have a significant impact on brain amyloid burden. In the Phase 3 trial, more than three-quarters of participants receiving donanemab had their amyloid lowered to “not elevated” levels by the end of the 18-month study. In the trials of donanemab, treatment was stopped once participants achieved this biomarker response to therapy. Accordingly, the FDA-approved label for the medication indicates that physicians may consider stopping treatment once amyloid has been reduced to “minimal levels on amyloid PET imaging.”

Full approval was granted because treatment with donanemab slowed clinical disease progression, compared to placebo, on the study primary outcome as well as all of the key secondary clinical outcomes—affirming its efficacy. Efficacy was greatest in patients who were deemed earliest in disease, defined in the trial using tau PET scans to determine whether participants had low/medium tau burden or fell into a higher tau burden group. That participants were required to have at least low/medium tau to be enrolled in the trials, had produced some conjecture

KISUNLA GETS FDA APPROVAL FOR ALZHEIMER’S DISEASE

about whether an approved label would require a similar requirement in clinical practice. But at a recent [FDA Advisory Panel](#), advisors were largely aligned on concerns that such a requirement would represent an unnecessary barrier to access and could lead to a widening of current healthcare disparities in the treatment of Alzheimer’s disease because of poor access to tau PET imaging in some communities. The approved label only indicates that patients should have the presence of amyloid confirmed prior to beginning therapy; there are no specific requirements on tau PET.

Donanemab joins lecanemab as the only approved disease-targeting therapies for Alzheimer’s disease. Beside the label indication of potentially stopping treatment after amyloid levels have been reduced, donanemab differs from lecanemab in a few other ways. Donanemab is administered through monthly infusions, while lecanemab requires twice-a-month infusions. Both treatments have the same important safety risks, namely Amyloid-Related Imaging Abnormalities (ARIA), which consists of bleeding or swelling in the brain. Because of this safety profile, and because treatment risks are higher in carriers of the e4 allele of the apolipoprotein E (APOE) genotype, the approval for both medications also indicates that [APOE testing](#) should be performed before prescribing. Comparisons of the two treatments’ safety and efficacy results are not appropriate, because differences in the patient populations in the trials are difficult if not impossible to account for. Donanemab has been announced a price of \$32,000 for 1-year, compared to \$26,500 for lecanemab.

Overall, this represents another incredible milestone in the research progress being made in Alzheimer’s disease. Important reminders are warranted, however. These drugs may slow, but do not seem to stop let alone reverse progression of clinical decline. If donanemab treatment is stopped after amyloid has been cleared from the brain, whether or when disease progression resumes is not yet known. ■

TRAINING AND EDUCATION

INSPIRING YOUNG MINDS

While other incoming high school seniors are sleeping-in late and spending their summer at the beach, 16 bright and motivated students from across Orange County participated in the 4th Annual Beall Scholar Program, a weeklong dementia neuroscience course.

Led by the trainee outreach group, Research and Education in Memory Impairments and Neurological Disorders (REMIND) and supported entirely by Joan and Don Beall, the Beall Scholar Program aims to inspire young people from especially underserved communities to pursue careers in geriatric medicine and neurodegenerative disease research. From July 15th to July 19th students learned about a variety of topics from UCI MIND faculty and trainees through lectures about basic neuroscience, frontotemporal degeneration, Parkinson's disease and Alzheimer's disease. They visited labs like Dr. Liz Chrastil's virtual reality suite to learn about how scientists study spatial navigation. They participated in demonstrations to understand, for example, how to measure electrical pulses and arousal in the brain. The program also included visits from several groups on campus to discuss college resources, including financial aid and admissions. The students explored major and career options with scientists, physicians, nurses, counselors and even current and recent undergraduates from schools across the country.

The program culminated with a Clinical Pathology Conference, a review of a case study of an individual who was a participant in the ADRC's Longitudinal Study and was followed to autopsy. Clinical Core leader Dr. David Sultzer, a psychiatrist, and neuropsychologist Dr. Michelle McDonnell reviewed the clinical presentation, Dr. Davis Woodworth, assistant project scientist, presented the available neuroimaging, and MD/PhD candidate, Jeremy Rouanet, presented the participant's neuropathological findings.

The students had the opportunity to weigh in on the final diagnosis before it was revealed and examine the tissue specimens from the case. The program closed with a session featuring family members of people who have or had dementia to better understand the human impact of these diseases.

The generous support from Joan and Don Beall allows UCI MIND and REMIND to host the program free of charge to the students. In fact, transportation, food,

materials, and a stipend are provided to encourage students to apply who may not have otherwise been able to participate. "The Beall Scholar program is vital as it provides students from more disadvantaged backgrounds the opportunity to learn and get involved with neuroscience here at UCI. I say this every year, but it's true, I really wish there was a program like this when I was at the same stage. It provides a service and experience that is unique to UCI and the faculty, staff, students and donors who make it happen," says Claire Butler, PhD, postdoctoral fellow in the Green Lab and REMIND Co-Chair.



Beall Scholars examine a human brain specimen with the UCI MIND Tissue Repository team.



The 2024 Beall Scholar Class flanked by program staff and REMIND Co-Chairs.



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The UCI MIND AD Research Center is supported by the National Institute on Aging (NIA) of the National Institutes of Health (NIH) under award number P30 AG066519.

This newsletter is supported in part by the California Department of Public Health, AD Program. Funding is pursuant to California Health and Safety Code Section 125275 - 125285.

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