

RESEARCHING WAYS TO MAKE MEMORIES LAST A LIFETIME

Frank M. LaFerla, Ph.D.

Alzheimer's disease is a complex, multisystem disorder that can only be tackled through multiple simultaneous lines of research designed to reveal the role of various disease mechanisms, identify new targets for treatment and therapeutic strategies, and uncover protective lifestyle strategies. Finding effective ways to prevent and ultimately treat dementia is the major research goal of UCI MIND. This goal is an inherent part of our fabric or DNA, which is why our vision is to research ways to make memories last a lifetime. We will continue on this path until Alzheimer's disease itself becomes a memory.

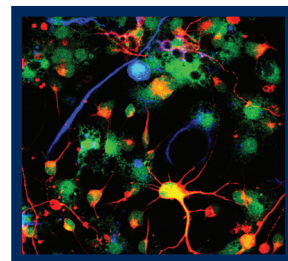
To achieve our goal, UCI MIND is engaging in a wide range of research, from innovative exploration of stem cell therapy to our longstanding studies of cognitive impairment in the oldest old and people with Down syndrome. Led by internationally distinguished faculty with a track record of innovation and expert clinicians, our studies seek to reverse the mechanisms that cause cognitive decline.

Research is a slow, evolutionary and sometimes tedious process that requires strict and rigorous methodology to evaluate existing hypotheses and provide evidence that either rejects or supports them. Your encouragement, support and direct

involvement as research volunteers are making it possible for UCI MIND to pursue six major areas of research.

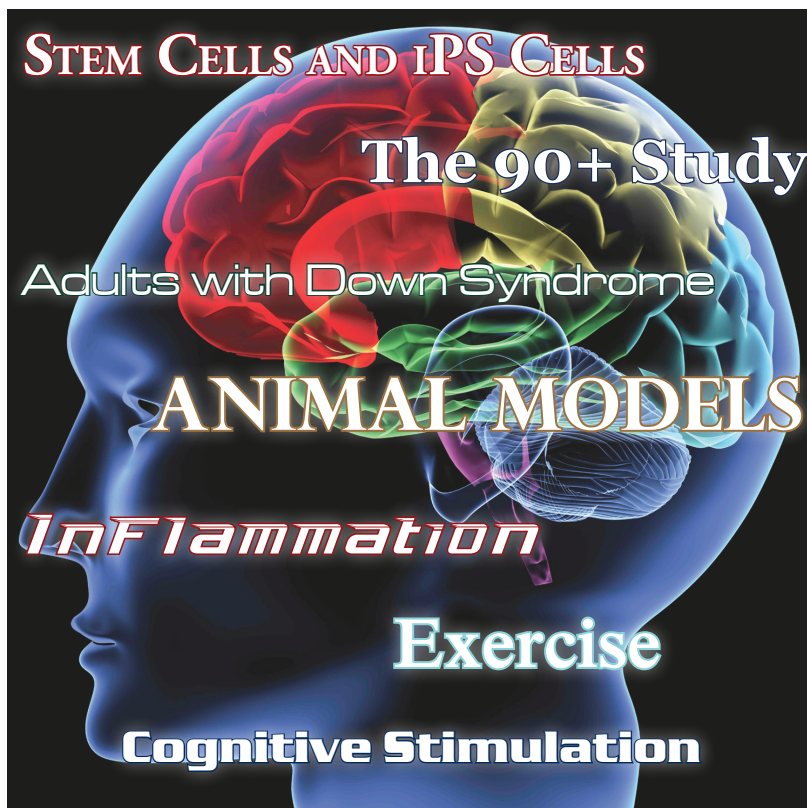
STEM CELLS AND IPS CELLS

Stem cell therapy for Alzheimer's disease is receiving greater attention, particularly with UCI MIND investigators pioneering this avenue of research. Stem cells are both controversial and exciting. The controversy surrounding stem cells is based on when the cells are harvested, with many individuals ethically objecting to the use of human embryos. UCI MIND investigators do not use embryonic stem cells in



their research. Likewise, it is critical to point out that many stem cells can be directly obtained from adults, thereby bypassing any ethical concerns.

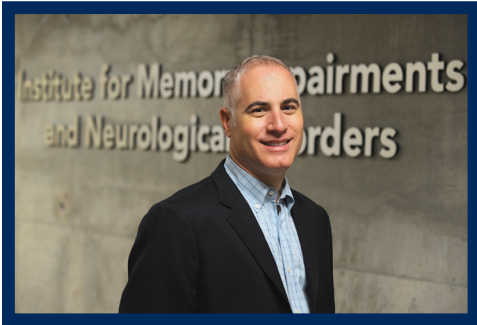
Few discoveries in biology have as great a transformative potential for altering modern medical research as induced pluripotent stem (iPS) cells. Enhancing our ability to study and understand the impact of disease in human cells in ways not previously possible, iPS cells are special because they are both pluripotent and immortal: capable of giving rise to



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From the Director...

Frank LaFerla, Ph.D.



As this newsletter hits your mailbox, we find ourselves, once again, in the middle of a busy holiday season. Amid the hustle and bustle, as the holidays prompt us to do, I've been thinking about our past and our future.

At UCI MIND, we've taken on the challenge of *researching ways to make memories last a lifetime*. Achieving our vision of a world in which Alzheimer's disease is but a memory brings with it responsibilities that we strive to fulfill in all we do at UCI MIND.

SCIENTIFIC INTEGRITY – As set forth in the national plan on Alzheimer's disease, our nationwide goal is to prevent and effectively treat Alzheimer's disease by 2025. Hence, we are doubling down on our commitment to adhere to the highest scientific standards. In science, there are no shortcuts, so we move forward diligently, step by step, generating findings that the medical and lay community can rely on, and laying the groundwork for innovation.

INNOVATION – Finding a cure for Alzheimer's disease demands stretching ourselves beyond "safe next-step science" into cutting edge efforts, such as the neural stem cell therapy that we've tested successfully in Alzheimer's mice, with improvements evident in both memory and synaptic connectivity. Now, we're moving this research forward through a disease team grant funded by the California Institute for Regenerative Medicine, with the goal of bringing neural stem cell therapy to human clinical trials in the next five years.

DISSEMINATION OF ACCURATE KNOWLEDGE – In a world where information about Alzheimer's disease – both accurate and inaccurate – is just a mouse click away, credibility is becoming increasingly difficult to judge. Hence, UCI MIND has assumed the critical responsibility of being the expert, trusted source of information about Alzheimer's disease and the related dementias in this community and beyond. Our internationally recognized researchers and clinicians will continue to make themselves available through events that reach 8,000-plus health care and aging services professionals, caregivers, and community members at large annually.

COMPASSION – While we strive to find a cure or a way to effectively prevent Alzheimer's disease, we remain committed to supporting the families living with dementia today. At our Memory Assessment and Research Center, our expert, caring clinicians and support staff handhold individuals with memory loss and their care partners through the diagnostic process, provide them with a roadmap for the future through comprehensive family conferences, and help them access community resources.

STEWARDSHIP – Our ability to advance knowledge about Alzheimer's disease depends on support from public and private sources, including many individual donors who give generously of their personal resources. We are committed to being good stewards of the funds we receive, maximizing the impact of every dollar. We thank you for your trust in us, and working together we can succeed in the battle against Alzheimer's disease.

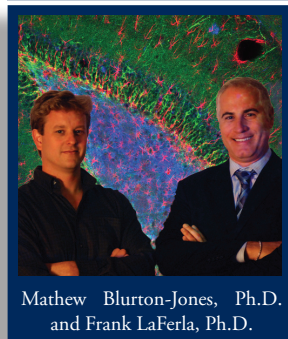
GRATITUDE – All of us at UCI MIND are grateful for the opportunity we have been given to make a difference in the lives of families living with Alzheimer's disease today and those affected in the future. We approach our work daily with deep appreciation for our supportive and generous community of friends.

As we enter 2013, we redouble our commitment to lead the way towards a world free of Alzheimer's disease and fulfill these responsibilities to our family of friends and donors, and the community at large.



IN THE NEWS

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



Mathew Blurton-Jones, Ph.D.
and Frank LaFerla, Ph.D.

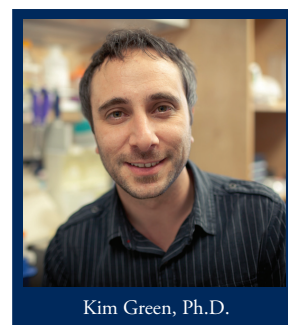
CIRM AWARD ENABLES PURSUIT OF STEM CELL THERAPY FOR ALZHEIMER'S

A \$20 million Disease Team Grant from the California Institute for Regenerative Medicine (CIRM) will enable UCI MIND to advance stem cell treatment of Alzheimer's disease in partnership with Stem Cell, Inc. of Newark, California. Led by Dr. Frank LaFerla, a world-renowned researcher in Alzheimer's disease who serves as the director of UCI MIND, and Dr. Mathew Blurton-Jones, Assistant Professor in the Department of Neurobiology and Behavior at UCI, the four-year project is designed to bring neural stem cell treatment into human clinical trials. Funding will support pre-clinical development of stem cell therapy using Alzheimer's mice. Promising early studies at UCI MIND have shown that treating Alzheimer's mice with neural stem cells can improve both memory and synaptic connectivity.

ALZHEIMER'S ASSOCIATION AWARDS THREE NEW INVESTIGATOR GRANTS

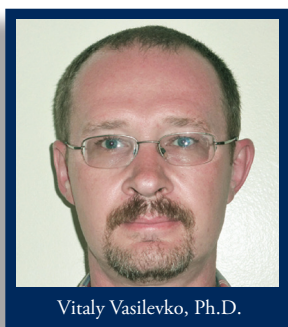
MICROGLIAL CELLS AS A POTENTIAL THERAPEUTIC TARGET

Dr. Kim Green will study the role of microglia, immune cells in the brain, in the formation of both beta-amyloid and tau pathologies. In brains affected by Alzheimer's disease, microglia abnormally "switch on" and may contribute to additional cellular, neuronal, and tissue damage that occurs. Dr. Green's research is designed to determine if microglia facilitate the formation of plaques and tangles through a specific molecular pathway. If so, microglia would represent a novel therapeutic target. Additionally, Dr. Green will elucidate the role of microglia in immunotherapy – a promising treatment for Alzheimer's disease currently in clinical trials. By understanding how immunotherapy facilitates the clearance of plaques and tangles from the brain affected by Alzheimer's disease, we can design more efficient ways to remove these pathologies.



Kim Green, Ph.D.

DEVELOPMENT OF VACCINE THERAPIES



Vitaly Vasilevko, Ph.D.

With his award, Dr. Vitaly Vasilevko will study vaccine therapies in transgenic mouse models of Alzheimer's disease. His goal is to develop vaccines against the beta-amyloid protein, one of the primary neuropathological hallmarks of Alzheimer's. In this study, vaccines will target highly pathogenic forms of beta-amyloid modified by pyroglutamate - an uncommon amino acid derivative - that resist normal enzymatic clearance and result in increased aggregation in the brain. Triggering the immune system to remove these pathogenic beta-amyloid species from the brains of transgenic mice has invaluable translational potential. Dr. Vasilevko's research can reveal important immunological targets for novel therapeutic approaches in persons affected by Alzheimer's disease.

ADVANCING STEM CELL THERAPEUTICS

Dr. Matthew Blurton-Jones was awarded a grant for his ongoing work in the development of neural stem cell therapeutics for Alzheimer's disease. In this project, Dr. Blurton-Jones and his team will genetically modify neural stem cells to enhance the degradation of beta-amyloid protein in the brain. Cells will be transplanted into the hippocampi of transgenic mice exhibiting both beta-amyloid pathology and neuronal death. The modified cells are expected to remove beta-amyloid, preserve neurons, and improve learning and memory. Through this effort, Dr. Blurton-Jones hopes to determine if target-specific modifications to neural stem cells can translate into promising new combined therapeutic approaches for patients with Alzheimer's.



Mathew Blurton-Jones, Ph.D.

Meet the Faculty

DAN GILLEN, PH.D.



Dr. Daniel Gillen, Associate Professor of Statistics, Epidemiology, and Public Health, serves as the leader of the Data Management and Statistics Core (DMSC) for the UCI MIND Alzheimer's Disease Research Center (ADRC). After earning his doctorate in Biostatistics at the University of Washington, Dr. Gillen started his career at the University of Chicago before joining the newly formed Department of Statistics at UCI in 2004.

Dr. Gillen is dedicated to identifying novel predictors of Alzheimer's disease and treatments for the condition while maintaining scientifically rigorous standards. He explains, "The acceptance of scientific hypotheses by the broader community demands supportive empirical evidence. In the real world, the results of scientific investigation can be clouded by variability in outcomes that may be due to unknown and/or uncontrollable factors. For example, a medication may, on average, be beneficial for treating a given condition in the population. Yet, there will still be some individuals for whom no benefit is observed. Statistics is a discipline that quantifies uncertainty in observed data by using probability to make statements about confidence in favor of, or against, scientific hypotheses." Dr. Gillen collaborates with multiple ADRC investigators, noting that statisticians are an integral component of successful research programs. "Statisticians play a crucial role in Alzheimer's research by refining scientific questions, designing efficient studies to answer those questions, and analyzing observed data to produce scientifically credible results. In doing so, we can identify markers and beneficial treatments faster while maintaining confidence in our conclusions."

Dr. Gillen's own research focuses on developing statistical models to address problems where adequate methods do not exist. He is well known for his efforts to sequentially test data as it is gathered, thereby enabling investigators to use fewer patients in studies and decreasing the cost, time, and patient burden often associated with clinical research.

Meet the Community Health Program Supervisor

PETER KNAUP



Peter's road to becoming the Community Health Program Supervisor for the Memory Assessment and Research Center (MARC) at UCI MIND has been a long and circuitous one. After brief stints in journalism and filmmaking, Peter began a career in retail and customer service management, which was foreshortened in 2001 when his mother was diagnosed with Alzheimer's disease. Upon taking on her care, and watching her cognitive and physical deterioration, Peter vowed to make a difference in the fight against Alzheimer's disease. Following his mother's death in 2005, Peter became a volunteer Public Policy Advocate for the Alzheimer's Association of Orange County, making yearly trips to Sacramento and Washington, D.C., to educate legislators about Alzheimer's and the toll it takes on caregivers. It was during these advocacy trips that Peter learned about UCI MIND. When the position of Patient Care Coordinator became available at the MARC, Peter jumped at the opportunity to use what he had learned as a caregiver to help others.

"Working directly with patients and caregivers at the MARC has been a blessing. It has given me a chance to share my experiences as a caregiver with families, who in turn have appreciated the opportunity to share their own feelings and experiences with someone who has been through the same circumstances."

For five years as a Patient Care Coordinator, Peter has helped guide families through the comprehensive assessment process, from the initial contact to the receipt of the final diagnostic report. In his new role, he plans on improving and streamlining administrative procedures to ensure the best patient and caregiver experience possible. Additionally, Peter has begun training as a support group facilitator with the Alzheimer's Association.

Peter is especially thankful for the support of his wife, Laurie, and labrador retriever, Clarence, with whom he enjoys both relaxing and traveling when not at work.

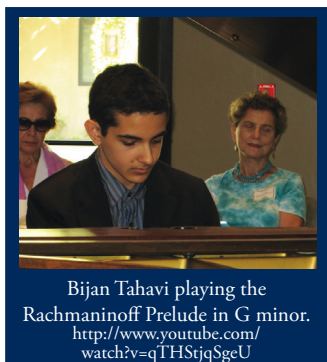
Appreciating ADRC Research Volunteers

Cordula Dick-Muehlke, Ph.D.

Since its inception in 1999, the NIH-supported Alzheimer's Disease Research Center (ADRC) at UCI MIND has relied on hundreds of research volunteers who have helped advance knowledge about the progression of normal aging to Mild Cognitive Impairment (MCI) and Alzheimer's disease by participating in our longitudinal study of aging and memory. Making a lifetime commitment, these volunteers, who include healthy older adults and individuals with MCI or a dementia like Alzheimer's disease, allow clinicians to track their cognitive and physical health annually, contribute biological specimens (e.g., blood, plasma, and cerebral spinal fluid), and agree to brain donation upon death. All data contributed by volunteers at the UCI MIND ADRC and 28 other federally funded Alzheimer's Disease Centers are made accessible to researchers worldwide. Our volunteers are, for example, helping us to better understand why some people remain cognitively healthy until death while others develop dementia; how lifestyle strategies, like engaging in regular exercise, can help reduce risk for dementia, and, the changes in biomarkers, as seen in brain images or cerebral spinal fluid, that foreshadow Alzheimer's disease and could lead to earlier diagnosis and treatment.



Dr. Cordula Dick Muehlke with Vance and Rita Moreira.



Bijan Tahavi playing the Rachmaninoff Prelude in G minor.
<http://www.youtube.com/watch?v=qTHStjSgeU>

To recognize our faithful research volunteers, the UCI MIND ADRC hosted its 1st Annual Appreciation Breakfast on July 31, 2012. Held at St. Mark Presbyterian Church in Newport Beach, the event featured a performance by a budding concert pianist, 14-year-old Bijan Taghavi. Dr. Frank LaFerla, Director of UCI MIND, kicked off the morning's program by expressing his personal appreciation to our ADRC volunteers for supporting UCI MIND's mission of *researching ways to make memories last a lifetime*. Following words of gratitude from Dr. Aimee Pierce, ADRC Medical Director, and Dr. Malcolm Dick, Neuropsychologist, clinical and support staff took turns acknowledging ADRC volunteers in 5-year increments, starting with those who joined the longitudinal study 20 or more years ago. While recognizing volunteers with appreciation certificates and the gift of an ADRC lapel pin, staff traced progress in Alzheimer's from 1992, when no treatments were available and humane care was the only option, to today, when UCI MIND is leading the way in developing stem cell therapies to combat the disease. A raffle drawing that included gifts ranging from a set of Tiffany and Company water glasses to a one-hour gondola ride, and centerpieces created by Susan Randhawa, LCSW, Senior Psychometrist, wrapped up the morning.

To learn more about UCI MIND's longitudinal study of aging and memory, or to volunteer, contact the Memory Assessment and Research Center at (949) 824-2382.



UNIVERSITY of CALIFORNIA • IRVINE

Alzheimer's Disease Research Center

Learn about your memory while advancing knowledge of memory and aging

Volunteers with **mild memory or thinking problems** are needed for a study on aging

Eligible participants will benefit from:

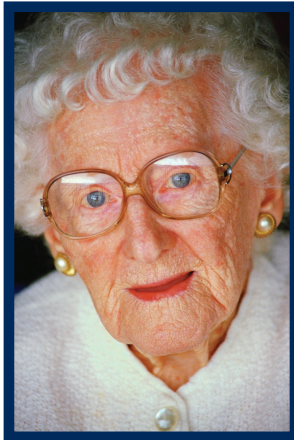
- Free comprehensive annual evaluations with feedback and recommendations from experts
- Opportunities to participate in additional studies (e.g., imaging, biomarkers, prevention, and clinical drug trials)
- The gratification of helping advance knowledge of aging and how to better treat Mild Cognitive Impairment, Alzheimer's disease, and other cognitive disorders

To participate, you must be 65 or older, have mild memory or thinking difficulties, and have an adult child, spouse or friend willing to answer questions about your everyday activities. If you would like to participate, or want further information, please contact Dr. Carrie Peltz at 949-824-2382, Option 3, or cpeltz@uci.edu.

every cell type in the human body and allowing robust expansion and unprecedented resource sharing. Notably, iPS cells can be derived from skin samples. Through a minimally invasive procedure, any person, even older adults, can easily donate the skin cells needed to develop iPS cells. Given the promise of iPS cells, UCI MIND is seeking to establish a National Alzheimer's Disease iPS Cell Bank as part of our Alzheimer's Disease Research Center. We believe this will be a valuable resource for the entire Alzheimer's research community and fits with our pioneering role in stem cell research.

THE 90+ STUDY

People 90 and older – known as the “oldest old” – are the fastest growing segment of the U.S. population, yet little is known about them. It is critical to understand the factors that are associated with longevity, particularly long life free of cognitive impairment. What makes it possible for some people to live to age 90 and beyond? What types of food, activities or lifestyles are associated with living longer? Answering these questions is not only important for academic reasons. Increasing numbers of oldest old present a public health challenge to promote quality, not just quantity, of life.



Interestingly, The 90+ Study has shown that people who drank moderate amounts of alcohol or coffee rather than abstained and were overweight or normal weight in their 70s and 80s rather than underweight lived longer. Cognitive and physical impairments are common, with over 40% of people 90 and older having dementia and nearly 80% being disabled. Curiously, about half of people with dementia over age 90 do not have sufficient neuropathology in their brains to explain the cognitive loss, but may have multiple, though very mild pathologies. Conversely, about half of the “normals” have pathology and may be either in the pre-clinical stages of a dementia or able to tolerate its buildup and remain cognitively intact. Most recently, it was discovered that 90+ individuals who had difficulty performing physical activities like walking had greatly increased odds of having dementia.

ADULTS WITH DOWN SYNDROME

Improvements in medical care of people with Down syndrome have increased their longevity substantially. Along with this increased longevity comes a higher likelihood of developing Alzheimer's disease. People with Down syndrome possess three copies of chromosome 21, where a key Alzheimer's gene, the one that gives rise to amyloid plaques, resides. Hence, people with Down syndrome make one-and-a-half times the amount of this protein and frequently develop Alzheimer's disease at earlier ages than other populations.



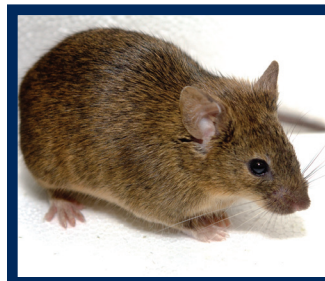
UCI MIND is one of only a few sites throughout the country that studies adults with Down syndrome.

This research has important implications not only for these individuals but also broadly for understanding Alzheimer's disease, as people with Down syndrome represent one of the largest groups to develop early onset Alzheimer's.

Research has shown that seizures are a major risk factor for cognitive decline in people with Down syndrome, a possible contributor being studied in other individuals with Alzheimer's disease as well. UCI MIND investigators have been on the cutting edge of enrolling people with Down syndrome in clinical trials and also in developing new technologies such as telemedicine to diagnose and care for these individuals.

ANIMAL MODELS

Significant insights into Alzheimer's disease and related dementias have occurred through studying genetically modified animals. Animal models have helped advance our understanding of the underlying mechanisms of Alzheimer's disease and proven to be invaluable in the preclinical evaluation of potential therapeutic interventions. Continuing refinement and improvements to yield the next generation of animal models will facilitate successes in producing greater



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Beyond Memory: The Behavioral and Neuropsychiatric Symptoms of Dementia

Cordula Dick-Muehlke, Ph.D.

When it comes to Alzheimer's disease and the other dementias, memory loss gets top billing. That's why UCI MIND and its community partners, the Alzheimer's Association of Orange County and Alzheimer's Family Services Center, turned attention to the less understood



Jim McAleer, President/CEO of the Alzheimer's Association - Orange County Chapter, helps to open this year's conference on World Alzheimer's Day.

yet highly prevalent behavioral and neuropsychiatric symptoms of dementia at the 20th Annual Southern California Alzheimer's Disease Conference, held on World Alzheimer's Day, September 21, 2012.

An audience of 560-plus professionals in health care and aging services, caregivers, and community members at large spent the day learning about the non-cognitive symptoms of Alzheimer's disease and other dementias from nationally known researchers and clinicians as well as a panel of individuals with Mild Cognitive Impairment (MCI) and their care partners. Through 41 exhibitors who generously sponsored the event, attendees also gained access to Orange County's rich array of dementia-related community services.



Conference drew a record audience of over 560 health care and aging services professionals, caregivers, and members of the community at large.

Across the day, six key points, as summarized here, emerged about the management of behavioral and neuropsychiatric symptoms in the dementias.

I. USE MEDICATIONS WITH CAUTION

Antipsychotics and other psychotropic medications are commonly used to treat behavioral and neuropsychiatric symptoms in dementia, but these drugs have limited benefit and may even cause harm, as emphasized by Dr. Lon Schneider of the University of Southern California. In

a series of studies, Dr. Schneider and his colleagues clearly demonstrated that atypical antipsychotics (e.g., Seroquel, Risperdal, and Zyprexa) have little benefit over placebo in treating symptoms such as agitation, aggression, and psychosis, come with significant side effects, and increase risk for death. In 2005, the FDA issued a "black box" warning against the use of atypical antipsychotics for dementia-related psychosis due to a heightened risk for death from stroke.

In his discussion of frontotemporal dementia (FTD), Dr. Adam Boxer of the University of California, San Francisco (UCSF), noted that no medications – psychotropics (e.g., atypical antipsychotics and anti-depressants) as well as cognitive enhancers used in Alzheimer's disease (i.e., acetylcholinesterase inhibitors and memantine) – are approved for FTD. Only anti-depressants (e.g., selective serotonin reuptake inhibitors/SSRIs and Trazadone) have proven effective in helping alleviate the neuropsychiatric symptoms of FTD. When used in this atypical dementia, acetylcholinesterase inhibitors (i.e., Aricept, Razadine, and Exelon) have worsened behavioral symptoms while memantine has further impaired cognition and the ability to perform activities of daily living.

Given the limitations of medications in the treatment of non-cognitive symptoms, speakers throughout the day cautioned professionals and family caregivers alike to (1) carefully weigh potential benefits of medications against their risks prior to initiating use, and (2) always try non-pharmacological approaches first to reduce behavioral symptoms. As Judy Cooper, who participated with her husband Jay, in a panel discussion involving individuals with MCI and their care partners, explained, she's decided not to treat Jay's hallucinations with medications for the time being. "When it is more bad than good, we will take the next step, but now it is more good than bad."

II. RULE OUT UNRECOGNIZED MEDICAL ILLNESSES

Unrecognized medical illnesses, use of inappropriate medications (e.g., anticholinergics), suboptimal prescribing, and polypharmacy, can all be the source of new

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behavioral symptoms or worsen existing ones, as described by Dr. Daniel Sewell of the University of California, San Diego. Upon reviewing the charts of 79 older adults who had been admitted to a psychiatric unit for a behavioral disturbance, Dr. Sewell and his colleagues found 34% had an unrecognized medical illness (e.g., constipation, urinary tract infection and pneumonia). To illustrate the impact of medical illnesses on behavior, Dr. Sewell gave the example of a person with both dementia and diabetes who refuses to eat, thus driving blood sugar levels down and precipitating confused, agitated behavior.

Whenever a new behavior emerges or an existing one worsens, clinicians and family caregivers ought to first rule out possible medical causes, including an acute medical condition, exacerbation of a chronic illness, or use of medications known to cause adverse events in older adults as detailed in the 2012 American Geriatrics Society Beers Criteria.

III. RECOGNIZE DIFFERENCES IN BEHAVIORAL AND PSYCHIATRIC SYMPTOMS AMONG THE DEMENTIAS

Like cognitive symptoms, behavioral and psychiatric ones do not look the same across Alzheimer's disease and the other dementias. Both Dr. Mario Mendez of the University of California, Los Angeles and Dr. Maria Luisa Gorno-Tempini of USCF highlighted differences between



Dr. Maria L. Gorno-Tempini, UC San Francisco, answers question.

the frontotemporal dementias, which include both behavioral and language variants. As described by Dr. Mendez, the behavioral variant is characterized by early and predominant changes in behavior and personality (e.g., socially inappropriate conduct, apathy, or compulsiveness). Dr. Mendez noted that affected individuals may have difficulty taking another's point of view, recognizing facial expressions, and stopping themselves from actions they know are wrong (e.g., stealing). In comparison, the language variants, as described by Dr. Gorno-Tempini, feature, for example, slow, halting, and effortful speech (i.e., progressive non-fluent aphasia) and the inability to understand the meaning of words (i.e., semantic dementia). As noted by Dr. Gorno-Tempini, tailoring one's communication style to the specific speech

and language impairments of the individual is essential for preventing misunderstandings and behavioral reactions.

Dementia with Lewy bodies (DLB) is still different in cognitive and behavioral presentation. Characterized by three core features – cognitive fluctuations, early hallucinations, and slowed parkinsonian-like movements – DLB may, as described by Dr. Aimee Pierce, also present with rapid eye movement (REM) sleep disorder, in which the individual acts out dreams. In fact, care partner Judy Cooper noted that her husband, Jay, developed REM sleep disorder a couple of years prior to being diagnosed with MCI due to Dementia with Lewy bodies.

IV. PARTNER FOR EFFECTIVE PROBLEM-SOLVING

Effectively evaluating and addressing dementia-related behavioral and psychiatric symptoms entails partnerships that involve the affected individual, family, and entire health care team.

Urging both physicians and other health care professionals to take a collaborative approach to dementia care, UCI's own Dr. Laura



Dr. Laura Mosqueda, UC Irvine Geriatrics, speaks with Dr. Alan Zamosky, Executive Director of Alzheimer's Family Services Center.

Mosqueda emphasized involving the person with dementia, family, and physician in a shared decision-making process when addressing medication use and other issues. Most importantly, if partnerships are to work, they must, as Dr. Mosqueda noted, involve listening, communication, clear expectations, negotiation, empathy, and compassion.

V. LISTEN TO PEOPLE WITH MCI AND THEIR CARE PARTNERS

Committed to including the voices of people with MCI and early Alzheimer's disease or another dementia, the Southern California Alzheimer's Disease Research Conference features a panel of affected individuals and their care partners each year. Participants in this year's panel shared their experiences of living with challenging behavioral and psychiatric symptoms such as depression and hallucinations while reminding the audience that there is life beyond the diagnosis of MCI or a dementia. Using a range of strategies to cope – such as focusing on the positive, drawing on spiritual resources, exercising regularly, engaging in activities that draw on remaining strengths, and participating in support groups – panelists demonstrated an ability to “rise above” daily challenges. As Steve Heins, who



Gincy Heins and her husband, Steve, who has MCI, share their experiences.

at despite his limitations.

While these couples demonstrated a remarkable resilience, or ability to “rebound,” their journey hasn’t been easy. In fact, at times, it was made more difficult by the health care professionals who didn’t take time to listen to them or explain conditions such as DLB or symptoms such as depression. In her “take home” message to the audience, Judy noted her frustration with professionals assuming DLB is the same as Alzheimer’s disease. “It’s often misdiagnosed; medical professionals need to learn about Lewy body; what it is and how it works; it’s not the same as Alzheimer’s.”



Judy Cooper and her husband, Jay, share what it's like living with his hallucinations, stemming from MCI due to Dementia with Lewy bodies.

Steve’s wife, Gincy, in turn directed her final comment to physicians in the audience, noting, “If you have a patient at risk for depression, spend a couple of minutes telling family members what to look for. Don’t just say, ‘Is he experiencing depression?’ Say, ‘Look for A, B, C, D, or E – if you see A and B, don’t wait for the next visit to follow up.’”

VI. ATTEND TO CAREGIVER STRESS

Behavioral and psychiatric symptoms of dementia are widely recognized as a significant contributor to caregiver stress. As summarized by Dr. Richard Schulz from the University of Pennsylvania, the prolonged stress of caregiving has been associated with depression, poor health and premature death. Caregiver stress may evidence itself through a variety of physical (e.g., disturbed sleep, headaches, gastrointestinal problems, pain, high blood pressure, or susceptibility to colds) and psychological (e.g., moodiness, depression, anxiety, irritability, or substance use) symptoms. In a series of collaborative studies investigating the effectiveness of “Resources for Enhancing

has MCI and struggled with depression, noted, “You have to learn your limitations so you can expand your horizons.” For example, while reading and writing are difficult for Steve now, he’s discovered acting as an activity he can excel

Alzheimer’s Caregiver Health” or REACH, researchers, including Dr. Schulz, learned that effectively reducing difficult behaviors involves teaching caregivers possible causes for and options to alleviate specific symptoms. For example, through REACH, the caregiver whose loved one becomes combative is taught how to calm the individual, look for a trigger, reduce danger and develop an emergency plan, and when to contact the doctor. Alternatively, a caregiver with a loved one who is having difficulty dressing is taught to buy practical clothes and lay them out daily in the order to be put on as well as to give step-by-step instructions and praise. Looking to the future, Dr. Schulz noted that families will increasingly be able to find support for decision-making and care through online sources, such as www.lotsahelpinghands.com, which offers a free social network and allows users to sign up for the purpose of helping each other.

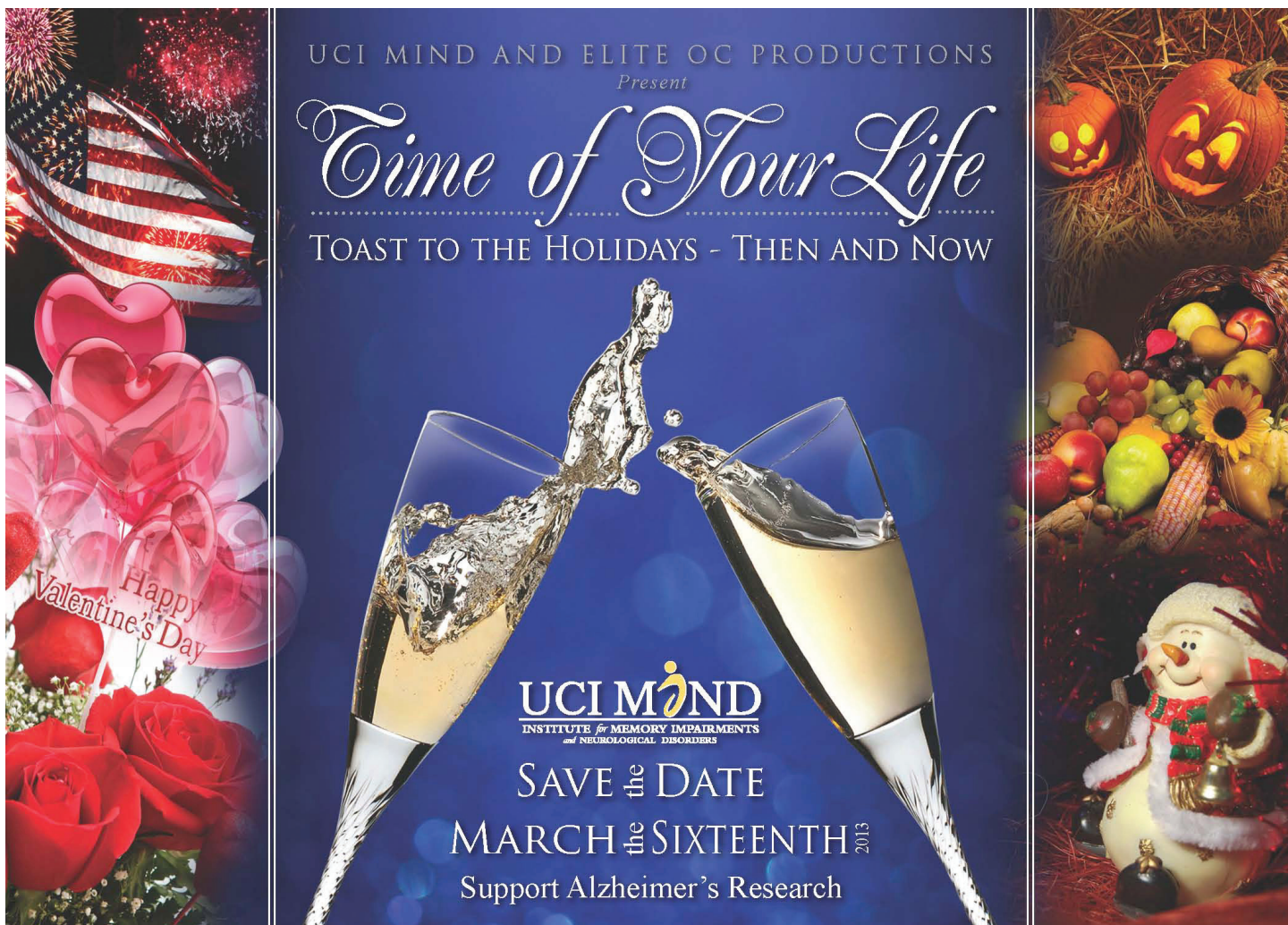
A FINAL THOUGHT - FOCUSING ON THE PERSON

With biomedical solutions such as medications not readily available to ease the behavioral and psychiatric symptoms of dementia, the conference reminded attendees to focus on the humanity of the affected **person**. While often thought of in terms of brain impairment, behavioral and psychiatric symptoms are, more often than not, expressions of need made when language escapes the person. Needs such as hunger, thirst, pain, fear, and loneliness expressed in behaviors demand a personal intervention grounded in knowledge of the person and the nuances of how dementia has affected the individual. Most importantly, such behavioral expressions require our empathy and compassion.

While we strive to find effective treatments and prevention strategies for Alzheimer’s disease and other dementias, all of us at UCI MIND stand in solidarity with the families affected today. Through research, education, and service to our community, we continuously seek to empower families to face their daily challenges with dignity, strength, and hope.



Dr. Frank LaFerla facilitates “Ask the Doc” panel of expert speakers.



**Mark your calendar to join us for the Time of Your Life on
Saturday, March 16, 2013!**

Join us at Time of Your Life 2013 to support research to move us closer to a world without Alzheimer's disease while celebrating your favorite holidays.

Our completely transformed UCI Student Center will feature the following experiences:

Valentine's Day
The 4th of July
Fall's Halloween and Thanksgiving
Holidays at the Lodge
And a Happy New Year's Eve countdown in the Big Apple.

Enjoy each holiday experience created for you by our generous partner, Elite OC Productions. Last year, they took us back to the 1960s. At our 2013 event, we will toast the holidays—then and now!

Food and drinks galore ❖ Dancing ❖ Entertainment ❖ A unique auction

Six o'clock until Midnight on Saturday evening, March 16, 2013.

Early Bird Special – Tickets \$200 per person until February 14, 2013; \$225 thereafter.

Sponsorships available and volunteers are encouraged.

Contact Linda Scheck at lscheck@uci.edu for more information.

UCI MIND is committed to researching ways to make memories last a lifetime.

All proceeds of this event will support Alzheimer's Research at UCI MIND.



GIVING AT UCI MIND

Helping UCI MIND Research Ways to Make Memories Last a Lifetime

DONOR'S STORY - A DAUGHTER'S CARING LOVE IMPACTS RESEARCH

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



Fascinated by understanding how the human mind works, Dr. Rosalyn Laudati chose to follow that special interest by pursuing a career in the field of psychology. She graduated from Brown University (B.A.), then the University of Hartford (M.A.), and finally earned her Ph.D. in psychology at the University of Iowa. She was President of the Orange

County Psychological Association and served on its board for many years. She has always sought to help people make behavioral changes that bring them happiness and enable them to live successful and meaningful lives.

Dr. Laudati has over 20 years of experience in treating adults. She finds helping people a privilege, not a job, and her work is a very important aspect of her life.

It is ironic that in recent years her personal life has become entangled with aspects of her professional life. Over the years she helped many individuals and families searching for answers about what to do for a loved one with dementia. Dr. Laudati helped them cope with the complex array of feelings and other psychological issues that can accompany caring for someone with a neurological disorder. She also advised them about trusted practical resources in the community and helped them develop support systems.

It was when her own mother was diagnosed with Alzheimer's disease in 2007 that she found herself walking along the same path many of her clients had traveled. The story is not all that unusual. Her parents lived on the east coast. Nothing appeared to be awry in all of their interactions, phone calls and frequent visits. However, when her father passed away, it became obvious that the family had been in denial. Her father had "covered up" her mother's memory problems and compensated for what was slowly fading from her ability

to function on her own. After the loss of her husband, Dr. Laudati's mother experienced a deep depression and needed more care.

Taking her own advice, Dr. Laudati researched the best senior care community for her mother. She is pleased that her mother has a high quality of life today, participating in daily routines and meaningful activities, such as making flower arrangements for dinner each night and setting the table. She is engaged and active within the limits of her growing dementia. Dr. Laudati visits her mother every day and remains close to her as they move through this new phase of their lives together.

Dr. Laudati is dedicated to the fight to end Alzheimer's disease so that other families won't have to experience its harsh realities. She has provided a number of meaningful contributions to support research at UCI MIND over the years and is an active member of the MIND Matters Club and Advisory Board. Her most recent contribution supports intriguing research being undertaken by Vinh Quang Nguyen, Ph.D., in collaboration with Malcolm Dick, Ph.D. Drs. Nguyen and Dick are comparing differences in memory for unfamiliar faces among cognitively healthy participants in the UCI MIND Alzheimer's Disease Research Center's longitudinal study and those who have Mild Cognitive Impairment (MCI) or Alzheimer's disease. Results of the study will advance the understanding of these differences and reveal if facial memory can be used effectively as a diagnostic tool.

When asked about the reason for her gifts, Dr. Laudati responded, "I want Dr. Frank LaFerla and his team at UCI MIND to find a cure for me and my own future and, of course, for others throughout the world. I feel a sense of urgency that we must find answers now and I believe that the researchers at this campus are poised to find those answers soon."

UCI MIND is grateful for Dr. Laudati's leadership, ongoing support, and generous contributions.

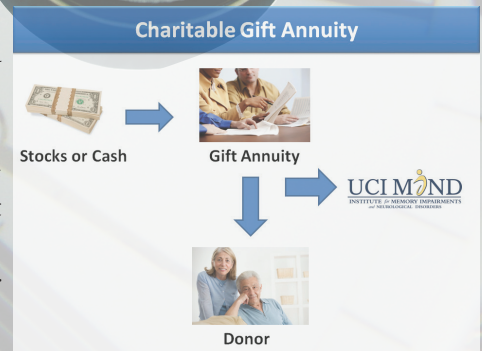
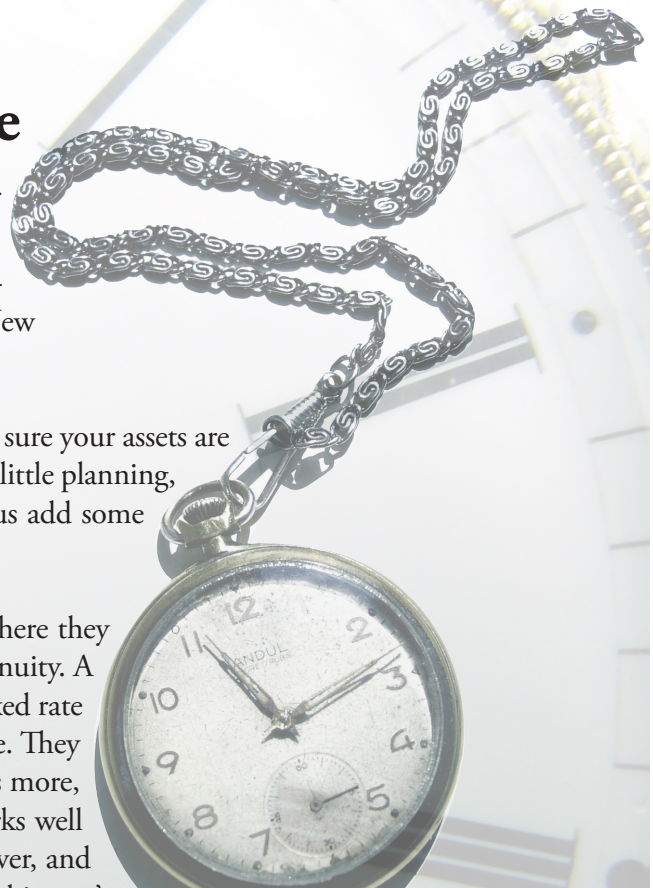
A Great Way to Bring 2012 to a Close

Everyone looks forward to the New Year and its promise of new opportunities, but did you know the old year might also yield rewarding returns? As you look ahead, consider some year-end decisions that can make a big difference, not just for the New Year, but for many years to come.

Think of the remaining days of 2012 as your chance to make sure your assets are working hard for you as much as they possibly can. With just a little planning, you can transform weak dividends into fantastic payments plus add some financial certainty to the end of your year.

Take another look at your stocks. If your dividends aren't where they need to be, you can use your stocks to fund a charitable gift annuity. A gift annuity is a contract where we agree to pay you cash at a fixed rate for the rest of your life. The payment rates are based on your age. They can be as high as 9.0%, and our rate will never change. What's more, there can be significant tax savings for you. This plan also works well with today's very low-rate CDs. Plan now before the year is over, and thank yourself with a charitable tax deduction to offset taxes on this year's return. Call or click for more information on ways to create reliable, fixed income that benefits you and will also help further our good work.

Call Linda Scheck at 949.824.3251 or Roland Ho at 949.824.6454 for more information on how you can create a reliable fixed income that benefits you and will also help others "make memories last a lifetime." You can also find more information on the charitable gift annuity on our website at <http://alz.uci.edu/giving/legacy-giving/>.



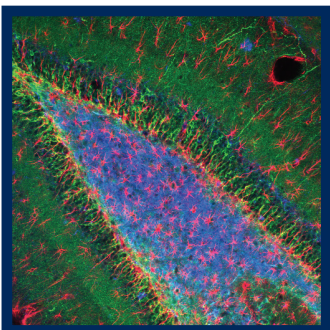
Research, Continued from page 6

concordance between preclinical studies and human clinical trials, and eventually lead to the introduction of novel therapies into clinical practice. UCI MIND investigators have played, and continue to play, a major role in this area.

For example, the 3xTg-AD mouse model developed at UCI is the first and only one to develop both plaques and tangles. Our triple transgenic mice have been widely used by researchers throughout the world, including over 150 investigators in 20+ countries, showing the worldwide impact of science conducted here at UCI MIND.

INFLAMMATION

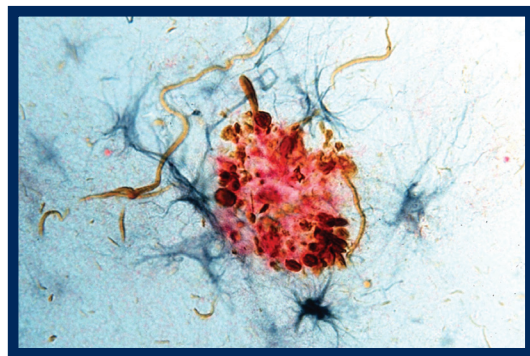
Inflammation is a fundamental protective response of the body. If it becomes dysregulated, inflammation can be a major cofactor in the pathogenesis of many



Continued on page 13

Research, Continued from page 12

chronic human conditions, including Alzheimer disease. Recent analyses of genome-wide association studies have identified at least 8 human genes that increase risk for Alzheimer's disease, and these 8 genes are all related to inflammation. Hence, there is a critical relationship between inflammation and Alzheimer's disease. As a matter of fact, inflammation is a key and invariant pathological feature of Alzheimer's disease pathology, and its impact on disease progression and neurodegeneration remains an area of active investigation here at UCI MIND. Because of the prominent role of inflammation, a large number of faculty labs are specifically investigating the role of inflammation in Alzheimer's disease as part of a cross-disciplinary team-based approach.



Given the central role of inflammation in Alzheimer's disease, our researchers are trying to develop new therapies based on manipulating immune function. For example, immunotherapy involves developing either active or passive immunization (vaccines) against critical components of Alzheimer's brain pathology. Like the work with the animal models, this area of research builds on previous findings, trying to constantly modify vaccination approaches to minimize side effects and improve safety and also increase efficacy.

PHYSICAL AND COGNITIVE STIMULATION

The benefits of physical and cognitive stimulation for brain health are now well-documented. As Benjamin Franklin once said, "exercise invigorates and enlivens all the faculties of body and of mind...It spreads a gladness and satisfaction over our minds and qualifies us for every sort of business, and every sort of pleasure."



UCI MIND researchers have been at the forefront of demonstrating that exercise promotes brain health, improves brain function and can reverse memory deficits in mice with Alzheimer's disease. Turns out that physical exercise increases the production of a key brain nutrient called brain-derived neurotrophic factor, which becomes reduced in the brains of people with Alzheimer's disease. As individuals age, the connections between neurons, or

synapses, are lost. Research shows that physical and cognitive stimulation increases these critical connections, enhancing brain function. So keep active, and don't forget the results described above indicating that individuals 90 and older who had difficulty performing physical activities like walking had greatly increased odds of having dementia.

UPS United Way Workplace Donors *Thank you!*



The group of UPS employees pictured above heard a brief presentation by Dr. Frank LaFerla about the importance of funding Alzheimer's research at UCI MIND. It took them only a few minutes before they stepped forward. They designated their workplace donations to benefit research at UCI MIND and since 2011, they have contributed \$10,500! They know how to get a job done!

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DONATIONS *from* March 2012 - September 2012

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 Gerald Bretts

Ms. Ina Zeleznick

In Honor of Phyllis Brin and

Jacqueline Wengrovitz

Ms. Deborah Brin

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Mr. and Mrs. William Emrich

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.

In Memory of Gene Buckley

Mr. and Mrs. Ken Smith

In Memory of Donna Crean

Dr. Jacqueline DuPont

Memorials Continued

In Memory of Donna Crean

continued

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In Memory of Mr. and Mrs.

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Sr. Martha Linhares

In Memory of Rebecca Yasuko Larsen

Ms. Debra D. Beers
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Dr. Christopher Coulter and Ms.
Pamela S. Newcomb

Memorials Continued

In Memory of Rebecca Yasuko Larsen

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A unique opportunity for you to

Ask the Doc



Dr. Frank LaFerla, PhD, director of UCI MIND, moderates a panel of researchers and clinicians in this open forum. Here is a chance to meet experts who will answer your most pressing questions about Alzheimer's disease, treatments, prevention, and caregiving.



Friday, February 15, 2013, 1:00 - 3:00pm

**Lakeview Senior
Center
20 Lake Road
Irvine, CA 92604**



This event is open to the public.



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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clinical assessments and diagnosis of memory complaints related to Alzheimer's disease and other dementias.

Editor: Cordula Dick-Muehlke, Ph.D., Director of Education
Layout: Shirley Sirivong, Volunteer



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.