Institute *for* Memory Impairments *and* Neurological Disorders

# MIND MATTERS

*Making Memories Last a Lifetime*

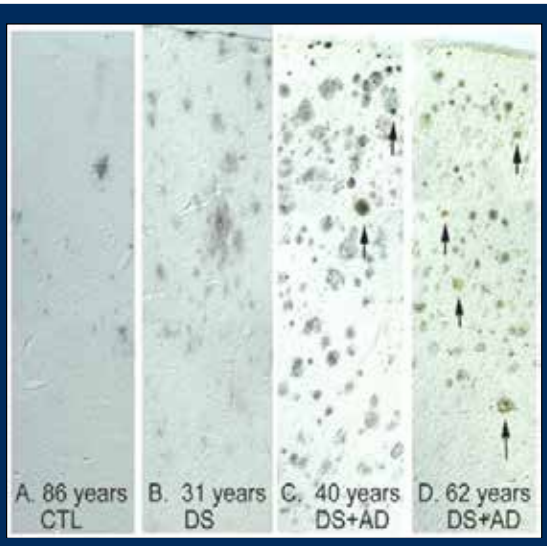
May 2013

University of California • Irvine

# Learning about Healthy Aging and Alzheimer's Disease from People with Down Syndrome

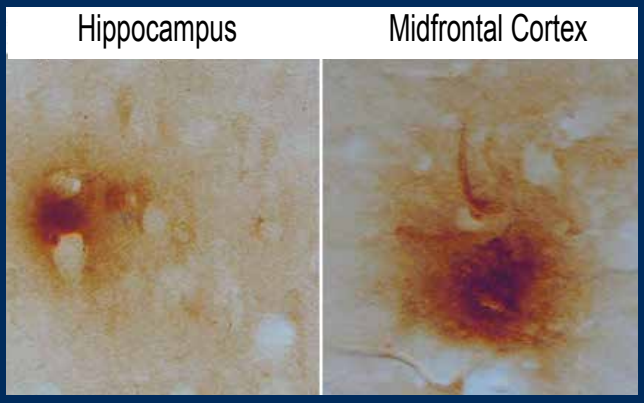
*Ira T. Lott, MD*

Down syndrome (DS) is the most common cause of genetically determined intellectual disability in the United States, affecting approximately 1 in 700 live births. An estimated 350,000 Americans have DS. Also called trisomy 21, DS results from a tripling of all or part of the 21st chromosome. The association between DS and Alzheimer's disease (AD) was established in 1948. Since then, we've learned that by age 40, all individuals with trisomy 21 have the characteristic amyloid plaques and neurofibrillary tangles of AD. Individuals with DS constitute the only population we know that has these ubiquitous changes of AD by mid-adult life.




*Progression of amyloid accumulation in DS compared to control brain*

One cause of the association between DS and AD is overexpression of the amyloid precursor protein gene on chromosome 21, which results in brain amyloid accumulation from an early age. Indeed, primitive brain deposits of amyloid have been seen as early as 4 months of age in infants with DS.




*Early onset Aβ in Down syndrome: Diffuse amyloid staining from the brain of a 4-month old child with DS, intact neuron (L)*

As a result, the processes of development and aging in DS provide a particular window on the mechanisms that lead to AD. UCI MIND is one of the few research centers nationwide that has had a longstanding and robust program in DS.

But the DS-AD connection is even more interesting. Despite the fact that plaques and tangles are universal by age 40 years, not every individual with DS develops dementia. While the prevalence of dementia increases with age, we follow many individuals in their 60s and beyond who have not experienced cognitive decline. The biomarkers that may signal cognitive decline are the subject of a current major research project funded by the National Institutes of Health (NIH) that involves many UCI MIND researchers.

We do know that amyloid is first deposited in the frontal lobe and entorhinal cortex of young adults with DS. These brain areas govern emotional reaction, executive functioning and memory processes. Although the brain cells appear normal in these early plaques, the neurons have a certain chemical profile which, in later life, results in "cell suicide" or

*Continued on page 6*

## From the Director... *Frank LaFerla, Ph.D.*


# Studying More than Just Alzheimer's Disease

Neurodegenerative disorders are a group of diseases that lead to the destruction and death of neurons in the nervous system. This umbrella term encompasses many common brain disorders, such as Alzheimer's and Parkinson's disease but also includes others that are less common, but no less debilitating, such as Huntington's disease and Lou Gehrig's disease.

To date, there have been over 103 drugs that have failed in Alzheimer's disease (AD) clinical trials. Hence, there is an urgent need to develop and evaluate new treatment strategies. Along these lines, UCI MIND is broadly focused on discovering and studying the pathways that underlie neurodegenerative disorders, and ultimately interested in finding ways to intervene to prevent, slow, or treat them. It is true that a significant amount of our efforts are focused on AD, which is proportional to the large number of individuals affected in our country, currently estimated at more than 5.4 million Americans. There is much, however, that can be learned by conducting cutting-edge research into other neurodegenerative disorders.

You may wonder how studying Huntington's disease will benefit you if you have a loved one afflicted with AD or conversely, if someone you know suffers from Lou Gehrig's disease, you may ponder how researching AD benefits you and your loved ones. It is true that these disorders affect different brain regions and thereby produce distinct clinical features, sometimes purely cognitive or motor dysfunction, or sometimes a mixture. Yet, all of the neurodegenerative disorders can be considered proteinopathies, diseases in which a specific protein misfolds and accumulates to toxic levels in the brain. For example, each disorder has its own specific protein that accumulates: amyloid and tau for AD and Down syndrome, huntingtin for Huntington's disease, prion protein for mad cow disease (i.e., Creutzfeldt-Jakob disease), and synuclein for Parkinson's disease. In some cases, a combination of proteins can accumulate as occurs in Lewy body dementia when amyloid, tau and synuclein build up and the patient experiences not only cognitive impairments but also Parkinson-like motor symptoms.

Even though different proteins accumulate and different brain regions are impacted, there are many biological processes that are commonly affected, including oxidative stress, brain inflammation, and changes in the ability to handle misfolded proteins, as if the cell's garbage disposal system were breaking down. The rich tapestry of neurodegenerative disease researchers at UCI MIND allows us to closely collaborate with each other and learn from the experiences that we derive in studying selective brain diseases.


In this issue of MIND Matters, we turn our attention to Down syndrome and its unique contribution to our understanding of AD. It is only through your support that we can maintain the breadth of research required to unlock the mysteries of AD and other neurodegenerative disorders. We thank you for your ongoing commitment to helping us *research ways to make memories last a lifetime.*

# IN THE NEWS

*Exciting discoveries, achievements, and updates from the Institute for Memory Impairments and Neurological Disorders*

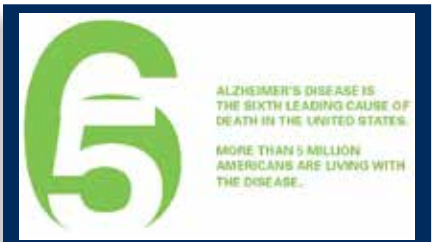
Longitudinal Study participants come in for an annual assessment.

## UCI MIND ADRC Longitudinal Study Grows to 300

In 2012, the UCI MIND Alzheimer's Disease Research Center (ADRC) set a goal of growing the number of research volunteers participating in its Longitudinal Study to 300. We are pleased to announce that 307 research volunteers, including cognitive normal older adults and individuals with Mild Cognitive Impairment or early Alzheimer's disease, now participate in the Longitudinal Study, which involves annual neurological, medical and neuropsychological evaluations and brain donation upon death. All information and biological specimens (e.g., blood, cerebral spinal fluid) contributed by our research volunteers are made available to researchers worldwide via a national database. To learn more about becoming a research volunteer, see the box on page 9 of this newsletter. Thank you to our research volunteers for their commitment to advancing knowledge about memory and aging.

## Alzheimer's Association Releases 2013 Facts and Figures Report

One in three seniors in the U.S. now dies with AD, according to the just-released *2013 Alzheimer's Disease Facts and Figures* report. In 2013, 450,000 people are expected to die of AD which is now the 6th leading cause of death nationwide. With a new person developing Alzheimer's every 68 seconds, the disease will cost the nation $203 billion in 2013, a number that is expected to escalate to $1.2 trillion by 2050. Given the widespread impact of AD, with over 5 million Americans affected and another 15 million-plus friends and family members involved in care, an urgent need exists to advance research into the causes and potential treatments for this disease. To read the full report, visit http://www.alz.org/alzheimers_disease_facts_and_figures.asp.




Someone develops Alzheimer's every 68 seconds.

Bijan Taghavi

## Award-winning Pianist, Bijan Taghavi, receives Scholarship Award

Bijan Taghavi, who entertained over 100 research volunteers attending the 2012 UCI MIND Alzheimer's Disease Research Center Appreciation Breakfast, recently received a scholarship award from the South Coast Symphony. Winning the "Young Stars of the Future" award in a concerto competition, Bijan performed the "Grieg Piano Concerto in A Minor" with the symphony on February 22nd. Born in November 1997, Bijan began his piano studies at the age of 3. He is a passionate musician, son of Guita Sharifi, Director of Operations at Alzheimer's Family Servicers Center. To hear the gifted Bijan play again, check www.LivingPiano.com for announcements of performances with his teacher and mentor, Robert Estrin, in Living Piano: Journey Through Time.

## Gene Hovatter is Oldest Graduate of Irvine Valley College

Gene Hovatter

Congratulations to Gene Hovatter, who received an Associate of Arts Degree from Irvine Valley College (IVC) at age 85. Recognized as IVC's oldest graduate, Mr. Hovatter, now age 86, has been a research volunteer in the UCI MIND Alzheimer's Disease Research Center's (ADRC) Longitudinal Study since October 1994. Serving as a "healthy control," Mr. Hovatter is helping UCI MIND understand the differences between successful agers who remain free of cognitive impairment and older adults who develop Alzheimer's disease or another dementia. We thank Mr. Hovatter for allowing us to assess his cognitive health annually and agreeing to donate his brain upon death for research. Our ADRC is continuously looking for older adults who are cognitively normal or starting to develop mild memory problems to volunteer for the Longitudinal Study. For more information, see the box on page 9 or call (949) 824-2382.

# Meet the Neuropathologist

## EDWIN S. MONUKI, M.D., PH.D.

Dr. Ed Monuki, Associate Professor and Acting Chair of the UCI Department of Pathology & Laboratory Medicine, is a recent addition to the UCI MIND Alzheimer's Disease Research Center (ADRC). We welcome him as the Co-Director of the ADRC Neuropathology Core. After training at Massachusetts Institute of Technology, UC San Diego, and multiple Harvard-affiliated hospitals, Dr. Monuki became a faculty member at the Brigham & Women's Hospital and Boston Children's Hospital. In 2001, he returned to Southern California to join UCI Pathology Services.

As well as helping direct the ADRC Neuropathology Core, Dr. Monuki will be involved in stimulating new research ideas and initiating work on an understudied, yet critical tissue in brain aging and neurodegeneration known as the choroid plexus. As an off-shoot of his work on the developing forebrain and its stem cells, Dr. Monuki recently described a first-ever method for generating choroid plexus cells from pluripotent stem cells, opening up a brand new area for studying and potentially treating Alzheimer's disease (AD) and Down's syndrome. His interest in AD is further motivated by his father, who has had dementia for nearly a decade, and his mother, who has struggled as his caretaker. "It seems like destiny that my family's struggles with dementia, my work on the choroid plexus, and the invitation to join one of the strongest centers in all of UCI have converged to provide an opportunity to make a unique impact on these dreadful neurodegenerative conditions and the people affected by them."

Additionally, Dr. Monuki brings his roles as senior editor/editorial board member on three neuropathology/neuroscience journals, standing member of the NIH Neurogenesis and Cell Fate study section, and Associate Director of the Medical Scientist (MD-PhD) Training Program to the task of further facilitating and promoting the activities of the ADRC.

# Meet the Patient Care Coordinator

## RUOBING "ROBIN" LI

When Ruobing "Robin" Li was searching for an opportunity to help advance research on Alzheimer's disease (AD), she had to look no further than UCI MIND. In October 2012, Robin joined the UCI MIND Memory Assessment and Research Center as its newest Patient Care Coordinator. Among other things, she is coordinating visits for our patients and research participants, as well as assisting with outreach efforts to the Chinese American community.

Robin previously worked as a geriatric case manager at the Orange County Council on Aging (COA). Robin provided guidance, support, and education to vulnerable individuals, including people with AD or another dementia, and their families. She conducted in-home assessments, managed care plans for frail elders and persons with disabilities, and educated her clients about community resources to support quality of life.

Robin also served as co-director of Linkages, case management program at the COA. In that role, she directed outreach efforts to help elderly persons continue living independently at home. Her many administrative responsibilities included writing grant proposals, conducting statistical analyses, training case managers, and creating program reports for state and federal funding agencies.

Robin is from Dali, Yunnan, China and is fluent in Mandarin. She earned her B.A. in English Languages and Literature at Southwestern Teacher's University in Chongqing, China. Before coming to the United States, she taught English to medical students at the Dali Medical College in Dali, China. She earned her M.A. in Sociology, with an emphasis in Gerontology, from California State University, Fullerton. In 2003, Robin was certified as a care manager by the National Academy of Certified Care Managers.

Robin's desire to educate extends beyond older adults. In her free time, she tutors people of all ages in Mandarin. Additionally, Robin enjoys staying active, and counts hiking and cooking among her favorite hobbies.

# Meet Research Volunteers Chris and Olive La Violette

Eric Doran, MS

When Chris was born in 1963, life expectancy for a newborn with Down syndrome (DS) was a little over 12 months of age, institutionalized care was the accepted norm and most physicians and scientists believed these children wouldn't achieve many of the normal developmental milestones. With loving care from his family and what his mother, Olive, describes as his innate determination to succeed, Chris, like so many others in his generation with DS, has demonstrated that much can be achieved. Chris would develop the skills necessary to talk, read, write, win numerous medals in Special Olympics, create original artwork and vote in every presidential election since Reagan-Mondale. While these achievements are remarkable, Olive is most proud of the fact that Chris developed into a well-mannered, caring and compassionate person. She describes Chris as "one of the world's beautiful people" and states "there is no question that my life has been infinitely blessed through him and that I am a much better person today because of him."

Chris in the 2nd grade, where he earned many "O's" (Outstanding) for his reading and penmanship.

Since a one-month old infant, Chris has faithfully participated in seven research projects related to DS. Studies Chris has participated in have investigated genetics, cognitive and behavioral features, brain structure and metabolism and, most recently, Alzheimer disease (AD) in DS. Since 1990 Chris and his mother have volunteered for studies that Dr. Ira Lott and other UCI MIND researchers are conducting to elucidate the relationship between DS and AD. Currently Chris, with Olive serving as his research partner, is part of the Alzheimer Disease Research Center (ADRC)-Down Syndrome Longitudinal Research Program through which he receives annual assessments of his neurological and cognitive function.

One of Chris' many holiday-themed original paintings.

Olive understood that Chris had a high likelihood of developing Alzheimer's but was forever hopeful that he would remain free of the disease. During one research visit, when Chris was 42 years old, she reported subtle changes in his functioning. He began forgetting where he put things, misspelling his name and confusing his phone number with his ZIP code. He was less interested in his artwork and music, had trouble following verbal direction, was walking more slowly and was taking more time to complete his daily activities. Chris had transitioned into the early stages of AD. Within 3-4 years his dementia progressed to the point that Olive could no longer manage his care at home and had to place him in a care facility; something she had avoided since his birth. Today his dementia has progressed to the point that he is completely dependent on others for assistance and less responsive to others. Watching Chris change is particularly difficult for Olive. "Chris once had an incredible memory; his mind was full with a never-ending flow of facts, thoughts, ideas, statistics (his favorite word), trivia and fond life memories. Today that it is all gone. It breaks my heart to watch Chris slowly lose all that he fought so hard to achieve."

Olive continues to visit Chris weekly and he enjoys these visits that often include periods of ball play during which he laughs with delight, listening to music, time for a tickle or two, and plenty of kisses from mom. Though these past years have been difficult, Olive is proud of the contributions Chris has made as a research participant, believing "parents of future children and adults with DS will have answers to some of the questions that were unknown to his father and me, especially those that relate to Alzheimer disease."

We are grateful to Chris and Olive for their past and continued participation in our DS clinic as well as research and particularly for sharing their story. If you or someone you know may benefit from services at our clinic, be interested in research participation, or like more information, please call the UCI Down Syndrome Research Program at 714-456-8443.

Chris and Olive during one of their recent Sunday visits.

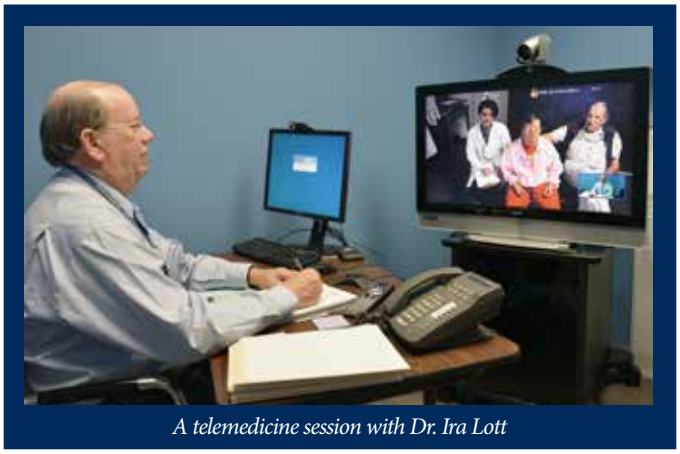
*Learning, Continued from page 1*

apoptosis. While this finding is of grave concern, it also provides a basis for hope, if a therapy for dementia which is safe, tolerable and effective is found for older adults with DS. Then stepping the intervention back to earlier age epochs may improve cognition in children and young adults with the disorder. This type of therapeutic window exists only in DS and unites the efforts of both pediatric and adult researchers.

Given the possibility of intervening early in life, individuals with DS would seem to be prime candidates for therapeutic trials. Unfortunately, until recently the opposite was true. It was said that the developmental disability made it impossible to diagnose dementia in DS or carry out successful clinical trials. Nonsense. Tests to accurately diagnose and follow dementia in DS have been developed at UCI and elsewhere. We published the first clinical trial for dementia in DS in 2002 and since that time many clinical trials have been forthcoming by our group and others. Under support of a previous NIH grant we successfully conducted a two-year randomized double-blind placebo-controlled trial of a therapeutic agent in DS with the same parameters as a major clinical trial for dementia in the general population. In fact, our researchers have found that people with DS are a joy to work with. The social skills of individuals with DS often exceed their intellectual strengths and their willingness to help enables full participation in trials that may benefit the aging process.

Clinical intervention trials, however, have little chance of being effective once dementia has begun in individuals with DS. We face the same challenge as AD researchers do, that is, to predict cognitive decline in order to begin intervention early. We have recently shown that seizures hasten cognitive decline in demented individuals with DS. Advanced EEG techniques may afford an opportunity for predicting dementia in DS. The "amyloid burden" in the brain can now be assessed with sophisticated functional brain imaging as can levels of amyloid and other suspect compounds in the spinal fluid. Measures of oxidative stress in mitochondria (see *Links to Pathogenisis*, page 8) may provide another means of predicting cognitive decline. In sum, ongoing research on DS at UCI MIND is focused on creating a predictive model of dementia in this population that will facilitate earlier intervention as new medications become available.

People with DS represent a health disparity for clinical trials. Many individuals live far from resources like our program at the UCI Medical Center and have typically been excluded as subjects for ongoing investigations. To begin remedying this disparity, we have been pioneering the use of telemedicine to reach individuals who live remotely from our medical facilities. Telemedicine is simply defined as the use of health care technology to render medical care when distance separates the doctor and the patient. In our program, the physician sees the patient in real time on a wide-screen TV and the patient sees the doctor in the same manner. We have carried out nearly 1,500 consultations in neuro-telemedicine and are convinced of both the reliability of and consumer satisfaction with this technology. Home monitoring of individuals with dementia is the next frontier for telemedicine and UCI is hard at work in developing technologies that will work efficiently for doctor and patient.



*A telemedicine session with Dr. Ira Lott*

Notably, there are some ways in which individuals with DS display healthy aging that may be informative to geriatricians and AD researchers. There seems to be a paucity of atherosclerotic complications in adults with DS as they age. In our database of several hundred adults, we have found no major complications from heart attacks, hypertension, or stroke. This experience is mirrored in other clinics for DS across the country. Also, adults with DS have a decreased frequency of certain types of solid tumors. These characteristics of people with DS may shed light on fundamental processes related to development and aging. By helping individuals with DS, we ensure that they have the highest possible quality of life and also help ourselves to age successfully.

*We wish to acknowledge the National Institutes of Health and the State of California for supporting our research and the Down Syndrome Association of Orange County for their generous funding of our pediatric clinic.*

# Links in the Pathogenesis of Down Syndrome and Alzheimer's Disease

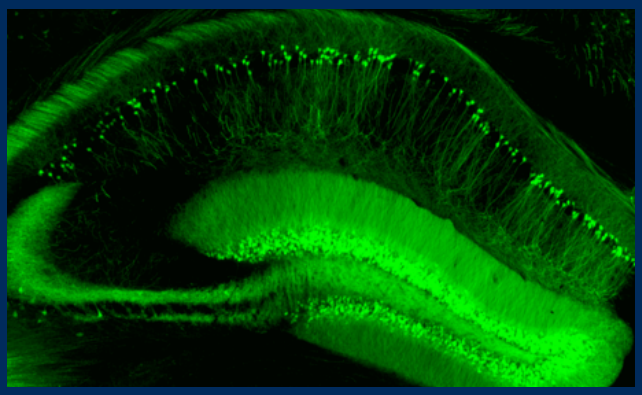
By Jorge Busciglio, Ph.D., and Maria D. Torres

Nearly 75% of middle-aged individuals with Down syndrome (DS) develop Alzheimer's disease (AD) neuropathology, including amyloid beta (Aβ) plaques and neurofibrillary tangles.

The high incidence of AD in DS offers a unique opportunity to further understand AD pathogenesis, identify biomarkers of cognitive decline and develop early treatments.

As noted in the earlier article by Dr. Ira Lott (see p. 1), development of AD in DS is related to the increased expression of the amyloid precursor protein (APP) gene, which is located on chromosome 21. APP is the precursor of Aβ, the main component of senile plaques and one of the hallmarks of AD pathology. Postmortem studies have shown that plaques and tangles develop as early as 30 years of age in persons with DS, but interestingly not all DS individuals with AD neuropathology develop symptoms of dementia. The early emergence of AD pathology in people with DS not only highlights the growing need for early treatments to halt the disease progression, but may also provide insights to prevent the development of AD.

In addition to the multiple medical and physical manifestations of DS (e.g., skeletal anomalies, craniofacial alterations, low muscle tone, increased incidence of congenital heart disease and seizures, abnormalities of the gastrointestinal track, and premature aging), the disorder is characterized by the presence of mild-to-moderate intellectual disability. DS individuals exhibit deficits in motor skills, language, learning and memory. Cognitive deficits are associated with morphological anomalies in the brain. Some of these abnormalities are observed in the structure of neuronal cells and include decreased number and aberrant architecture of dendritic spines. Dendritic spines are small protrusions found in neuronal extensions called dendrites. Dendrites are the information input region of neurons, and dendritic spines constitute principal sites of connections between neurons called synapses. Defects in the shape of spines usually reflect structural alterations in synapses, which are believed to contribute to the malfunction of neuronal circuits in the brain and to intellectual disability in DS. The mechanisms involved in the structural alterations of dendritic spines in DS are not known.



*Hippocampal region of a transgenic mouse containing a green fluorescent protein inside neurons, which makes possible detailed morphological and structural studies using imaging techniques*

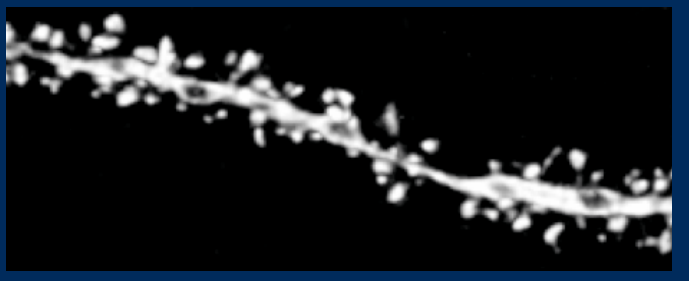
Research in our laboratory is aimed at understanding the molecular mechanisms underlying dendritic spine pathology in DS. We are investigating the role of astrocytes, a type of glial cell in the brain, in spine defects. Astrocytes provide support for and modulate the function of neurons. We identified thrombospondin-1 (TSP-1), an astrocyte-secreted protein, as a critical factor that modulates dendritic spine development. Additional experiments showed that TSP-1 production is reduced in DS astrocytes. Reduced TSP-1 levels produce pathological changes in dendritic spine structure. These alterations can be prevented by addition of recombinant TSP-1, suggesting an important role for TSP-1 in the formation and modulation of dendritic spines. TSP-1 deficiency may be associated with defects in the number and morphology of spines seen in DS and other neurological disorders. In fact, defects in dendritic spine structure and function have been widely reported in AD patients and linked to neuronal dysfunction and cognitive impairment. These novel findings provide a mechanistic rationale for the exploration of TSP-1-based

*Continued on page 8*

*Links in Pathogenesis, Continued from page 7*

therapies to treat spine and synaptic pathology in DS and other neurological disorders.

We are also actively researching the mechanisms of mitochondrial dysfunction and oxidative stress in DS. Mitochondria are the main sites of energy generation in cells. DS cells exhibit reduced mitochondrial activity, which ultimately contributes to a series of pathological changes, including increased generation of free radicals within cells and intracellular accumulation of Aβ. Oxidative stress and Aβ production and accumulation are critically involved in AD pathogenesis. In addition, mitochondria play a critical role in cell death signaling pathways. Increased levels of free radicals as observed in DS lead to higher rates of mitochondrial DNA mutations, which can initiate programmed cell death, another important feature present in AD brains. Recent work from our laboratory indicates that reduced mitochondrial activity in DS is part of a cellular adaptation to prevent cellular damage by free radicals and to preserve basic cellular functions. Interestingly, down regulation of mitochondrial activity to prevent oxidative damage has been observed in several different organisms and cell types. Thus, strategies to protect mitochondria and block free radical production may be useful in both DS and AD.



*High magnification of a portion of a dendrite with multiple dendritic spines*

To date, there is no cure for DS. Existing treatments are directed at alleviating or preventing clinical complications such as congenital heart defects or gastrointestinal blockage. Additionally, physical and speech therapy are available to further assist in improving quality of life for people with DS. Nutritional therapies have been used to enhance cognition although there is little data supporting their effectiveness. Antioxidants such as resveratrol, celastrol, vitamins, and coenzyme Q10 are characterized by their ability to protect cells against oxidative damage through the clearance of free radical intermediates and by delaying the oxidation of cellular constituents. Antioxidants can improve the survival of DS neurons and prevent neuronal death, while improving spatial learning in a mouse model of DS. Given the genetic and phenotypic complexity underlying DS, specific therapeutic interventions have been limited. The significant increase in life expectancy that individuals with DS enjoy today must be complemented with effective treatments to enhance cognition and prevent age- and AD-related cognitive decline. Dendritic spine pathology has been associated with intellectual disability in DS and other neurological disorders, yet no therapeutic approach exists to prevent or restore spine structure and function. This is a promising area of research, which may pave the way for the discovery of new treatments to ameliorate neuronal connectivity and brain function in DS and other neurodevelopmental and neurodegenerative conditions.

*Supported by the National Institutes of Health, the Alzheimer's Association and the State of California Department of Public Health Alzheimer's disease initiative.*

# ReMIND Hosts 4th Annual Emerging Scientists Symposium

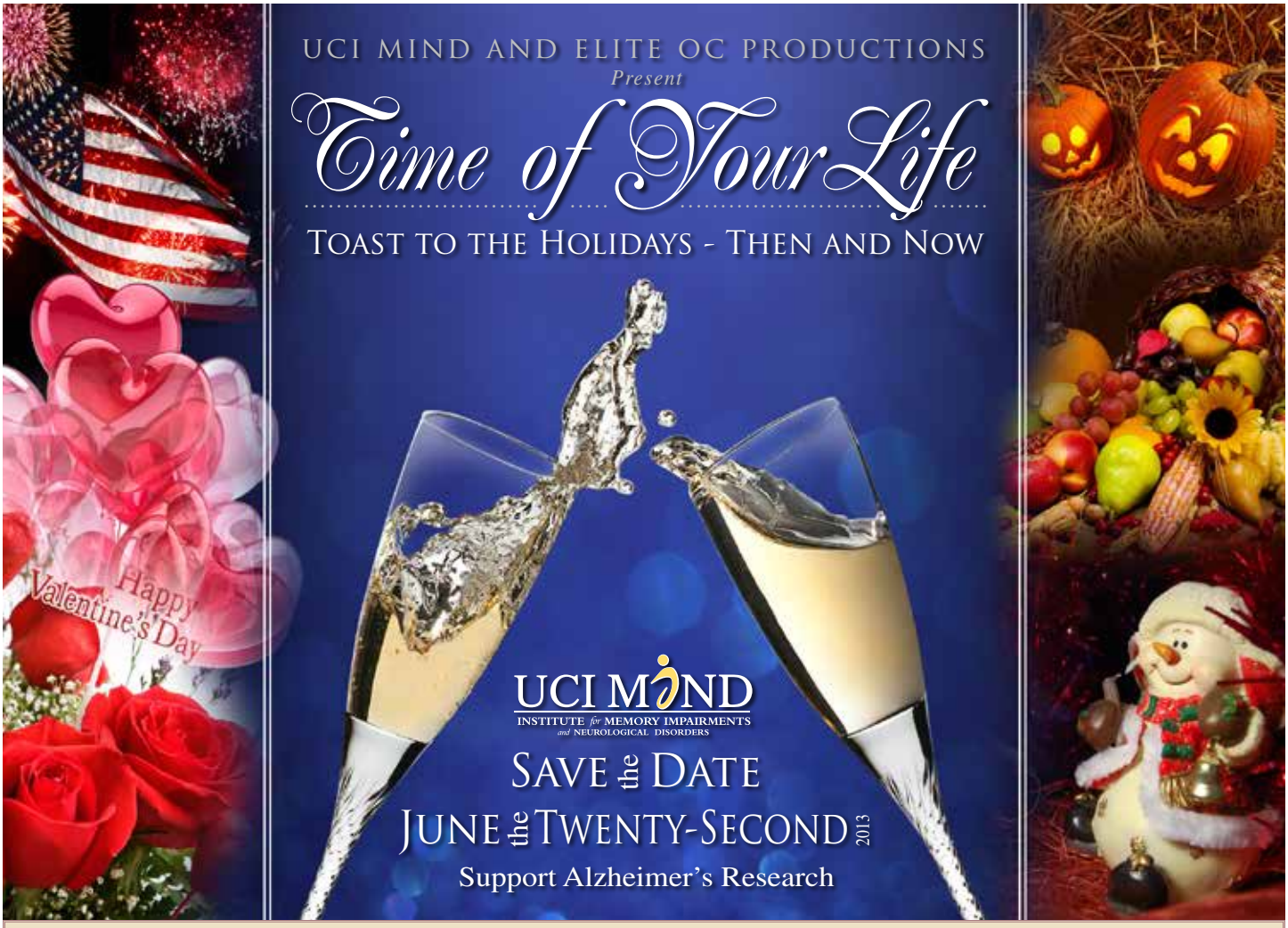
Rachel Rice

Founded with the goal of promoting the advancement and discussion of neurological research, ReMIND (Research and Education in Memory Impairments and Neurological Disorders) held its 4th Annual Emerging Scientists Symposium on February 21, 2013 at the University Club on the UCI campus. Drawing over 100 attendees from the UCI community, the event featured research presentations by fourteen graduate students and five postdoctoral scholars, demonstrating the breadth and depth of the research carried out at UCI.

*Nicholas DiPatrizio, PhD (far left), and Annie Vogel-Ciernia (far right) stand with Dr. Frank LaFerla, Director of UCI MIND, and Dr. Clive Svendsen, Director of the Cedars Sinai Regenerative Medicine Institute.*

Opening comments from Dr. Frank LaFerla, Director of UCI MIND and faculty advisor for ReMIND, were followed by five sets of talks, each chaired by a distinguished UCI professor. Annie Vogel-Ciernia and Dr. Nicholas DiPatrizio received awards for best graduate student and postdoctoral research presentations, respectively. The symposium concluded with a keynote address by Dr. Clive Svendsen, Director of the Cedars Sinai Regenerative Medicine Institute, who spoke about employing stem cells as potential therapeutics for both Lou Gehrig's disease (ALS) and Parkinson's disease.

The graduate student-run ReMIND organization is co-chaired by Sam Marsh, Erin Burke, and Rachel Rice, who organized the symposium. ReMIND is greatly appreciative of support received from the Sue and Bill Gross Stem Cell Center, Office of Research, Graduate Division, Department of Neurobiology and Behavior, and the School of Biological Sciences.




**Mark your calendar to join us for the Time of Your Life on Saturday, June 22, 2013!**

5:30 – 11:00 P.M. at The Hangar at the Orange County Fairgrounds
Support Alzheimer's Research at UCI MIND

Celebrate the Holidays – Then and Now
***Valentine's Day***
***Halloween and Thanksgiving***
***Holidays at the Lodge***
***and a Happy New Year's Eve countdown in the Big Apple.***

It will be a unique experience! You will enjoy an evening of virtual-video images enveloping you in enchanting holiday sights and scenes.

There will be memorable holiday foods and drinks all evening long. Live entertainment, dancing, a unique auction and more are in store.

Co-Chairs Jacqueline DuPont and Marc Carlson, Linda and Burton Young, Rosemary and Rand Sperry, Alice and Sean Cowell and Dana and Tom Chou invite you to an Elite OC Productions event to raise funds for UCI MIND.

Early Bird Special – Tickets $200 per person until May 5, 2013; $250 thereafter.
Ultimate Premiere Reserved Tables of ten - $3,000. Sponsorship opportunities are available.

For further information contact: Linda Scheck, 949-824-3251 or lscheck@uci.edu
www.mind.uci.edu

# Time of Your Life Co-Chairs are Not Taking Their Roles Sitting Down!

Marc Carlson and Dr. Jacqueline DuPont
Linda and Burton Young

Our Co-Chairs are determined to raise funds for Alzheimer's research at UCI MIND. It is unusual to have five couples co-chair a fundraising event. But that is exactly what Jacque DuPont and Marc Carlson, Dana and Tom Chou, Alice and Sean Cowell, Rosemary and Rand Sperry, and Linda and Burton Young have joined together to do.

Each couple has been touched directly by caring for a close family member who has the disease. These couples want to find ways to stop others from being diagnosed with Alzheimer's disease. They have each pledged to contribute personally to help underwrite the Time of Your Life and to ask others to join them in doing so as well.

Rosemary and Rand Sperry

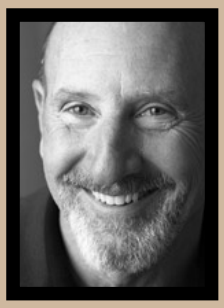
The event has the potential to raise large amounts to fund UCI MIND researchers. For the first time, our donors can contribute to the event online. You and your friends and colleagues can purchase tickets to attend the event, buy a table, become a sponsor or make a donation online. Any amount counts.

Dana and Tom Chou and Alice and Sean Cowell

You can use our ten Co-Chairs as your example. Go to the Time of Your Life website and join us. Ask your friends to join you by attending this exciting event celebrating the holidays – then and now. Make a difference. Be part of the solution.

*For a special message about the Time of Your Life event, use your mobile device and a QR Code app to scan the code to the right.*

## *Donors Join in Challenge to Fund Research*



*Supporting Kenneth R. Chiate's challenge match to fund Alzheimer's research in the LaFerla lab in memory of his wife, Jeannette Chiate, are the following donors to UCI MIND:*

Ronald R. Berkholtz
Linda M. Birke
John R. Cadarette, Jr.
Lawrence D. Canarelli
Gary and Peggy Chiate
Richard and Marcia Chiate
Convergent Wealth Advisors
Catherine and Nathaniel Estacio
William and Adrienne Frumovitz
Martin and Mimzy Goodman
Bobby and Fran Green, Starwood Group, LP
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Michael S. Lurey and Laurie Hasencamp
John F. and Jodie McGuire
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# GIVING AT UCI MIND

*Helping UCI MIND Research Ways to Make Memories Last a Lifetime*

## Innovative Ways to Support Research

Linda Scheck, (949) 824-3251, lscheck@uci.edu

His wife suffered from Alzheimer's disease; she was diagnosed at 58 and succumbed to it ten years later. During her illness, he explored many treatment options to no avail. He turned his loss and frustration into action. He sent an appeal to his friends and colleagues telling them that he would match their donations dollar-for-dollar.

He told them that researchers need "fresh new theories to pursue and funds to pursue them," and that, although he had contributed to many worthwhile causes, he had never asked anyone else to make a donation. He was making an exception this time because he strongly believes so much more can be accomplished with adequate funding for new and promising research. That is how Kenneth R. Chiate was able to raise a substantial amount for a challenge appeal to fund a promising research study being undertaken in the lab of Dr. Frank LaFerla, Director of UCI MIND.

Another man, who had cared for his wife with Alzheimer's disease for many years, attended a Behind the Scenes Tour of UCI MIND. He heard the research presentation, toured the laboratory and held a human brain in his hands. He saw the potential and hope of research was limited only by funding. When his wife passed, he remembered. He thought of the researchers who were eager to pursue treatment options that had promise but who could not move forward because they lacked funds. These researchers might be able to discover treatments that could have helped his wife. He decided to donate a one-time, anonymous, substantial gift that holds the promise of discovery.

Diane Mondini, who owns Caring Companions at Home, has found a way to donate in an innovative manner by joining forces with A Charity for Charities, "Community Cents." She sends a percentage of her credit card transaction fee savings, garnered through the unique charity, passing them on to UCI MIND. She designates these continuous, ongoing, monthly earnings to Alzheimer's research. It is not complicated for her business and while the monthly donations are modest, they add up over the months and years.

A family devastated by a parent's Alzheimer's disease formed a family foundation to support causes important to them. This family recently donated funds to support educational outreach for UCI MIND, helping to underwrite the popular "Ask the Doc" forums.

The grandchildren of a woman named Betty, who lived in the Midwest and had suffered from dementia for many years, wanted to honor the grandmother they all adored. They felt helpless in their need to do something until deciding to form a family foundation in their grandmother's name. They established Betty's Foundation and started raising money. They held garage sales, jewelry parties, musical events – as Betty loved music and dancing – silent auctions and harbor cruises. In a period of a few short years, they raised thousands of dollars for research at UCI MIND.

Some donors have requested anonymity. Others have allowed us to use their names. All are part of the slowly expanding number of individual donors and foundations in our community supporting our mission of *researching ways to make memories last a lifetime.*

Research today translates into hope for tomorrow. Are there any creative ways you can imagine that would make it possible for you to invest in discovery?

# Leaving a Legacy of Hope...

Have you ever thought about what kind of legacy you will leave and how you will be remembered? What will be your legacy? Most of us define legacy as a bequest or will, a financial gift we give after we die. It can be seen as more than just the transfer of money. A legacy can also pass on your values and philosophy of life to the loved ones you leave behind. You can let your heirs know what you consider important and set an example of societal stewardship.

When you think about your legacy, you may consider your memories, your family and others in your life who have influenced you and those whom you have touched. What if you could expand your legacy? What if you could have a broader impact on the world, one that would not only perpetuate your memory, but also change the world for the better?

When you leave a bequest to UCI MIND, you can have this kind of impact. Your legacy gift can perpetuate your memory and help find a cure for Alzheimer's disease.

Leaving UCI MIND as a beneficiary of your estate has other benefits as well. For instance, your estate gift may help your heirs and your estate mitigate taxes.

We would like to invite you to consider being a part of our grand vision by creating a lasting legacy for yourself that enables UCI MIND to *research ways to make memories last a lifetime.* Call our UCI Director of Planned Giving, Roland Ho, at 949-824-6454 to find out more about how you can create your legacy.

Dr. Lowell and Ina Zeleznick

## UCI MIND Matters Club

You are invited to join the MIND Matters Club.

Are you eager to learn more about recent discoveries in Alzheimer's research at UCI MIND and elsewhere? Are you interested in meeting experts in the field of cognitive fitness? Are you interested in promoting your own cognitive health as you support research at UCI MIND?

The MIND Matters Club may be for you. It is a group of individuals committed to helping UCI MIND expand our understanding of Alzheimer's disease and other neurodegenerative disorders through research, education and service to the community.

Members of the MIND Matters Club receive such benefits as quarterly private receptions featuring expert speakers on cognitive fitness; a quarterly news brief highlighting recent discoveries; an annual appreciation event at the home of Director, Frank LaFerla, Ph.D., offering an opportunity to "meet and greet" UCI MIND researchers; and, if desired, a confidential annual memory screening and personalized brain health consultation, including a review of your risk factors.

The MIND Matters Club recognizes donors who contribute $1,906 or more annually to UCI MIND. Contact Linda Scheck, Director of Development and Donor Stewardship at 949-824-3251 or lscheck@uci.edu to discuss this unique donor club supporting Alzheimer's research at UCI MIND.

# DONATIONS *from* September 2012 - March 2013

We thank the following benefactors who are making a difference in supporting our mission of *making memories last a lifetime* through research directed at uncovering the causes of memory impairments and neurological disorders such as Alzheimer's disease. Through our discoveries and outreach we are helping achieve the goals of diagnosing Alzheimer's disease earlier, treating it effectively and supporting affected individuals and their families.

## Honoraria

***In Honor of Mrs. Betty Abrams***
Dr. and Mrs. Marvin Abrams

***In Honor of Shelton Babin***
Mr. Robert G. Perez

***In Honor of Paul and June Hunter***
Mr. Paul E. Hunter

***In Honor of the 53rd Birthday of our daughter, Cheryl Pytlarz***
Mr. and Mrs. Bill Emrich

***In Honor of Linda Scheck***
Dr. Donald Hansen

***In Honor of Helen S. Simpson***
Mr. and Mrs. Robert Naeve

***In Honor of my Birthday!***
Ms. Barbara Stroup

## Memorials

What a wonderful way to commemorate a loved one and to help support Alzheimer's disease research. Many families choose to make a lasting donation in memory of a friend or loved one in lieu of flowers. Once the memorial donations have been received, a thank you acknowledgment is sent to the donor.

As requested by the donor, we notify the family or other appropriate individual of the gift. All donors are recognized in the MIND Matters newsletter, unless the donation is designated as anonymous.

## Memorials Continued

***In Memory of Betty Abrams***
Dr. and Mrs. Marvin Abrams

***In Memory of Virginia Barry***
Mr. and Mrs. Mike Hablitzel

***In Memory of Judy Berman***
Ms. Aylene Kovery and Phil Moser
Ms. Eileen Lafferty

***In Memory of John Briones***
Mr. and Mrs. Mark DeBono

***In Memory of Mrs. V. J. Coates***
Mr. and Mrs. Nathaniel Brenner

***In Memory of Mr. and Mrs. William W. Drewry***
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***In Memory of John R. Feehan***
Ms. Dorothy Feehan and
Ms. Kathleen Malinski

***In Memory of Donald Geib***
Ms. Mary Geib

***In Memory of Bryan Hsiung***
Ms. Victoria Hsiung

***In Memory of Dr. Marion Jabczenski***
Mr. and Mrs. David Emery

***In Memory of Paolo La Ferla***
Mr. and Mrs. Hsin Liu
Drs. Stephanie and James Moore
Ms. Linda Scheck

## Memorials Continued

***In Memory of Mr. K. L. Liu and In Honor of Luter Liu***
Ms. Linda Scheck

***In Memory of Douglas Maron***
Ms. Shari L. Maron

***In Memory of Modena J. McFarlane***
Mr. Harlan Leonard

***In Memory of Carol (Becky) McGaugh***
Ms. Audrey M. Schneiderman

***In Memory of James W. Robertson***
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***In Memory of Carmen Ruiz***
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Ms. Alison Jones

***In Memory of Gordon Smale***
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***In Memory of Lou Steele***
Mr. Boyd Steele

***In Memory of Einar Stefferud***
Mr. and Mrs. Jerry Sweet

***In Memory of Edna West***
Ms. Joyce Bragg

***In Memory of Rebecca Yasuko Larsen***
Ms. Gillian Bradshaw

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Ms. Diane Mondini, Caring Companions at Home, A Charity for Charities
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Mr. and Mrs. Raymond Otte
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Mr. and Mrs. Wellington White
Ms. Kimberley Yourman

*Join us for...*

# Ask the Doc

Professor Frank LaFerla, director of UCI MIND, moderates a panel of clinicians and researchers who will answer your most pressing questions about Alzheimer's disease, treatments, prevention, and caregiving.

**Wednesday, May 29, 2013, 1:00 - 3:00pm**

**Laguna Woods Village - Clubhouse 3**
23822 Avenida Sevilla, Laguna Woods, CA 92637

Open to the public. Individuals who are not residents of Laguna Woods Village must RSVP at (949) 824-2382, press option 4, and leave a message or email mpsoares@uci.edu.





## How can I Support UCI MIND Alzheimer's Research through United Way Workplace Giving?

Even though UCI MIND is not a United Way member agency, you CAN designate your workplace donations through United Way to support our research. Not widely promoted, designating United Way donations is an important option for people who want to use this vehicle to support Alzheimer's research.

Simply indicate on your United Way Campaign form at your workplace that your donation should go to "UCI Foundation to support UCI MIND Alzheimer's Research." Our 501(c)(3) Tax ID# 95-2540117 is for "UCI Foundation" – so that is how we should be designated on your payroll deduction form.

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# Research Today. Hope Tomorrow.

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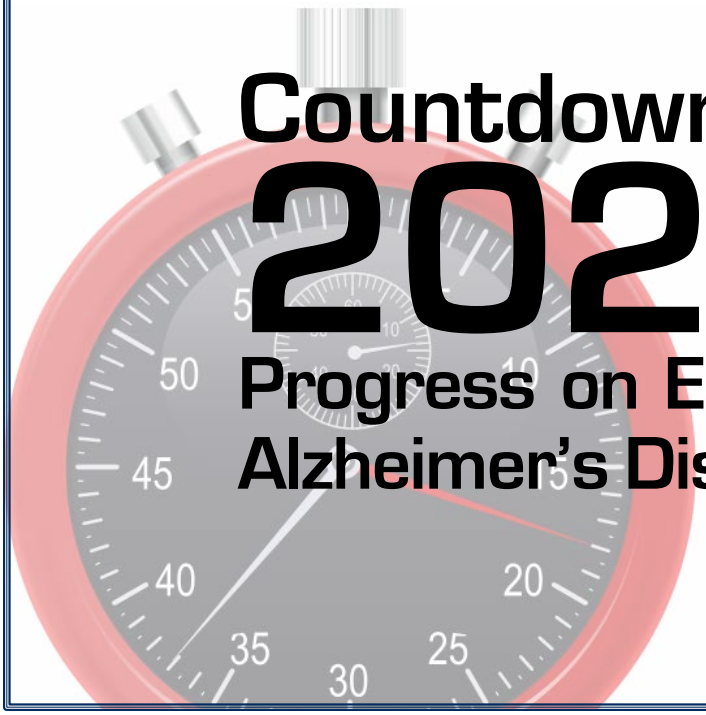
*Editor: Cordula Dick-Muehlke, Ph.D., Director of Education*
*Layout: Marcelo Soares, Education Coordinator*

## 24th Annual Southern California Alzheimer's Disease Research Conference

September 20, 2013 • Hilton Orange County / Costa Mesa



## Countdown to 2025

## Progress on Ending Alzheimer's Disease

### Register Online Today

act.alz.org/24thAnnualResearchConference

To register by phone or for questions, contact Marcelo Soares at (949) 824-9896, or mpsoares@uci.edu.

**Early bird registration by August 2, 2013**

- $200 for professionals seeking continuing education units
- $85 for family caregivers, students, and individuals with MCI or dementia

*Hosted by UCI MIND in partnership with the Alzheimer's Association, Orange County Chapter*

UCI MIND Institute for Memory Impairments and Neurological Disorders

alzheimer's association
the compassion to care, the leadership to conquer