UC Irvine Institute *for* Memory Impairments *and* Neurological Disorders

MIND MATTERS

A Quarterly Publication of UCI MIND

Winter 2016

NEW GRANT TO DISCOVER CRITICAL BIOMARKERS FOR ALZHEIMER'S DISEASE IN PEOPLE WITH DOWN SYNDROME

Ira T. Lott, MD

KAREN DELANEY HAS PARTICIPATED IN UCI MIND'S DOWN SYNDROME PROGRAM FOR OVER TWO DECADES

Adults with Down syndrome are at high risk for developing dementia of the Alzheimer type. Most individuals with Down syndrome develop the pathological hallmarks of Alzheimer's disease (amyloid plaques and tau tangles) by their 30's and 40's and a high percentage (estimates of up to 80%) eventually develop clinical signs of dementia as they age into their 60's. These risk figures make people with Down syndrome the largest genetically "at-risk" population in the world; a population that has been estimated to be more than 250,000 in the US and over 16,000 in California. In the past several decades we have seen a dramatic increase in longevity in persons with Down syndrome, which has resulted in more people living into the high risk years for Alzheimer's type dementia.

People with Down syndrome are born with an extra copy of chromosome 21. Having three copies of chromosome 21, instead of the normal two, leads to a host of cognitive and physical symptoms that define the syndrome, including intellectual disability and distinctive facial features. The development of Alzheimer's disease in Down syndrome is linked to the additional copy of the amyloid precursor protein (APP) gene on chromosome 21 that results in 50% greater levels of both APP mRNA and amyloid protein. This increased production of amyloid is responsible for the early formation and accumulation of amyloid in the brains of people with Down syndrome. Why persons with Down syndrome develop the brain changes of Alzheimer's disease in mid-life and not all will go on to develop Alzheimer's type dementia is one area of focus of UCI MIND researchers. Another focus has been on longitudinal data to identify biomarkers that may predict conversion to Alzheimer's type dementia.

UCI MIND investigator, Ira T. Lott, MD, is a co-principal investigator for a grant to identify biomarkers of Alzheimer's disease in adults with Down syndrome. Dr. Lott's team will receive $4.7 million as part of a $37 million effort to uncover predictive biomarkers. This NIH initiative establishes funding for two research teams that will pool data and standardize procedures, increase sample size and collectively analyze data that will be available to the research community. Dr. Lott's team includes UCI MIND researchers and colleagues from Columbia University Medical Center in New York City, Kennedy Krieger Institute/Johns Hopkins University in Baltimore, Massachusetts General Hospital/Harvard University in Boston, and the University of North Texas Health Sciences Center in Fort Worth.

They will assess an array of biomarkers to identify and track Alzheimer's-related changes in the brain and cognition in over 300 volunteers with Down syndrome ages 40 years and older. The measures include:

- Positron emission tomography (PET) scans that track brain levels of amyloid and glucose consumption (energy used by brain cells); MRI of brain volume and function; and levels of amyloid and tau in cerebrospinal fluid and blood;
- Blood tests to identify biomarkers in blood, including proteins, lipids and markers of inflammation;
- Blood tests to collect DNA for genome-wide association studies that identify the genetic factors that may confer risk or protect against developing Alzheimer's disease;
- Evaluations of medical conditions and cognitive and memory tests to determine levels of function and monitor any changes.

KAREN DELANEY AND HER MOTHER, RUTH DELANEY, VISIT WITH DR. LOTT AS PART OF KAREN'S ANNUAL RESEARCH PARTICIPATION. WITH THIS SIGNIFICANT NEW AWARD FROM THE NIH, THE DELANEYS ARE HOPEFUL THE RESULTS WILL LEAD TO EARLIER DETECTION, MEANINGFUL TREATMENTS, AND ULTIMATELY, PREVENTION OF ALZHEIMER'S DISEASE.

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FROM THE DIRECTOR

Andrea Tenner, PhD

Dear Friends,

Happy New Year from all of us at UCI MIND! We hope that your holiday season was safe and enjoyable. We hope too that your 2015 ended optimistically, as it did for the field of Alzheimer's disease research and for UCI MIND specifically.

The December announcement that Congress passed a federal budget that would increase Alzheimer's disease funding by more than 60% was met with joy by researchers nationwide. The additional $350 million brings AD funding to more than $900 million, an increase that—while overdue—could not have come at a more critical time. Now is a very exciting time in the history of Alzheimer's disease research, with innovative research programs able to test novel hypotheses and promising candidate therapies. The increase in funding will accelerate the rate of elucidating the underlying causes of dementia and identifying new targets for specific inhibition of detrimental events as well as for the promotion of brain health. The funding demonstrates a realization that in order to achieve the goal of eliminating Alzheimer's disease, the nation must invest the resources needed to do so. In addition to generating hope for those affected by the disease, this new commitment should also encourage junior investigators to continue in their efforts to contribute to solving this crisis.

Even before the announcement, as you have noted from the newsletters in 2015, it was an optimistic time at UCI MIND. The successes of 2015 were capped at year's end by the funding announcement for Dr. Ira Lott and his team (page 1). Their newly funded grant will permit cutting edge studies of Alzheimer's biomarkers in persons with Down syndrome for the coming five years. These lines of study could hold keys to unlocking new treatments, not only in people with Down syndrome, but also in people with other genetic or even sporadic forms of Alzheimer's disease. Please join us in congratulating Dr. Lott on this important accomplishment.

At the conclusion of 2015, we also thanked those who make our research possible. We held two end-of-year events, honoring both research participants and the friends and supporters of the Institute (page 3). We were thrilled to honor many individuals at these traditional festivities, including our Chief Administrative Officer, Andrea Wasserman, who has devoted 27 years of service (and is still going strong) to UCI MIND. Next year, we anticipate combining our year-end celebration with the UCI MIND Gala on December 3, 2016, at the Balboa Bay Resort in Newport Beach. We hope you will join us, thank you for your support, and encourage you to stay tuned – 2016 is sure to be an exciting and productive year.

RESEARCH PARTICIPATION OPPORTUNITIES

The A4 Study

If you are a healthy older adult with normal memory, this could be the right time for you to join the fight to prevent the memory loss of Alzheimer's disease (AD). The **Anti-Amyloid Treatment in Asymptomatic Alzheimer's study (the A4 study)** is a clinical study for older individuals (65 to 85 years of age) who may be at risk for memory loss due to AD. The A4 study is investigating a new drug intervention that may reduce the impact of a protein known as "amyloid" or "beta amyloid" forming plaques in the brain. Scientists believe that accumulation of amyloid in the brain may play a key role in the eventual development of AD-related memory loss. The A4 anti-amyloid investigational drug targets amyloid build-up in the brain with the aim of slowing memory loss associated with the development of AD.

The A4 study at UCI is enrolling people between the ages of 65 through 85 with normal thinking and memory function but with evidence of amyloid plaque buildup in the brain. Physicians and researchers will use PET amyloid imaging scans to determine whether a potential participant has evidence of elevated amyloid buildup. Individuals with elevated amyloid on the PET scan will be eligible to become participants in the A4 clinical study. For more information, contact Beatriz Yanez, RN at **(949) 824-3250** or email **byanez@uci.edu**.

MRI Research Studies of Memory. We are recruiting volunteers for participation in MRI research studies of memory and cognition. Sessions are 1-2 hours. Must be 60 years or older. You will be compensated for your participation. Located on the UCI campus.

Contact Liz Murray at **949-824-0314** or email **yassalab@uci.edu** for more information.
Principal Investigator: Dr. Michael Yassa

YASSALAB
Translational Neurobiology Laboratory

UCI MIND CELEBRATES THE HOLIDAYS

On December 14th, UCI MIND celebrated the holidays with an annual appreciation reception for all the inspiring individuals who give their time, blood, and cerebrospinal fluid to participate in our research studies and clinical trials. Without our participants, we would not be able to advance our mission of researching ways to make memories last a lifetime. The holiday appreciation reception was a warm and encouraging event with over 100 participants and family members. Attendees enjoyed festive jazz music by "The Standards," raffle prizes, and remarks from Dean Frank LaFerla, Director, and Dr. Joshua Grill, Associate Director, of the UCI MIND Alzheimer's Disease Research Center (ADRC). A special thank you to Vivante, Assured In-Home Care, Caring Companions at Home, and Guardian Angels for helping to sponsor this special event.

DR. ADAM BOXER PRESENTED AT THE 16TH ANNUAL HOLIDAY LECTURE AND DINNER

UCI MIND also held its 16th Annual Holiday Lecture and Dinner on December 10th. The evening began with a fascinating lecture on "Developing Alzheimer's therapies by studying non-Alzheimer's dementias" from Associate Professor and Neurologist of the Memory and Aging Center at UC San Francisco, Dr. Adam Boxer. Following the lecture, Dr. Andrea Tenner presented a year in review, highlighting some of UCI MIND's most exciting accomplishments in 2015.

A special part of this annual holiday event is to recognize the next generation of outstanding researchers with the Carl W. Cotman Scholar's Award, an award in honor of UCI MIND's founding Director, Dr. Carl Cotman. From the elite group of young scholars at UCI MIND, Natalie Goldberg and Dr. Janine Kwapis were selected for the 2015 Scholar's Award. Natalie is a doctoral candidate in the Neurobiology and Behavior program who joined the lab of Dr. Mathew Blurton-Jones in 2012. Janine received her PhD from the University of Wisconsin-Milwaukee and joined the lab of Dr. Marcelo Wood in 2014 as a post-doctoral trainee. UCI MIND congratulates Natalie and Janine on their accomplishments and promising futures in the field of neurodegenerative disease research.

DRS. CARL COTMAN AND ANDREA TENNER PRESENTED THE PRE-DOCTORAL AWARD TO NATALIE GOLDBERG

DRS. CARL COTMAN AND ANDREA TENNER PRESENTED THE POST-DOCTORAL AWARD TO DR. JANINE KWAPIS

Also presented annually is the UCI MIND Award, an honor bestowed upon an individual who has made the highest level of contribution to the mission of UCI MIND. The 2015 award was presented to Andrea Wasserman, Chief Administrative Officer of UCI MIND. Andrea began her career as Staff Research Associate for Dr. Cotman in 1989 and has been with UCI MIND since its inception as an Organized Research Unit in 1995 (then called the Institute for Brain Aging and Dementia). Andrea has been instrumental in the continued and consistent funding of UCI MIND and its researchers, and she is truly the cornerstone of our success. UCI MIND congratulates Andrea and thanks her for her longstanding leadership and commitment to advancing our mission.

ANDREA WASSERMAN WITH HER PARENTS, ANDY AND SYDELL WALENCEWICZ; CHILDREN, LAUREN AND BRENT; AND HUSBAND, JAY

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The current research funding is the culmination of a collaborative effort on Down syndrome and Alzheimer's disease within the Alzheimer's Disease Research Center (ADRC) and UCI MIND that has existed for over 20 years. UCI's ADRC was the first NIH funded center to focus on this relationship between Down syndrome and Alzheimer's disease.

Along with identifying the pre-existing factors for Alzheimer's disease, the ultimate goal of the research is to identify the susceptibility to dementia in time for treatment interventions to prevent dementia in Down syndrome. This may afford people with Down syndrome the same opportunities for early treatment as those at risk for Alzheimer's disease in the general population.

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Research Today. Hope Tomorrow.

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Editors: Joshua Grill, PhD and Chelsea Cox, MPH, MSW