



## ANTI-AMYLOID THERAPIES: WHERE ARE WE NOW?

*Aimee L. Pierce, MD & Joshua D. Grill, PhD*

The "amyloid hypothesis" posits that the abnormal accumulation of amyloid-beta in the brain is the first step in a cascade of biological changes leading to Alzheimer's disease. The amyloid hypothesis remains a dominant theme on the international Alzheimer's disease research agenda, especially in drug development. Of the over 60 therapies currently being tested in human clinical trials as potential disease-slowing treatments or preventions for Alzheimer's disease, more than half target amyloid in some manner.

But the recent news for anti-amyloid therapies has been discouraging. Bapineuzumab, the first anti-amyloid treatment to complete phase 3 trials (the last phase before FDA approval) failed to slow disease progression when tested in patients with mild-to-moderate dementia. Solanezumab, the second anti-amyloid treatment to complete phase 3 trials similarly failed to demonstrate efficacy in mild-to-moderate dementia, as well as in mild dementia. Do these negative results mean we should abandon the amyloid hypothesis? Certainly not.

Other anti-amyloid therapies have generated great enthusiasm in early phase trials because of an ability to remove amyloid from the brain at unprecedented levels, suggesting that all anti-amyloid therapies are not created equal. Additionally, many researchers believe that any anti-amyloid therapy will be most effective if started as early in the disease process as possible. This makes prevention studies in asymptomatic older adults, like the A4 Study and the soon-to-launch EARLY study, all the more critical in the larger Alzheimer's disease research agenda.

The world urgently needs new treatments to slow, stop, or prevent Alzheimer's disease and researchers desperately want to discover such treatments. Unfortunately, science takes time, resources, and partnership with large numbers of volunteer participants. The next few years will reveal several important results that will shed light on the validity of the amyloid hypothesis. While UCI MIND remains at the forefront of these and other studies that examine anti-amyloid therapies, we will also perform studies on non-amyloid therapies, some of which are already underway. And we will not rest until we transform the care of Alzheimer's disease. To learn more about clinical trials at UCI MIND, please contact our research coordinator at **949.824.0008** or [research@mind.uci.edu](mailto:research@mind.uci.edu).

## Promising Junior Investigators Awarded Prestigious Grants

UCI MIND congratulates five postdoctoral fellows in the laboratories of Drs. Frank LaFerla, Masashi Kitazawa, and Kim Green, who were recently awarded prestigious grants. Many of the passionate young researchers at UCI MIND are driven by personal experiences to find improved treatments, preventions, and cures for Alzheimer's disease and related dementias. Dr. Stefania Forner, an Alzheimer's Association Research Fellowship (AARF) recipient states, "We are made of memories, and the thought of such a disease capable of disassociating us from the people we love and the world made me want to be a part of a team of researchers who are fighting not only for a better understanding of the disease, but for a cure." Dr. Forner's project investigates the relationship between brain cells' actin cytoskeletons and the loss of synapses (connections between brain cells) in Alzheimer's disease. Dr. Lindsay Hohsfield, another AARF recipient and young investigator who has been personally impacted by Alzheimer's disease, will test a drug regimen hypothesized to regulate microglia, immune cells believed to be chronically over-activated in Alzheimer's disease.

Dr. Siok Lam Lim's AARF project also investigates microglia, examining whether a novel regulator may be key to turning on and off immune responses as treatments in Alzheimer's disease, and Dr. Heng-Wei Hsu's project will explore the role of a protein found in brain blood vessels (called LRP1) in inflammation and amyloid-beta clearance from the brain. Lastly, Dr. Alessandra Martini, recipient of the Larry L. Hillblom Fellowship Research Grant, will evaluate how excessive signaling of inflammatory receptors drives cognitive decline. Dr. Martini shares, "as I saw my grandfather and so many others lose their memories, it became obvious to me that I should pursue this path and join efforts with a team of admirable researchers to understand and fight this devastating disease."



From left: Drs. Heng-Wei Hsu, Siok Lam Lim, Alessandra Martini, Lindsay Hohsfield, and Stefania Forner

## FROM THE CO-DIRECTORS

Frank M. LaFerla, PhD & Joshua D. Grill, PhD



Dear Friends,

As 2016 came to a close, we communicated to you that we were at a critical but hopeful juncture in the history of Alzheimer's disease research. Several exciting studies were on the horizon and we anticipated a significant increase in National Institutes of Health (NIH) funding for Alzheimer's disease research.

As 2017 begins, this hope has given way to uncertainty. With a new administration and no approved federal budget as of February 1, researchers are understandably nervous. In regard to NIH funding, it is unclear what actions will be taken by President Trump and his nominee to lead the Department of Health and Human Services, Representative Tom Price (R-GA). Rep. Price is a known budget hawk, but when asked during his confirmation hearings about the very low levels of Alzheimer's disease research funding, relative to

the large numbers of afflicted Americans, he responded that it is "absolutely imperative" to ensure a better proportionality of resources.

The truth is, we don't yet know what to expect from the new administration or the incoming Secretary about the NIH budget or funding for Alzheimer's disease research. What we do know is that greater investment in Alzheimer's disease research is needed now more than ever. We will continue to pursue every opportunity to see research accelerate at UCI MIND—be it through NIH funding, foundation grants, or philanthropy. Substantial work remains to be done to change the way we treat Alzheimer's disease, and we will work tirelessly until we achieve a world without Alzheimer's disease and other dementias—a world where memories last a lifetime. We hope you will join us in this commitment.

### Down Syndrome and Alzheimer's Disease Conference



On January 21, over 150 health care professionals and family members of individuals with Down syndrome attended an educational conference hosted by Alzheimer's Orange County, *Medical, Scientific, and Practical Advances in Down Syndrome and Alzheimer's Disease*. Esteemed UCI MIND researcher, clinician, and director of the Down Syndrome Program, Dr. Ira T. Loft, presented current research on the risk factors, diagnosis, and treatment of individuals with Down syndrome and Alzheimer's disease. His lecture was followed by moving stories from a panel of caregivers moderated by manager of the Down Syndrome Program, Eric Doran. Conference attendees were connected with valuable community resources, including Down Syndrome Association of Orange County, Regional Center of Orange County, Caregiver Support Groups at Alzheimer's OC, and Dr. Loft's Down Syndrome Program at UCI. If you would like to learn more about these resources and more, please contact Eric Doran at **714.456.8443** or [edoran@uci.edu](mailto:edoran@uci.edu).

### What Can We Learn from the Sleeping Brain?

The 23rd UCI Distinguished Lecture Series on Brain, Learning, and Memory hosted by UCI MIND, UCI Ayala School of Biological Sciences, and UCI Center for the Neurobiology of Learning and Memory was held on February 7 at the Irvine Barclay Theatre. Dr. Ruth Benca, UCI MIND faculty member and Professor and Chair of Psychiatry and Human Behavior, delivered a lecture on sleep and brain health to over 850 community members, the largest attendance for this series to date. Dr. Benca's engaging presentation first addressed why humans need sleep and some of the common disorders that interfere with the critical sleep process. She then discussed what sleep tells us about the brain, including the possible link between sleep and Alzheimer's disease. She noted more research is needed to understand this relationship, including whether amyloid-beta protein is cleared from the brain during sleep and whether treating sleep disorders may reduce the risk for or slow Alzheimer's disease. Visit our YouTube page to view the full lecture: [www.youtube.com/user/UCIMIND](http://www.youtube.com/user/UCIMIND)





## Holiday Appreciation Reception Honoring Research Volunteers

On December 14, UCI MIND hosted a holiday appreciation reception honoring the most important members of our research team, participants and their study partners. Currently, there are 300 volunteers enrolled in our Longitudinal Study, which follows healthy people with and without memory problems annually until the end of life. More than 40 others are involved in clinical trials of promising new therapies. Through their commitment to research, our volunteers help us understand the differences between people who develop cognitive problems leading to Alzheimer's disease and those who do not, changes in biological markers that could lead to earlier diagnosis and targets for new treatments, and the safety and efficacy of potential therapies. If you or someone you know would like to learn more about the Longitudinal Study and other research participation opportunities, please contact our research coordinator at **949.824.0008** or [research@mind.uci.edu](mailto:research@mind.uci.edu).

## A DECEMBER TO REMEMBER

Over 300 loyal friends and supporters of UCI MIND launched the holiday season with a *December to Remember* gala at the Balboa Bay Resort on December 3. The gala, led by co-chairs Roger and Lucy Lisabeth, honored distinguished faculty member, Dr. Ira T. Lott, community leaders, Burton and Linda Young, and UCI alumna, Elsa Ramon.

The event, recognized by the *Los Angeles Times-Daily Pilot* and the *Orange County Business Journal*, was the most successful to date, raising \$375,000 to support Alzheimer's disease research at UCI. UCI MIND extends sincere gratitude to the planning committee, underwriters, and sponsors who helped make the event possible.

Please save the date for the next UCI MIND gala on **December 2, 2017**, at the Balboa Bay Resort, and contact Linda Scheck for sponsorship opportunities: **949.824.3251** or [lscheck@uci.edu](mailto:lscheck@uci.edu).

### 2016 GALA SPONSORS

Alzheimer's Orange County  
The Beaumont Family in Honor of Dr. Jacque DuPont  
Tim and Steph Busch  
Caring Companions at Home  
The Chou Family in Memory of Doris Chou  
The Crean Foundation  
Elite OC Productions  
Irvine Cottages  
Roger and Lucy Lisabeth  
The Friends of Roger and Lucy Lisabeth  
Monster Loans  
Robert and Virginia Naeve in Memory of Helen Simpson  
San Clemente Villas by the Sea  
Silverado  
Sperry Commercial  
Sperry Equities  
Wells Fargo



UCI MIND award recipient and director of the Down Syndrome Program, Ira Lott, MD



Honorees Linda and Burton Young with son (left) and UCI alumna honoree, Elsa Ramon (center right)



Drs. Frank LaFerla and Joshua Grill with CEO of UCI Health, Dr. Howard Federoff (center)



Gala co-chairs Roger and Lucy Lisabeth (center right) with family

## Charitable Bequest



Philanthropy accelerates research and many individuals choose to include philanthropic research support among their final gifts. A bequest, or will, to support research at UCI MIND creates a legacy in your name that funds ongoing research to find answers to the neurological disorders that disrupt so many lives today. The sample language below can be used by you and your legal counsel to name UCI MIND as a beneficiary:

"I give to the University of California, Irvine Foundation, (tax id # 95-2540117) located in Irvine, California (description of gift; i.e. percentage of estate, specific dollar amount etc.). This gift shall be used to benefit research at UC Irvine's Institute for Memory Impairments and Neurological Disorders, UCI MIND."

Once your estate documents are complete, contact Roland Ho, Senior Executive Director of Planned Giving, at **949.824.6454** or [roland.ho@uci.edu](mailto:roland.ho@uci.edu). You will be invited to become a member of the University's Legacy Society. To learn more, contact Linda Scheck, Director of Development at **949.824.3251** or [lscheck@uci.edu](mailto:lscheck@uci.edu).

**UCI** University of  
California, Irvine  
Institute for Memory Impairments  
and Neurological Disorders  
2646 Biological Sciences III  
Irvine, CA 92697-4545

Non Profit Org.  
US Postage  
PAID  
Santa Ana, CA  
Permit No. 1106

 Follow us on Facebook @UCIrvineMIND

 Follow us on Twitter @UCIMIND

MIND MATTERS is a publication of the UCI Institute for Memory Impairments and Neurological Disorders in collaboration with the Alzheimer's Disease Research Center (ADRC) and the California Alzheimer's Disease Centers (CADC). The ADRC is funded by a grant from the National Institute on Aging and supports and promotes interdisciplinary research on Alzheimer's disease. The CADC is funded by the California Department of Public Health. The CADC provides expert clinical assessments and diagnosis of memory complaints related to Alzheimer's disease and other dementias.

**EDITORS:**

Joshua Grill, PhD & Chelsea Cox, MPH, MSW

## 28th Annual Southern California Alzheimer's Disease Research Conference

**UCI MIND** Institute for Memory Impairments  
and Neurological Disorders

**Alzheimer's** | ORANGE COUNTY

# The Elephant in the Room

## Sensitive Subjects in Dementia Care



End  
of Life

Driving  
Risk



Elder  
Abuse

Intimacy



Psychiatric  
Symptoms

Physician  
Aid in Dying



Friday, September 22, 2017

7:30 AM - 3:30 PM

Irvine Marriott Hotel

### Exhibitor Information:

kleinkm@uci.edu  
949.824.9475

### Registration Information:

adriana.bakhoun@alzoc.org  
949.757.3721