WHAT A DIFFERENCE A YEAR MAKES: ADVANCES IN ALZHEIMER’S DISEASE CLINICAL CARE

The last twelve months have seen dramatic and important changes in the clinical practice of caring for people with Alzheimer’s disease (AD). In July, the FDA converted the “accelerated” approval of the monoclonal antibody lecanemab to a traditional full clinical approval. This was the first full approval for a new drug for AD since 2003 and marked a major milestone for the field, built upon decades of research and numerous clinical trials with thousands of research volunteers, all of whom deserve credit in this major advancement.

The full approval, which indicates that lecanemab is a treatment for “early AD” (including patients with Mild Cognitive Impairment and mild dementia), also sparked other major changes to clinical practice. The Centers for Medicare and Medicaid Services (CMS) changed their approach to coverage of anti-amyloid therapies. Lecanemab and aducanumab had both been previously granted accelerated approval but were not covered by CMS unless patients were treated as part of a CMS-approved randomized study. Now, CMS has indicated that they will cover the cost of fully approved anti-amyloid therapies much more broadly for Medicare recipients. Moreover, they have indicated that they will also cover the biomarker tests needed to determine if a patient is appropriate for treatment. This includes amyloid PET imaging that confirms AD is a cause of a person’s cognitive impairment.

They will also cover the costs of MRI scans that are needed to ensure that patients are not experiencing adverse reactions to the treatment. These changes will reshape the experience of many patients receiving a diagnosis of AD, though there remains tremendous work left to do. These treatments slow, but do not stop, disease progression. Understanding the long-term benefits of treatment, beyond the 18 months examined in the clinical trials, will require further study, as will the impact on later stages of disease, when the burden and cost of care become most significant.

Another major milestone came on July 31st when CMS announced that they also would cover dementia care coordination programs. These programs aim to provide families information, resources, and guidance as they navigate the journey of caring for a loved one with dementia.

Together, these advances will transform the clinical practice of caring for people living with cognitive disorders. Yet, more progress is needed to achieve the ultimate goal of treatments that stop, reverse, or prevent AD and other causes of dementia.
Dear Friends of UCI MIND,

We hope you have had an excellent summer and are enjoying fall. As you can see in this newsletter, it has been a busy time at UCI MIND and in the field of AD research. Things are changing for the better for families dealing with AD (page 1). This progress was made possible only because of the diligent work of researchers and contributions of people enrolled in research studies over the last several decades. For more than four decades, this has included UCI MIND founding director, Dr. Carl Cotman, who made substantial research contributions (page 3).

This summer and fall, UCI MIND researchers received new funding (page 4) and awards (page 12) and again shared their progress at the annual Alzheimer’s Association International Conference this year in Amsterdam (page 10). We continued to emphasize education and training (page 10), including our annual Southern California AD Research Conference (page 5) and our Beall Scholar Program to inspire Orange County high schoolers (page 13). Our December to Remember Gala (page 6 and 7) will honor Lauren Miller Rogen and Seth Rogen for their support of this aspect of our mission.

Progress in the field is tangible and exciting, but it does not come without risks (page 11). UCI MIND looks forward to continuing to play leadership roles in making discoveries that move the field forward but also ensuring the responsible and optimal means of introducing new progress into the lives of people affected by age-related brain diseases. As ever, we are grateful for the support of our local community. We know we are all in this fight together.

Joshua D. Grill, PhD  
Director, UCI MIND
The Retirement of Our Founding Director and a Giant in the Field, Carl Cotman, PhD

Dr. Carl W. Cotman, the founding director of UCI MIND, distinguished Professor of Neurology and Neurobiology and Behavior, and a pioneer in the field of aging research was honored on Tuesday, September 12th at the Beckman Center of the National Academies of Science and Engineering in Irvine. Colleagues and proteges, family and friends gathered with Dr. Cotman to share stories about the famed scientist’s long and storied career.

Dr. Cotman received his PhD in Biochemistry from Indiana University and in 1967 joined the faculty at UCI, first in the department of Psychobiology (today known as Neurobiology and Behavior) and later in Neurology. Dr. Cotman is recognized worldwide for his innovative research on the neurobiology of aging, AD and other forms of dementia. He was instrumental in elucidating basic mechanisms of cell loss and amyloid aggregation, as well as the effects of exercise and other factors on aging and disease.

The event included speeches and video tributes from more than twenty-five colleagues and family members, a reception and a dinner to honor the achievements of the world-renowned scientist. Faculty from UCI and beyond took to the podium to discuss the many ways in which Dr. Cotman impacted their lives and paved the way for modern AD research, including James Geddes, PhD, Professor Emeritus from the University of Kentucky; Patrick Kesslak, PhD, Vice President of Clinical Development and Medical Affairs at Alzheon; Robert Rissman, PhD, Professor of Physiology and Neuroscience at USC; and Bruce Miller, MD, Distinguished Professor of Neurology at UCSF.

Dr. Caleb Finch, a celebrated professor in the department of Gerontology at USC, recalled his experience partnering with Dr. Cotman to form the USC-UCI Alzheimer’s Disease Research Center (ADRC), one of the original five centers funded by NIA in 1984. Dr. Cotman went on to form the UCI ADRC, which began independent funding in 2000. He was the founding director of UCI MIND, established in 1995. Dr. Malcolm Dick, retired neuropsychologist with the UCI ADRC, spoke about Dr. Cotman’s foresight in forming one of the ten recognized California Alzheimer’s Disease Centers at UCI, which has brought specialized clinical care to AD patients and their families for over 25 years. Dr. Ira Lott, professor of pediatrics at UCI, lauded Dr. Cotman for helping him establish the Down syndrome cohort at the ADRC before the importance of studying these patients was widely recognized by the field.

Others discussed the sheer number of research discoveries made by Dr. Cotman. Dean Frank LaFerla discussed Dr. Cotman’s many accomplishments including publishing 780 articles, many in high impact journals like Nature, Science, and the New England Journal of Medicine. Several former students who are now established scientists in their own right described Dr. Cotman’s collaborative approach, strong work ethic and his scientific rigor. Aileen Anderson, PhD, Brian Cummings, PhD, Elizabeth Head, PhD, and Mathew Blurton-Jones, PhD, emphasized Dr. Cotman’s passion for mentorship, scientific discourse and thoughtful debate. Several speakers told stories of how he helped many of his students find jobs and reach the next level in their careers. Throughout his career Dr. Cotman mentored more than 200 students.

Through his daughter, Cheryl, Dr. Cotman shared words of wisdom for his friends and fellow scientists, “Be bold in your ideas and forward in your thinking.” May we all endeavor to live Dr. Cotman’s words and follow in his giant footsteps.
On Saturday, September 9th, the UCI Center for Aging Research in Down Syndrome (CFAR-DS) and UCI MIND co-hosted the UCI Down Syndrome Showcase. Over 250 people attended this one of a kind event that was held at the Irvine Barclay Theatre. The showcase was a collaborative effort to celebrate the creative and artistic talents of individuals with Down syndrome and an opportunity for the public to learn about the research being conducted at UCI to identify the factors that impact their health and well-being.

In the lobby area were crafts, paintings, and other exciting creations by children and adults with Down syndrome. The talent show, arranged by the Down Syndrome Association of Orange County (DSAOC), starred performers with Down syndrome singing, dancing, performing martial arts, and more. The opportunity to connect directly with the community garnered positive feedback from attendees of the event, the Board of Directors of the DSAOC, and UCI staff and students. To learn more about the UCI CFAR-DS please visit cfar-ds.uci.edu or email cfar-ds@uci.edu.

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FUNDING AWARDS FROM THE ALZHEIMER’S ASSOCIATION

Through the Alzheimer’s Association International Research Grant Program, two UCI MIND faculty members were recently awarded grants totaling $700,000 to further their work in AD research. Gregory Brewer, PhD, Professor of Biomedical Engineering received a Zenith Fellows Award to study blood biomarkers for dementia, and Thomas Lane, PhD, Chancellor’s Professor in the department of Neurobiology and Behavior, was awarded the ALZDISCOVERY grant to explore COVID-19 and risk for AD. This comes after recent news of Lisi Flores Aguilar, PhD, who received nearly $200,000 from the Alzheimer’s Association this summer for her work on cerebrovascular disease in AD and Down syndrome. Congratulations to all!
In addition to pursuing discoveries in Alzheimer’s disease and related dementias (ADRD), UCI MIND also serves the community by delivering the latest research in the field to Orange County and beyond. Our annual research conference highlights the important role we play in this regard. In partnership with the Alzheimer’s Association Orange County Chapter and Alzheimer’s Orange County, we hosted the 34th Annual Southern California AD Research Conference at the Hilton Irvine on Friday August 25th, 2023. The theme of this year’s hybrid conference was “Sex and Gender in Dementia Research and Care” and explored the discoveries made in how sex and gender affect AD and other neurodegenerative diseases, and the areas that remain in need of study.

Michelle Mielke, PhD, from Wake Forest University opened the program discussing disparities in the rates of ADRD between men and women. Timothy Hohman, PhD, from Vanderbilt University shared the latest research about the role genes play in understanding sex differences in AD. Elizabeth Mormino, PhD, from Stanford University and Sarah Banks, PhD, from the University of California, San Diego, each spoke about the progression of biomarkers in AD with Dr. Mormino focusing on the interplay between the APOE gene and neuropathology and Dr. Banks focusing on cognitive measures. Associate professor in the department of Neurobiology and Behavior at UCI, Elizabeth Chrastil, PhD, discussed sex differences in spatial navigation in AD and whether the ways in which we navigate could be an early predictor of disease. Amanda Smith, MD, a clinician scientist at the University of South Florida, showed the limited data available on sex differences in the safety and efficacy of AD treatments and clinical trials. Jason Flatt, PhD, MPH, from the University of Nevada, Las Vegas, shared his research on disparities in sexual and gender minority caregiving.

The afternoon concluded with a panel discussion including caregivers from different gendered perspectives: a son, a daughter, a husband, and two wives. Video recordings from this conference will be made available on our website in the coming months.
Dear UCI MIND Friends & Families,

I am delighted to invite you to our 13th Annual December to Remember UCI MIND Gala. This, our signature fundraising event, generates critical support for our research mission to make discoveries to better understand, diagnose, treat and ultimately end AD.

The event is also a wonderful opportunity to honor key supporters of this mission. This year we pay tribute to two very important advocates inspiring change and accelerating progress in Alzheimer’s care, research, and particularly training the next generation of clinicians and scientists. Lauren Miller Rogen and Seth Rogen have been supporters of our field for over a decade. Their lives were touched in 2012 when Lauren’s mother was diagnosed with early-onset AD. They co-founded Hilarity for Charity (HFC) to motivate the next generation of advocates by using humor as a form of activism. They have raised millions of dollars to award free, quality in-home care to families in need of respite and support. They are also founding partners of our UCI MIND RAMP program, providing UCI medical students a research experience after their first year, which we hope will influence their career choices toward our cause.

Lauren and Seth’s dedication to our field is unmatched, and we are excited to honor them. Please mark your calendars and join us on December 9.

Dr. Joshua Grill
LAUREN MILLER ROGEN  
Co-Founder, Hilarity for Charity

Lauren Miller Rogen is a screenwriter, director, producer, and philanthropist who was profoundly affected by Alzheimer’s when her mother, Adele, was diagnosed with early onset Alzheimer’s at 55 years old. With her husband Seth Rogen, Lauren co-founded Hilarity for Charity (HFC) to harness hope and humor while caring for families impacted by AD, inspiring the next generation of Alzheimer’s advocates, and being a leader in disease prevention research and brain health education. Since then, HFC has raised more than 20 million dollars and awarded over 405,000 hours of in-home family care. Lauren is on the board of California’s Institute of Regenerative Medicine and sits on the California Alzheimer’s Task Force. In 2022, Seth and Lauren were awarded The Public Leadership in Neurology Award from the American Brain Foundation for their work to advance public awareness, research, and understanding of neurological diseases.

Lauren’s artistic accomplishments include starring in, co-writing, and producing the film For A Good Time Call and directing the Alzheimer’s-themed dramedy Like Father, starring Kristen Bell and Kelsey Grammer.

SETH ROGEN  
Co-Founder, Hilarity for Charity

Seth Rogen is an award-winning actor, writer, producer, director, entrepreneur, and philanthropist.

He produced and starred in Hulu’s Emmy® Award-winning series Pam & Tommy and the Peacock docuseries Paul T. Goldman. Recently, he starred in Apple TV+’s Platonic and Steven Spielberg’s semi-autobiographical Academy Award®-nominated film The Fabelmans. He produced and starred in the film Teenage Mutant Ninja Turtles: Mutant Mayhem, as well as the animated adaptation of The Super Mario Bros. Movie, in which he voiced the iconic “Donkey Kong.”

Next, Seth is starring in the Sony and Black Bear Pictures’ film Dumb Money, as well as starring in and producing an Apple TV+ Untitled comedy series. He is producing the Paramount+ spinoff TV series, Tales of the Teenage Mutant Ninja Turtles and Amazon’s Sausage Party: Foodtopia.

Seth became a New York Times best-selling author for his book, Yearbook. In 2019, he launched Houseplant, a Canadian cannabis company dedicated to product quality and consumer education. The company has since expanded to the United States and added a line of home goods to its collection.

In 2012, Seth and his wife Lauren Miller Rogen founded Hilarity for Charity (HFC), a national non-profit dedicated to changing the trajectory of AD.

gala.mind.uci.edu
Hilarity for Charity
Bringing Light to Alzheimer’s

A national non-profit organization founded by Seth Rogen and Lauren Miller Rogen, HFC cares for families impacted by Alzheimer’s disease, inspires the next generation of Alzheimer’s advocates, and is a leader in brain health research and education.

CARE FOR CAREGIVERS

Care Grants
The HFC In-Home Care Grant Program relieves caregivers, giving them time to rest, recharge, and focus on their personal and professional life. Delivered with our partner, Home Instead, HFC’s Care Grants provide 3-6 months of free, professional, in-home care.

Online Support Groups
HFC’s Online Support Groups are free, frequent, and designed to help caregivers navigate any stage of Alzheimer’s disease.

Caregiver Wellness Programs
HFC provides free, educational, interactive, and informative online events to support caregivers, especially around their own health and well-being.

CARE FOR BRAINS

HFCUniverse
HFC's groundbreaking digital platform, HFCUniverse, is transforming the way young people learn about, talk about, and support others dealing with an Alzheimer’s diagnosis. The platform fosters a sense of community, reduces stigma surrounding the disease, and promotes brain health education.

DRIVE AWARENESS & INSPIRE CHANGE

YMAA Powered by HFC empowers and activates high school and college students across the U.S. to change the trajectory of Alzheimer’s disease through education, awareness, and collective action. Our aim is to reduce the stigma associated with Alzheimer’s disease and dementia by promoting disease education, providing opportunities to connect and support those affected by the disease, and inspire a generation of youth to take action to protect their own brain health by learning about and practicing brain healthy habits. We also recognize the growing community of students who are providing or helping to provide care to someone living with Alzheimer’s and aim to support caregiving youth with a range of resources and programs.

$20M
raised to support family caregivers, brain health education, and prevention research.

405K+
hours of in-home care relief awarded through our Caregiver Respite Grant Program.

850K+
people reached, on average, through our program grants, events, and social media each year.

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UCI MIND JOURNEYS TO AMSTERDAM FOR AAIC

In July, UCI MIND researchers journeyed across the Atlantic to Amsterdam, Netherlands, to present their work and meet with collaborators at the Alzheimer’s Association International Conference (AAIC). As always, UCI MIND had a strong presence at the annual conference. Among others, the MODEL-AD investigators, including Kim Green, PhD, Andrea Tenner, PhD, Grant McGregor, PhD, Vivek Swarup, PhD, and Andrea Wasserman, shared the most recent results from their program in an effort to increase use of the new tools they have developed for global investigators. Mathew Blurton-Jones, PhD, presented work on using induced pluripotent stem cells to study sex-based effects of vascular contributors to cognitive impairment. Maria Corrada, ScD, and Davis Woodworth, PhD, both chaired sessions at the meeting, and the 90+ Study that they work on had more than five posters and presentations. Negative top-line results were presented for the NEAT study, a clinical trial of nicotinamide in early AD; the basis of which came from work performed in UCI MIND labs.

Elizabeth Head, PhD, and her lab were heavily featured at the conference with several students presenting posters, including Ellie Andrews for her work on sex differences in AD pathology in Down syndrome. Postdoctoral scholar and Alzheimer’s Association awardee, Lisi Flores-Aguilar, PhD, gave an oral presentation on cerebrovascular pathology in the presence of AD in people with Down syndrome. All told, more than 30 posters and presentations were delivered by UCI investigators at this important meeting.

JOSHUA GRILL NAMED CARLA LIGGETT AND ARTHUR S. LIGGETT, MD, ENDOWED CHAIR IN HONOR OF FRANK M. LAFERLA, PHD

Earlier this year we announced the creation of the Carla Liggett & Arthur S. Liggett, M.D. Endowed Chair in Honor of Frank M. LaFerla, PhD. By committee selection, UCI MIND Director Joshua Grill, PhD, was chosen to be the inaugural recipient of the endowed chair. The annual funding received will be used to support his lab’s research. Dr. Grill is a professor in the departments of Psychiatry and Human Behavior and Neurobiology and Behavior and has been a faculty member of UCI since 2015. His research interests lie in identifying means to improve AD clinical trial design and understanding the ethical challenges of AD biomarker disclosure in research and clinical practice.
Quest Diagnostics recently announced the launch of a direct-to-consumer blood test to detect amyloid plaques in the brain. The test examines the ratio of Aβ42/Aβ40 in the plasma. Based on the Quest website, the test results are provided in numeric fashion, as well as on categories of low, intermediate, and high risk of amyloid presence in the brain (with lower numbers on the plasma Aβ ratio associated with higher likelihood of amyloid being present in the brain). There appears to be a high degree of overlap on test results among those with elevated compared to not elevated amyloid (assessed with brain PET scan, the current gold standard), making clear interpretation for some results difficult. It is not clear what proportion of results would be intermediate, which might also be considered “indeterminant.” The test costs $399 and is being marketed for repeated use for individuals to monitor their risk of AD.

Research into AD blood tests have exploded in recent years. The technology used in this offering from Quest is similar to previous tests, such as the Precivity test from C2N Diagnostics. New plasma tests, likely to enter practice in the near future, may hold even greater promise for higher precision and fewer indeterminant test results.

The main difference with this Quest plasma test is that it is being offered directly to consumers, rather than as a tool for expert clinicians to use as part of their work. We continue to believe that these tests are best used in the hands of expert clinicians, given that the implications of undergoing such tests and understanding their results are complex, multifactorial, and worthy of discussion with an expert.

In particular, the marketing of the new test, including quotes from a Quest medical director, indicate that they plan to make this test available to cognitively unimpaired individuals who are interested in better understanding their risk for AD in the future. This, for us, raises concerns.

We understand the desires of individuals to better recognize their personal risk for cognitive impair-
Every research project aims to establish data that can be analyzed to answer a scientific question. Given this fact, the ADRC at UCI MIND has a Data Management and Statistics Core that guides the Institute in designing and analyzing its many research studies. As medical science progresses and expands, and the era of big data emerges, the need for qualified biostatisticians will only further grow.

To address this need, Daniel Gillen, PhD, Professor and Chair of the department of Statistics at UC Irvine and leader of the UCI ADRC Data Management and Statistics Core, has organized a competitive summer program that teaches undergraduates from around the country important concepts in biostatistics and study design, with the goal of energizing the next generation of data scientists. The Irvine Summer Institute in Biostatistics and Undergraduate Data Science (ISI-BUDS) program ran for a second straight summer this year in July. The six-week program included meals, on-campus housing and travel stipends and supported 15 students in 2023. Funded by the National Heart, Lung and Blood Institute and the National Institute of Allergy and Infectious Diseases, the program included lectures, hands-on lab activities and workshops to teach the students everything from statistical modeling to scientific writing and communication, as well as career paths. As part of the program, the students participated in a research project utilizing the statistical tools they gained from the curriculum with a UCI faculty member, including some UCI MIND faculty, such as Ira Lott, MD, Edwin Monuki, MD, PhD, and Joshua Grill, PhD. At the conclusion of the six weeks, the students presented their research at a symposium.

Mrs. Andrea Wasserman was recognized on Thursday, October 26th at the 52nd Annual UC Irvine Lauds and Laurels awards ceremony for her long and dedicated career at UC Irvine. The Lauds and Laurels award is given to UCI supporters, faculty, and employees who demonstrate “exemplary service.” Andrea joined UCI MIND in 1988 when she took a position as a staff research associate in the lab of Dr. Carl Cotman. She worked in Dr. Cotman’s lab for 8 years helping to run his experiments and manage his lab. From 1996 to 2008, she managed the ADRC Tissue Repository, where neuropathological specimens are processed, stored, analyzed and shared. In 2008, she was appointed chief administrative officer (CAO) for UCI MIND and the ADRC, and has led the Institute’s administrative department ever since. As CAO, Andrea has many vital responsibilities including overseeing all aspects of staff personnel, grants management, lab space maintenance, special projects, and is even known to don a lab coat and provide tours of UCI MIND, including walking visitors through a demonstration involving a human brain. Congratulations Andrea!
For the third consecutive summer, UCI MIND hosted fifteen Orange County high school students who were selected to participate in a unique scientific experience. The Beall Scholar Program, named for its supporters, Joan and Don Beall, was launched in 2021 to help increase interest in neuroscience and geriatric medicine in underrepresented students from the local community. UCI MIND’s trainee led group, Research and Education for Memory Impairments and Neurological Disorders (REMIND), has planned and led the program since its inception.

Students spent one week immersed in the study of neurodegenerative diseases and brain aging at UCI. Each day began with a faculty lecture from renowned scientists, including Leslie Thompson, PhD, Craig Stark, PhD, Gyorgy Lur, PhD, and Liz Head, PhD. The program included hands-on visits to UCI MIND laboratories. Students strapped on virtual reality goggles in Dr. Liz Chrastil’s laboratory to learn about spatial navigation research, and to experience the tasks undertaken by participants in her studies. They visited Dr. Tom Lane’s laboratory to learn about cell culturing and neuroinflammation. They also held and examined a human brain and spinal cord. Additionally, they participated in a neurophysiology laboratory to learn about the sympathetic nervous system.

REMIND leaders delivered talks and demonstrations on study design, health disparities research, and laboratory bench techniques. The students also had the chance to hear from campus organizations to discuss, among other things, college admissions, choosing a major, and financial aid. The engaged students were very active, asking questions and connecting with UCI MIND faculty and trainees, as well as their fellow Beall Scholars. Said one scholar, “I enjoyed every minute! It was an incredible experience.”

A fundamental component of the program involves mentoring; each Beall Scholar is paired with a REMIND leader for the entire academic year. Nearly half of the scholars selected this year will be the first in their family to attend college and their mentors, many of whom were the first in their own families to attend college, will help them navigate the college application to admissions process.

What makes the Beall Scholar Program particularly special is its inclusivity and accessibility. Daily transportation, meals, materials, and a stipend are provided to encourage students who may not normally have the means to attend a program like this to apply.

“I felt so honored to be able to connect with the graduate students, mentors, and professionals who all do work in such an important field. Every panel, workshop, and group project positively pushed me to look forward to the future of my career, and also the future of Alzheimer’s disease in Orange County,” said one Beall Scholar.