SPRING 2017



We Need Your Participation A Full Menu of Studies Open for Enrollment

The UC San Diego, Shiley-Marcos Alzheimer's Disease Research Center (ADRC) is one of the original five of the now 32 Alzheimer's Disease Centers across the country supported, primarily, by the National Institute on Aging. Our ADRC was established in 1984 to translate research advances into improved diagnosis and care for persons with Alzheimer's disease (AD) and related disorders while also focusing on finding ways to prevent, treat, and ultimately cure these conditions. Over the years, we have served as a site for clinical trials of medications currently approved for the treatment of AD, as well as novel but unfortunately unsuccessful clinical trials. Progress in AD depends on gaining a better understanding of mechanisms of disease, on methods for early detection and diagnosis, and on ways of improving quality of life for patients and caregivers. The participation of research volunteers has been essential to our efforts, and we are deeply grateful to you.

In this special issue of Currents, we are proud to bring you an overview of a wide range of investigations currently underway through our ADRC. These studies are open for enrollment and provide many different avenues to advance knowledge and treatment. We hope these will excite your interest and we look forward to advancing our progress together.



Dr. Nguyen and Dr. Chen working with the transcranial Doppler machine

Understanding a Relationship Between Cerebral Vascular Disease and Alzheimer's Disease

By Branko Huisa, MD

Vascular dementia is one of the leading causes of dementia after Alzheimer's disease. However, cerebral vascular disease seems to be a common finding in many patients with Alzheimer's disease. Increasing numbers of studies are now recognizing an important relationship between Alzheimer's and dysfunction of brain vessels. Indeed, a combination of Alzheimer's and vascular factors could be the most common explanation for cognitive impairment in the elderly. This study aims to look at the relationship of simple measurements of vascular markers with Alzheimer's markers.

We are currently offering transcranial Doppler (TCD) and pulse wave velocity evaluations to all Shiley-Marcos ADRC participants. These studies are optional but they can provide important information about your brain vessels and how that is affecting your thinking. TCD is a non-invasive method that measures the cerebral blood flow in order to study the main arteries of the brain. A helmet is used to fix the doppler probes to detect the cerebral arterial blood flow. (See photo.) Pulse wave velocity (PVW) measures the stiff*continued on page 2*

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ness of large body arteries. We have found that stiffness of large arteries is associated with cognitive impairment. PWV is also a non-invasive technique that uses a blood pressure cuff on the leg and a small sensor (like a pen) placed on the neck at the level of the carotid artery to detect the arterial pulsation. Both studies usually take 45 minutes to complete.

Contact Nicole Evangelista: nevangel@ucsd.edu or call (858) 552-8585 ext. 6992 for more Information.

Brain Function and Brain Structure of Human Memory

By Christine Smith, PhD

Persistent memory impairment is the hallmark of Alzheimer's disease (AD) as well as amnestic Mild Cognitive Impairment (aMCI), which is thought to be a transitional stage between healthy aging and AD. New and better tools are needed to identify people who will develop MCI and AD. Early detection of MCI and AD will help people plan for their future and help physicians know who to treat when treatments become available.

We are developing a new cognitive test that measures memory for the past by asking about notable news events and trivia. This test may shed new light on the cognitive decline that leads to MCI and AD. But little work has been done to reveal which brain structures and connections support performance on the test. We want to find out! In our study, we will see if our new test serves as an early estimate of cognitive and neural decline associated with the development of AD.

We are looking for Veterans with or without memory problems to participate. After a 2-hour visit to assess your cognitive abilities, we will schedule 2-3 Magnetic Resonance Imaging (MRI – NO RADIATION) sessions at the UCSD campus in La Jolla (1 hour each). While in the scanner, you will take computer-administered tests of memory where you will be asked to remember facts or short sentences. After each scanning session, you will take a computer-administered test outside of the scanner (1 hour each). Finally, we will collect a saliva sample to measure a genetic risk factor for AD. Participants will be compensated up to \$290 for the entire study and will receive a picture of their brain.

If you are interested in learning about our study and your eligibility, contact Dr. Christine Smith at (858) 552-8585 Ext. 7128.

Towards an Understanding of Sleep Disturbance and Cognitive Decline

By Joanne Hamilton, PhD

Sleep disturbances, including insomnia, sleep apnea, excessive napping, and active dreaming, are common complaints for the aging population. A growing body of evidence identifies specific sleep disorders associated with different causes of cognitive decline. For example, REM Behavior Disorder, which causes disruptive activity during dreaming, can occur in Parkinson's disease and Dementia with Lewy Bodies years before other symptoms emerge and is an important risk factor for development of dementia. The presence of obstructive sleep apnea is commonly associated with Alzheimer's disease (AD). Sleep apnea disrupts sleep consolidation and is associated with cognitive impairment. In one longitudinal study, better sleep consolidation weakened the risk of developing AD, slowed the rate of annual cognitive decline, and decreased neurofibrillary tangle density. A new explanatory framework that links poor sleep quality to the development of cognitive decline has been advanced. Researchers have identified a pathway running beside the brain's vascular system that aids the flow of cerebral spinal fluid through the brain and is responsible for the clearance of soluble proteins, including Aβ and Tau. This so-called "glymphatic system" is driven by pulsation of the cerebral arteries and is dependent upon sleep. Thus, chronic disruption of sleep may result in buildup of proteins that are associated with development of common neurodegenerative diseases.

We are currently recruiting for a study to further investigate the relationship between sleep disturbance and cognitive decline in hopes of improving early detection of neurodegenerative disease. We are recruiting individuals with Mild Cognitive Impairment, Alzheimer's disease, Parkinson's disease, and Dementia with Lewy Bodies. Study participants will complete a roughly 3-hour visit to answer questions about their sleep and behavior and to test brain activity, memory, and attention. Participants will be asked to measure their sleep at home with minimally disruptive sleep equipment. No medication or longitudinal follow-up is required. Participants can be compensated for their time and travel.

Please call Kefron McCaw, PsyD at (619) 798-6048 for more information.



The Impact of Combined Behavioral Interventions on Cognitive Outcomes in MCI

By Amy Jak, PhD

Amy Jak, PhD is conducting a study investigating the "Impact of Combined Behavioral Interventions on Cognitive Outcomes in MCI" to learn more about the impact of daily activity on people's thinking as they age. We are currently recruiting individuals who are between the ages of 60-80, who are not currently exercising or participating in any computer training course, are noticing changes in thinking or memory or who have mild cognitive impairment, and are generally medically healthy. Study participation would entail undergoing testing of memory and thinking and wearing a pedometer to track daily walking and/or participating in a computer cognitive training program.

For more information, contact Andrew Rauch at (858) 642-6375 or aarauch@ucsd.edu.

Vascular and Biomarker Influences on Cognitive Aging

By Christina Wierenga, PhD

Cerebrovascular disease (CVD) risk factors such as hypertension, obesity, hyperlipidemia, diabetes, and metabolic syndrome have been linked to cognitive decline and higher risk for dementia. These risk factors may represent potential targets to delay or prevent age-related cognitive decline. Our research group is currently enrolling Veteran participants in a study that aims to reveal the link between the vascular and neurodegenerative process of Alzheimer's disease (AD) and the emergence of clinical symptoms. The overarching goal is to use new neuroimaging techniques to improve early detection, diagnosis, and intervention to delay or prevent AD onset. We will examine cognitive, vascular, and brain function in 120 English-speaking Veterans without dementia who are aged 65 or older and do not have dementia, but do have cerebrovascular disease risk factors. Assessments include standardized cognitive testing, state-of-the-art structural and functional MRI of the brain, comprehensive non-invasive vascular function assessment (including carotid ultrasound), lumbar puncture to analyze cerebrospinal fluid AD biomarkers (including beta amyloid and tau), physical activity belt to assess physical activity/ sedentary level, and a cheek swab for DNA analysis. This study will improve our understanding of how Alzheimer's disease and cerebrovascular risk factors affect cognitive abilities and memory. We hope that this will improve early detection of risk for cognitive decline and identify therapeutic targets to slow the progression of the disease at the earliest stage, when preventive interventions are likely to be most effective.

For more information, contact Jessica Osuna at (858) 552-8585 Ext. 5793.



Intervention for Healthy Brain Aging Study By Zvinka Zlatar, PhD

The WISE Lab (Wellness Initiative for Senior Enrichment) at UC San Diego is currently recruiting older adults between the ages of 65 and 80 to participate in the "Intervention for Healthy Brain Aging Study." This study is a novel healthy aging intervention aimed at improving brain health and cognitive functions in older adults who are NOT currently very physically active (those who perform less than 60 minutes per week of moderate to high intensity exercise leading to light sweating and increased heart rate in the past 6 months).

You may qualify if: a) you are in good overall health, b) you own a smartphone [Android or iPhone], c) you are able to walk independently, d) are not currently experiencing memory problems and have not been diagnosed with any neurological conditions, including dementia or mild cognitive impairment, e) qualify to undergo magnetic resonance imaging (MRI), f) and perform moderate intensity exercise – resulting in at least light sweating – for less than 60 minutes per week in the past 6 months.

The "Intervention for Healthy Brain Aging Study" will randomly assign participants to a home-based exercise condition or a home-based healthy aging education condition for three months. Visits to UC San Diego campus will occur prior to, at 6 weeks, and following the intervention - CURRENTS

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(12 weeks). These visits will consist of fitness and cognitive testing, brain MRI, and face-to-face training with a health specialist. During the intervention period, you will receive regular phone calls from study staff. You will be compensated for participating.

If you or someone you know is interested in participating in this study, please contact the WISE Lab at (858) 822-7737.

Novel Locus Coeruleus Markers of Inflammation and Risk of Alzheimer's Disease

By Jeremy Elman, PhD

Aggregation of β -amyloid (A β) and tau neurofibrillary tangles are considered hallmark characteristics of Alzheimer's disease (AD). However, there is evidence that significant Aß deposition may occur decades before behavioral impairments, and recent autopsy studies suggest abnormal tau may be present prior to age 30. This long prodromal state may present a critical period in which to inititate treatment. Existing biomarkers of AD pathology are costly and difficult to obtain. In contrast, pupil dilation is an easily obtained measure of mental effort and is closely linked to locus coeruleus (LC) function. The LC may be the initial site of tau pathology, and damage to this structure increases inflammation and contributes to AD progression. We previously found that altered pupil dilation is associated with MCI status, changes in brain activity, and cognitive performance. The goal of this research is to provide evidence for the role of LC damage in AD progression, and to explore the utility of novel biomarkers of LC dyfunction as early screening tools for AD risk.

The experiment will involve a 30-minute pupillometry session in which you perform a few different cognitive tasks while we measure your pupil size with a handheld device. In addition, we will draw 10mL of blood. Both of these procedures will take place at the Shiley-Marcos ADRC. On a separate day, you will come in for a magnetic resonance imaging (MRI) scan on the UC San Diego campus. The scan lasts approximately 20 minutes. We are interested in enrolling individuals who: do not have a diagnosis of Alzheimer's disease, are not currently taking anti-cholinesterase medication, and do not have glaucoma or other eye diseases affecting both eyes.

For more information, contact Jeremy Elman, PhD at (858) 534-6842 or jaelman@ucsd.edu.

Behavioral Assessment of Network Dysfunction in Preclinical Alzheimer's Disease

By Diane Jacobs, PhD

The brain changes associated with Alzheimer's disease (AD), such as a build-up of amyloid plaques, begin years before memory impairment and other symptoms of the disease begin to interfere with daily functioning. This is often referred to as the preclinical phase of AD, since there are no obvious symptoms of the underlying brain changes. Traditional neuropsychological measures, such as list-learning tests, may not have sufficient sensitivity to detect subtle cognitive changes associated with the preclinical phases of AD; therefore, novel measures are needed.

It has been hypothesized that the brain changes associated with preclinical AD may disrupt functional neocortical networks (i.e., networks of distinct brain regions that interact with one another in order to perform a task). If disruption of neocortical networks is among the earliest consequences of AD pathology, then cognitive-behavioral measures that assess functional integrity within and between neocortical systems could be particularly useful for detecting cognitive change in preclinical AD. Examples of such measures include memory binding tasks, which require the integration of separate pieces of information into a single coherent whole (e.g., face-name pairing), and sensory binding tasks, which require integration of information from distinct cortical regions (e.g., color and shape) into the representation of a single object (e.g., an orange triangle). Prospective memory - or remembering to perform an action at some point in the future – also requires the integration of abilities associated with distinct brain regions (e.g., attention, executive control, memory, sequencing, etc.), and measures of prospective memory may also be useful in preclinical AD. Dr. Diane Jacobs is conducting a study to assess and compare these novel cognitive-behavioral measures, as well as examine the association of performance on these tasks with AD biomarkers. She is recruiting healthy controls from the ADRC longitudinal study for participation.

For more information, contact Christina Gigliotti, PhD at (858) 822-4800.

There is much work being done throughout the world with research studies. I would like to take part in the cure. Leave something of yourself for the world so that you can participate in its future.
— Victor, diagnosed with Alzheimer's disease 9

Healthy Bilingual Aging and Alzheimer's Disease

By Tamar H. Gollan, PhD

Sometimes I'll start a sentence in English y termino en español. Bilinguals easily and fluently switch languages when they want to, but also avoid switching when they need to speak in just one language. Recent studies suggest that this constant management of two languages in the bilinguals' daily life may be a form of 'mental exercise' - increasing their ability to function relatively better in the presence of brain damage (compared to people who know just one language). The Bilingualism and Aging lab is actively investigating how the ability to speak two languages changes with increasing years of experience using two languages, and in bilinguals with Alzheimer's disease. Most of the time we take language for granted, even in assessment of cognition. But memory testing, and other cognitive tests often given to determine if mental abilities might have declined, require language use. Little information is available on how such tests should be interpreted when testing bilinguals - a problem our lab is actively seeking to solve. We have discovered some language tests that appear to be uniquely sensitive for detecting Alzheimer's disease in bilinguals, and ongoing adaptations of this same test might eventually be useful for assessment of monolinguals and bilinguals alike.

We are looking for people over 65 who speak Spanish and also know a little or a lot of English, or individuals who speak English and also know a little or a lot of Spanish. Most bilinguals have one language they feel more comfortable speaking and report that speaking in their other language is a bit, or even much, more challenging. Perfect bilinguals are rare. We are recruiting all types of bilinguals.

For more information, contact Rosa Montoya, MS at (858) 246-1269.

Longitudinal Cognitive ERP Studies: Advancement for Alzheimer's Disease (AD) Clinical Trials

By Jim Brewer, MD, PhD, UC San Diego and John Olichney, MD, UC Davis

Cognitive Event-Related Potentials (ERPs) are a non-invasive measure of the brain's electrical and synaptic activity. ERPs offer precise measures of the speed of cognitive processes, and many ERP components have shown sensitivity to the early stages of Alzheimer's disease (AD).

This study, funded by the National Institute of Aging, plans to enroll 100 elderly participants aged 60-90 over the next 2 years (55 with normal cognition, 25 with amnestic Mild Cognitive Impairment, and 20 with mild AD dementia). The procedures of the protocol include longitudinal cognitive ERPs/EEG (3 annual studies over 2 years), brain MRI (2 annual studies), amyloid-PET (at study entry), and neuropsychological testing. The ERP data will be collected while participants perform simple tasks of attention, memory, and language over a 2-3 hour period. The ERP paradigms chosen for this study have demonstrated high sensitivity to early AD, and a systematic study comparing the relative sensitivity and stability of the ERP components is needed as new imaging biomarkers show sensitivity to early AD, even in its "preclinical" stage. The ERP studies will be conducted in the cognitive electrophysiology lab of Marta Kutas, Professor of Cognitive Science, on the UCSD campus.

This project will advance the ability to conduct multicenter ERP studies of AD, develop infrastructure, and refine methodology, with the long-term goal of determining how cognitive ERPs can be best used to detect and track changes in AD pathophysiology. This proposal aims to advance our knowledge of how to use ERPs in AD clinical trials as both entry criteria (e.g. identifying those at greatest risk) and as biological markers of treatment response.

For more information, contact Jessica Bercow at (858) 822-4800.

Cardiovascular Disease

By Katherine Bangen, PhD

The purpose of this study is to learn more about mild cognitive impairment (MCI), a condition that has been associated with increased risk of developing Alzheimer's disease. We will assess cognitive functioning, brain structure and function using MRI, and different proteins (called biomarkers) in blood in older adults with MCI and those with normal cognition. Studies suggest that blood-based measures of inflammation, glucose, and vascular functioning may influence risk of developing Alzheimer's disease. This study may aid in early detection of brain changes and help us determine which combination of blood-based biomarkers, cognitive markers, and neuroimaging markers help us predict whether people with mild cognitive problems are at high risk of having worsening memory problems over time, or of progression to Alzheimer's disease.

You may be eligible for the study if you are between the ages of 55-85 and have normal cognition or MCI. Participants undergo cognitive testing, MRI, blood draw, echocardiogram, and a non-invasive assessment of vascular health. These assessments are completed over 2-3 visits to UCSD. Participants will receive a total of \$100 through direct deposit as compensation for completing the study.

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For more information, contact Nicole Evangelista at (858) 552-8585 extension 6992 or nevangel@ucsd.edu.

Chronic Stress and Caregiving

By Guerry, Peavy, PhD, UC San Diego and Ann Mayo, RN, DNSc, University of San Diego

Caregivers of individuals with Alzheimer's disease (AD) experience significant, often prolonged stress. This can lead to poor health and difficulties with thinking or cognition (e.g., memory, problem solving) that challenge their ability to meet the demands of the caregiver role. Caregivers with a spouse with AD are often vulnerable, not only to difficulties associated with caregiving, but also to the increasingly harmful effects of stress due to aging.

Differences between Hispanic and non-Hispanic caregivers in cultural and genetic characteristics may lead to differences in how they react to chronic stress. Hispanics are the largest minority in the United States, but there are few studies addressing the consequences of stress on Hispanic caregivers of an AD spouse. We have obtained a California state grant to measure cognitive change in Hispanic and non-Hispanic caregivers that may result from chronic stress. We will also investigate how specific factors that may increase the chances of developing AD combine with the prolonged stress of caregiving and aging to affect cognition.

We have recently begun to recruit subjects who are at least 55 years of age and functioning normally in their daily activities. There will be four groups: 1) Hispanic individuals caring for a spouse with AD; 2) non-Hispanic individuals caring for a spouse with AD; 3) Hispanic individuals married to a cognitively normal spouse who is functioning independently in daily activities; and 4) non-Hispanic individuals married to a cognitively normal spouse who is functioning independently in daily activities.

If you are interested in participating and would like additional information, please call the Shiley Marcos ADRC (858) 822-4800, and ask to speak to Amanda Rodriguez, our bilingual psychometrist. You may also call Dr. Guerry Peavy at (858) 246-1272 for information.



Our Journey on Planet Alzheimer's

By Jayne Slade

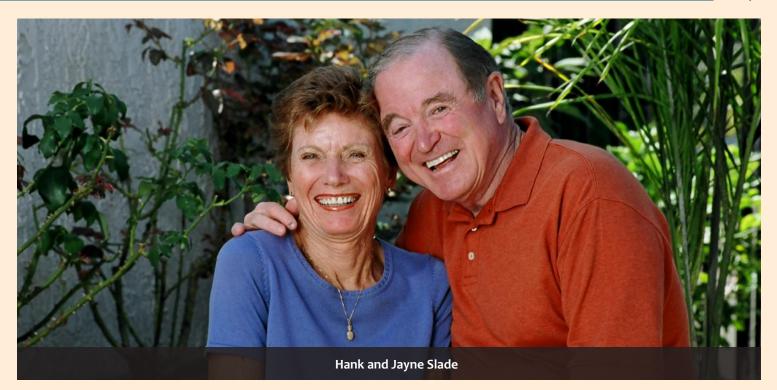
I am an ordinary person who made a success out of caregiving by learning how to allow my husband to feel relevant, loved, listened to, and cared for. I was married for 57 years to an energetic, vibrant, fun loving man. Then Alzheimer's disease showed up at our front door. I lost my husband, Hank, 5 years ago in July of 2012. He spent his last four years in a wonderful Alzheimer's community where I spent my days with him.

Our journey on Planet Alzheimer's, began in about mid-1995. Hank was forced to retire in 1996 when he could no longer perform the necessary executive skills as general manager of a large tennis club. I immediately reached out for resources and the Alzheimer's Association (now Alzheimer's San Diego) led me to UC San Diego and the Shiley-Marcos ADRC.

When your spouse has Alzheimer's, things usually begin happening slowly. You don't lose the person all at once, but as if a puzzle is being taken apart piece by piece instead of being put together. I lost my best friend, my confidante, my lover, the father of my children, my handyman, my companion, my husband. It progressed to not having meaningful conversations and discussions and I began to realize I was basically living alone in our house, even though my husband was physically there.

Alzheimer's is a compelling and tenuous road of learning for the family and loved ones and most certainly an overwhelming shock for the person losing his or her memory. It is a long road to travel, and if you think that San Diego proper has too many potholes, those of us who have ridden, or are riding, in Alzheimer's shoes, would love to gift you with an additional number of the 1000's of potholes we experience along the way. I learned an enormous amount personally, not only about the disease, but about myself.

From my personal experience, I can definitively say that there are blessings to be enjoyed if one only just looks. The problem is that family caregivers are so busy figuring things out and covering all bases that oftentimes the blessings aren't noticed. In my case I decided to look for some in each day and was rewarded in that regard many times. The greatest one of all was that Hank knew me to the end. He didn't know anyone else, but he knew me. I also met many, many wonderful people who I would have never encountered had it not been for Hank's disease. I found out how strong and resilient I was in coping with the daily life presented to us by Alzheimer's. Keeping our sense of humor was an absolute must and I can still remember Hank's loud



and boisterous laugh as we shared our world. In the first stages of the disease, Hank would laugh it off with friends and associates by saying, "I have CRS - I can't remember stuff," although he didn't use the word stuff.

A couple of years into Hank's diagnosis a new drug for Alzheimer's was approved by the FDA – Namenda/memantine. His neurologist at UCSD prescribed it right away. I do believe that it enhanced his daily living abilities for some pe-

riod of time. In that sense, his personal dignity was preserved longer. Because my husband died from Alzheimer's (confirmed by brain autopsy at the Shiley-Marcos ADRC), his journey during the last stages was not so uncomfortable for him because his brain was slowly being devoured by plaques

All of us need to keep working with all the tools at hand to stop the disease before it starts, to interrupt the disease so it halts progression, and to find a cure when one is already afflicted.

and tangles. As for myself, I can't describe the emotional pain of seeing it happen. When his life stopped, I was happy for him that he no longer had to endure his life as it was.

So, what does research mean to me? Research spells HOPE in one form or another for everyone. Hank collected and cut out every article written about Alzheimer's research during his illness for as long as he was able, creating excessive files that spelled out his wish for something to hang on to – that maybe it would be a "cure" for him. In the past 30 years of Alzheimer's disease research there have been many failed drug trials. There is no cure. Has that discouraged the researchers? I would guess that is hasn't. It has disappointed them, but along the way they have gained vast amounts of relevant information. Researchers feel fortunate to be in the field at this exciting time. San Diego is the hub of this research and is respected as being a leader throughout the world.

I am a facilitator for an Alzheimer's caregiver support group at the Shiley-Marcos ADRC. We have spouses and members in our group who participate in studies and clinical and

> drug trials. They are willing to participate for future generations and many donate their brain for autopsy at death. They are greatly appreciated. As their facilitator, I am giving back to this community in the only way I know how, by using the knowledge I gained to assist others in their struggle. All of us need to keep work-

ing with all the tools at hand to stop the disease before it starts, to interrupt the disease so it halts progression, and to find a cure when one is already afflicted. My greatest and only personal tool I had to fight the disease with Hank was love, trying to make sure he knew I was with him all the way and would not abandon or give up on him. It worked. It really, really worked. When his life was finished, I had no regrets. I had done everything of which I was capable to make his life with Alzheimer's livable, bearable, and normal, even though we had many "new normals." I am a happy, well-adjusted, independent widow and I am quite sure that would make Hank happy, as well.

Observational Studies

COGNITIVE AGING LONGITUDINAL STUDY (ALSO AVAILABLE IN SPANISH)

PI: Douglas Galasko, MD CONTACT: Tracey Truscott, LCSW (858) 822-4800 or ttruscott@ucsd.edu TIME INVOLVED: Minimum 5 years

DESCRIPTION: The purpose of this study is to learn how the brain changes as we age. This is an observational study with no medication, with behavioral, medical, and cognitive data collection and testing as well as a neurological exam. This is done annually from the time of enrollment to death. Information about strategies for healthy

brain aging is provided, as is feedback about one's annual performance on cognitive testing. We continue to obtain blood and CSF samples to match up changes in chemicals we can measure in the blood and CSF with changes in cognition and brain structure.

REQUIREMENTS: Age 65 and older if normal cognition or diagnosis of MCI or early dementia due to Alzheimer's, FTD, or DLB; study partner; LP and MRI required; brain autopsy required.

ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE 3 (ADNI)

PI: James Brewer, MD, PhD CONTACT: Tracey Truscott, LCSW (858) 822-4800 or ttruscott@ucsd.edu TIME INVOLVED: Up to 5 years

DESCRIPTION: The primary goal is to discover, optimize, standardize, and validate clinical trial measures and biomarkers used in ongoing Alzheimer's disease research. The Alzheimer's Disease Neuroimaging Initiative (ADNI) plays a central role in improving treatment trials. Since the study's launch, ADNI Investigators with regulators in both the US and abroad have facilitated the design of major completed and ongoing drug trials. ADNI 3 is a contin-

LONGITUDINAL STUDY BIOMARKER RESEARCH

PI: Douglas Galasko, MD **CONTACT:** Beata Santiago (858) 822-4800

Research into biomarkers - measurements that inform us about a disease process - is an increasingly important component of trying to understand the complex changes in the brain in aging, Alzheimer's disease and related disorders. We, and other researchers worldwide, are engaged in building a detailed picture of brain structure and biochemistry through the use of brain imaging techniques and the analysis of cerebrospinal fluid. These measures have helped to improve how we diagnose, follow, and evaluate treatment for Alzheimer's. Measuring how biomarkers change over time is important in assessing interventions, and has helped us to more rigorously evaluate new approaches to treatment and even prevention. Researchers are trying to build a detailed map of brain changes on the trajectory to Alzheimer's disease to determine who may be at risk and who might be protected. Participants in our longitudinal study have likely undergone a lumbar puncture procedure so that their cerebrospinal fluid could be analyzed for levels of

uation of this work. ADNI 3 is a non-randomized, natural history, non-treatment study. Clinical/cognitive, imaging (MRI and PET scans), biomarker, and genetic characteristics will be assessed across the three cohorts: Normal controls (NC), Mild Cognitive Impairment (MCI), and mild Alzheimer's disease (AD). Visits will occur annually for MCI and AD subjects and biennially for NC subjects.

REQUIREMENTS: Age 55-90; have normal cognition or a diagnosis of MCI, or AD; have a study partner; have overall good general health. Subjects are required to undergo MRI and PET scans and undergo a lumbar puncture.

biomarkers such as amyloid beta protein and tau protein. While this one time CSF collection is valuable since volunteers can be compared to one another, having more than one data point within an individual person is even more valuable, as it can enable us to understand patterns of change in biomarkers. Having longitudinal biomarker data can provide us with specific information about how those changes in CSF over time may relate to changes in imaging biomarkers and cognitive test data.

Dr. Galasko and colleagues at the ADRC would like to collect a follow-up sample of cerebrospinal fluid from all longitudinal participants who are willing to undergo a second lumbar puncture procedure. Many of the studies outlined below will use CSF data in their analyses and would benefit significantly from data that is collected in the same timeframe as the information gathered in their unique protocols. As with your previous LP, you will be compensated \$100.00 for participation in this optional additional study procedure. Please contact Beata Santiago at the Shiley-Marcos ADRC to schedule this additional LP appointment at your earliest convenience (858) 822-4800.

Clinical Trials for Persons with Normal Cognition

A4: ANTI-AMYLOID IN ASYMPTOMATIC AD (*ENROLLMENT CLOSING SOON, BUT WE ARE STILL SCREENING)

PI: Douglas Galasko, MD	clonal antibody that helps the body rid the brain of beta
CONTACT: Tracey Truscott, LCSW	amyloid) on persons with no symptoms of AD. Solan-
(858) 822-4800 or ttruscott@ucsd.edu	ezumab is administered via monthly infusions.
TIME INVOLVED: 3 years DESCRIPTION: This randomized, double-blind, placebo controlled trial will assess solanezumab (a passive, mono-	REQUIREMENTS: Age 65-85; Normal cognition; study partner; MRI and PET scans required; lumbar puncture optional.
	F

<u>A5</u>

PI: Douglas Galasko, MD CONTACT: Tracey Truscott, LCSW (858) 822-4800 or ttruscott@ucsd.edu TIME INVOLVED: 54 months of treatment (4.5 years); 35 visits over 54 months

DESCRIPTION: A5 is a clinical trial similar to A4. The purpose of the study is to test a new drug (JNJ-54861911) which is being developed by Janssen Pharmaceuticals. JNJ-54861911 is a beta-site amyloid precursor protein cleaving enzyme inhibitor (BACEi) that is being developed for the treatment of Alzheimer's disease (AD) by reducing production of amyloid-beta (A β) fragments. Accumulating amyloid aggregates trigger a pathophysiological cascade (including acceleration of tau pathology) that leads to progressive neurodegeneration, neuronal loss, and cognitive impairment.

We are recruiting subjects who are asymptomatic and at risk for developing Alzheimer's dementia due to evidence

of elevated amyloid accumulation based on CSF or amyloid PET imaging. Drug is administered orally once a day. Some people who were screened for the A4 trial but did not qualify may be eligible for A5.

REQUIREMENTS: Age 60-85; Subjects 60 to 64 years of age must also have 1 of the following 3 conditions:

- a. A positive family history for dementia (minimum of 1 first degree relative)
- b. A previously known APOE4 genotype
- c. A previously known biomarker status demonstrating elevated amyloid accumulation in CSF or PET

With or without subjective memory complaints, should not be receiving acetylcholinesterase inhibitor and or Memantine, 7 MRIs, 4 Lumbar punctures, 4 PET scan, study partner is required.

Clinical Trials for Persons with AD

DISCOVER

PI: Douglas Galasko, MD CONTACT: Tracey Truscott, LCSW (858) 822-4800 or ttruscott@ucsd.edu TIME INVOLVED: Up to two months and will require at least five study clinic visits including a three-day stay at the clinical research unit. Compensation will be provided to enrolled participants.

DESCRIPTION: Posiphen is an experimental drug developed as an anti-amyloid medication that may delay Alzheimer's disease (AD) onset or slow the progression

of possible AD-related brain damage due to amyloid buildup. Participants in Discover will help researchers learn if the experimental drug is both safe and tolerated. This is a randomized, double-blind, placebo-controlled study with a 50/50 chance of receiving the experimental drug.

REQUIREMENTS: Age 55-85; diagnosis of MCI or mild Alzheimer's disease; MMSE 24-30; study partner, MRI scan, lumbar puncture, willing to undergo extended stay in clinical research unit (2 nights).

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EMERGE: BIOGEN (BIIB037)

PI: James Lohr, MD CONTACT: Lorraine Cheng, MA (858) 229-2283 or LOCHENG@ucsd.edu TIME INVOLVED: 2 years	a human monoclonal antibody, and it is being evaluated to determine whether it can remove the amyloid plaques and slow the progression of symptoms in early AD.
DESCRIPTION: The purpose of this study is to evalu- ate the efficacy and safety of Aducanumab (BIIB037) in persons with early Alzheimer's disease. Aducanumab is	REQUIREMENTS: Age 50-85; diagnosis of Alzheimer's disease; MMSE 24-30; study partner; PET and MRI scans; able to have monthly infusions.
TRIAD: AVANIR (AVP-786)	
PI: James Lohr, MD CONTACT: Lorraine Cheng, MA (858) 229-2283 or LOCHENG@ucsd.edu TIME INVOLVED: 16 weeks	to dementia of the Alzheimer's type. AVP-786 is a combi- nation product of d6-DM with quinidine sulfate (Q) that interacts with multiple receptors to decrease behavioral disturbances associated with AD.
DESCRIPTION: The purpose of this study is to evaluate the efficacy, safety, and tolerability of deuterated [d6]- dextromethorphan hydrobromide/quinidine sulfate (d6- DM/Q or AVP-786) in persons with agitation secondary	REQUIREMENTS: Age 50-90; MMSE 6-26; study partner; moderate to severe agitation/aggression. Visits take place at the La Jolla VA and VMRF facilities.
UC CURES	
PI: Shauna Yuan, MD CONTACT: Tracey Truscott, LCSW (858) 822-4800 or ttruscott@ucsd.edu TIME INVOLVED: 52 weeks	Salsalate is a non-steroidal anti-inflammatory (NSAID), which is used to treat arthritis. Salsalate is being tested here for its property to inhibit tau acetylation, thus pre- venting tau aggregation.
DESCRIPTION: Double blind, randomized, placebo con- trolled, pilot PK/PD, evaluating tau acetylation inhibitor salsalate for mild-to-moderate Alzheimer's disease.	REQUIREMENTS: Age 50-85 with diagnosis of AD; MMSE 14-30. Subject agrees to LP, MRI, PET (amyloid and tau), cognitive testing and must have a study partner.
BI 409306	
PI: Gregory Light, MD CONTACT: Joyce Sprock (619) 471-9455 or jsprock@ucsd.edu TIME INVOLVED: 17 visits during treatment period of 14	ways via increase of cGMP to strengthen LTP and synaptic plasticity leading to memory enhancement. Phase 1c clini- cal safety study, randomized into 25mg or 100mg dose groups. Compensation and travel assistance provided.
days DESCRIPTION: The investigational drug in this study is a potent selective phosphodiesterase 9 (PDE9A) inhibitor, which is believed to target glutamatergic signaling path-	REQUIREMENTS: Age 55-85, diagnosis of AD; MMSE 18-26; stable treatment for 3 months if taking memory medications.
AC IMMUNE (ANTI-AMYLOID VACCINE STUDY)	
PI: William Mobley, MD, PhD CONTACT: Asmaa Al-Hamdani	impact Alzheimer's related brain changes in people with Down syndrome.
(858) 249-2525 or aalhamdani@ucsd.edu TIME INVOLVED: 24 months (2 years)	REQUIREMENTS: Diagnosis of Down syndrome; 25-45

DESCRIPTION: It is well known that individuals with Down syndrome (DS) develop Alzheimer's at a much higher rate than the general population. This research study will test whether an investigational vaccine can **REQUIREMENTS:** Diagnosis of Down syndrome; 25-45 years of age; do not have any other serious illnesses; have a caregiver/ informant that can answer questions about the participant; 22 visits, 7 vaccine injections, 5 MRI, clinical, laboratory, and cognitive testing.

Clinical Trials for Persons with Mild Cognitive Impairment or Probable AD

ABBVIE M15-566

PI: Shauna Yuan, MD CONTACT: Tracey Truscott, LCSW (858) 822-4800 or ttruscott@ucsd.edu TIME INVOLVED: 92 weeks of treatment; 33 visits over 24 months

DESCRIPTION: The purpose of the study is to test a new drug (ABBV-8E12) which is being developed by AbbVie Pharmaceuticals. ABBV-8E12 is a humanized IgG4 monoclonal antibody against human microtubule associated protein tau. It targets soluble extracellular tau in the brain, which has been implicated in the development and spreading of tau pathology. ABBV-8E12 may be able to block soluble tau aggregates, or seeds, from propagating between cells and thereby decrease the spreading of tau pathology and slow down Alzheimer's disease. Drug is administered an infusion once a month.

CURRENTS

REQUIREMENTS: Age 55-85; stable on memory medication for 3 months or no memory medications; 8 MRIs, 3 Lumbar punctures, 1 PET scan; study partner is required. MMSE 22-30.

UCSD Movement Disorder Center – Research in Parkinson's Disease & Related Disorders

We are actively seeking patients that meet the following criteria: diagnosed with early or late Parkinson's disease (PD); Semantic Variant Primary Progressive Aphasia (PPA); Progressive Supranuclear Palsy (PSP); Frontotemporal Dementia with Amyotrophic Lateral Sclerosis (FTD-ALS); Essential Tremor (ET); Parkinson disease with Dementia (PPD); and Healthy controls (spouses or relatives of potential participants).

INTERVENTIONAL STUDIES: BIOLOGICAL STUDIES FOR EARLY PD

- SURE-PD Inosine for Early PD (active)
- Antibodies Against α-Synuclein (active; with limited anti-Parkinson's treatment)

INTERVENTIONAL STUDIES: PDD PATIENTS

• SYNAPSE study for PDD Patients (active)

<u>OBSERVATIONAL STUDIES: FOR PD & FRONTOTEMPORAL DEMENTIA (INCL. PSP AND CBD)</u>

- Advancing Research and Treatment for Frontotemporal Lobar Degeneration (ARTFL) (active)
- Four Repeat Tauopathy Neuroimaging Initiative Cycle 2 [4RTNI-2] (active)
- Developing T Cell Based Biomarkers for Autoimmunity in Parkinson's Disease (active)

For more study specific information or to refer patients, please contact Dr. Litvan's research coordinators directly – Kimberly Thomas at (858) 822-5751 or kktoo8@ucsd.edu or Cindy Lawrence at (858) 246-2537 or clawrence@ucsd.edu.



You may have heard of clinical trials and research studies but are not sure what they are or if you want to join one. This booklet provides information to help you decide if participating in a clinical trial or study is right for you, a friend, or family member.

Whatever the motivation, when you choose to participate in research, you become a partner in scientific discovery. Your contribution can help future generations lead healthier lives. Major medical breakthroughs could not happen without the generosity of clinical trial participants—young and old.

Please contact the ADRC at (858) 822-4800 to receive your complimentary copy.

UPDATES IN QUALITY OF LIFE PROGRAMS



Hearing the Voices of People with Dementia – An Interactive Theatre Performance

To Whom I May Concern is a nationwide non-profit interactive theatre program whose mission is to support and give voice to people living with early-stage dementia. The program reaches out to people who feel silenced by dementia and encourages them to share their experience before an audience of their peers, caregivers, the public, and professionals. Authentic narratives collected from people with dementia across the country are read by actors in a scripted play. Then a panel of people with dementia follows to provide discussion so the audience can better learn about the experience of living with Alzheimer's.

On March 1 2017, the Osher Lifeline Learning Institute at UC San Diego partnered with the Shiley-Marcos ADRC to host a performance of To Whom I May Concern in San Diego. Approximately 75 people attended the play. Osher President, Jim Wyrtzen, opened the event and introduced the actors who were all volunteers of the OSHER Theatre World Group. The reading was approximately 45 minutes.

After the reading 3 panelists with early-stage Alzheimer's who are members of Shiley Marcos ADRC weekly earlystage support group shared their own experiences of living with Alzheimer's. Tracey Truscott LCSW, social worker with the ADRC, helped to facilitate a question and answer discussion as Teresa, Karen, and Barbara told their own brave and honest stories. When asked about some of the frustrations of living with a diagnosis Karen stated, "My friends are wonderful and they mean well, but I am not an invalid and I don't need help getting out of a car. I can still walk." When Barb was asked whether she tells others she has Alzheimer's, she stated that she tells people about her diagnosis because she "doesn't want people to think I'm stupid." Barb stated that most people are understanding when she tells them. Teresa has a very positive outlook on her life. Her neurologist at UC San Diego showed kindness and patience with her when he gave her the diagnosis in her 50s, and that made all the difference in the world to her.

An audience member made a comment about a part of the play when one actor stated, "Just give me a minute", referring to how fast people talk and how hard it can be for a person with Alzheimer's to keep track of a conversation. The panelists with dementia shook their head in agreement with audience members who asked about slowing down conversation speed so that those with memory impairment have time to respond and participate.

Dr. James Brewer, interim director of the Shiley-Marcos ADRC, closed the event with a discussion of the research opportunities at the ADRC and answered questions about Alzheimer's and related disorders.

Weeks after the play reading, participants with early-stage dementia in both the ADRC's weekly support group and the monthly young-onset dementia support group have been having meaningful discussions about the content and experience of the play. Teresa stated that she resonated most with the discussion about slowing down conversation. She reflects that trying to keep up with conversation can be difficult and it is hard to just "butt in" and ask to be considered. Her message, however, is clear: "I have something to say!"

For more information see www.towhomimayconcern.info

Introducing the Musical Biographies Project

The Shiley-Marcos ADRC cares deeply for persons with memory disorders and their loved ones as demonstrated in the wide-range of creative and supportive opportunities provided through our Quality of Life Programs. We understand the importance of attending to the whole person, including the many social and emotional aspects of coping with cognitive changes and the impact that these changes have daily life and relationships. on Research has demonstrated that music therapy, reminiscence therapy, and scrapbooking (used for highlighting a person with dementia's unique social history), all have positive outcomes for persons with dementia and their caregivers. Benefits range from increasing socialization and meaningful communication to reducing depression and agitation.

The Musical Biographies Project is a new partnership between Villa Musica and the UC San Diego Shiley-Marcos Alzheimer's Disease Research Center that will provide individuals living with early-stage Alzheimer's or a related disorder and their caregivers a platform for creating memory books inspired by a musical playlist. Participants will work with Villa Musica and Shiley-Marcos ADRC staff to identify music that inspires memory, such as memory of an important occasion, an event, or an era. During the 4-week sessions, 4-6 persons with early stage dementia and their caregivers will meet weekly with a music therapist from Villa Musica and an ADRC staff person. Participants will ask friends and family to help them select 4-5 songs for their "playlist." The participants will listen to each song, recount the memories it inspires, and create scrapbook entries. Family members and caregivers will be actively involved in adding to the project by collecting photos, anecdotes, and textiles to give context to the memory. Upon completion of the project, it is anticipated that the special playlist will be added into a longer playlist and loaded onto an iPod. The program will be evaluated to assess its impact on the participants' mood, communication, and other wellness-related responses.

If you have early-stage dementia and have a loved one who can accompany you, please contact Tracey Truscott, LCSW at (858) 822-4800 for more information or to register for the "Musical Biographies" program. This program will be offered twice a year at Villa Musica in Sorrento Valley and is free-of-charge. Research participation is not a requirement for enrollment.



MUSEUM OF ART January 13, May 12, September 8

MINGEI INTERNATIONAL MUSEUM February 10, June 9, October 13

TIMKEN MUSEUM OF ART March 10, July 14, November 10 MUSEUM OF PHOTOGRAPHIC ARTS April 14, August 11, December 8

Join us on the second Friday of each month from 2:00 - 3:00 at one of these exceptional San Diego museums for a unique docent-led discussion and tour. Museum docents engage people with mild-to-moderate Alzheimer's or a related disorder and an accompanying family member or friend in discussions about the artwork to stimulate visual and verbal abilities and to spark memory. Memories at the Museums alternates between the four co-sponsoring museums that are all located in central Balboa Park. Museum admission and tours are *free of charge* to participants.

Each monthly tour is limited to 8 pairs (16 participants total). Pre-registration is requested. Please call Tracey Truscott, LCSW at the Shiley-Marcos Alzheimer's Disease Research Center at (858) 822-4800 to register for a tour.

Shiley-Marcos ADRC Presents the First Shiley Lecture



Brad Hyman, MD, PhD

A few years ago, Darlene Shiley made a generous new donation to the Shiley-Marcos ADRC. After some discussion, we decided to use these funds to support a distinguished researcher who would come to UCSD, give a public lecture for the research community, and also meet with interested fac-

ulty. The goal of the annual Shiley lecture is to update scientists regarding novel areas and developments, and potentially to foster new collaborations.

We were excited to launch this series by having Brad Hyman, MD, PhD, deliver the first lecture on February 28, 2017. Dr. Hyman is a distinguished and highly productive researcher who directs the Alzheimer's Disease Research Center at Massachusetts General Hospital in Boston. A theme of his research is to model and better understand how and where different molecules initiate and contribute to the progression (or spread) of Alzheimer's pathology. He uses a variety of different animal models as well as growing nerve cells in culture to build up an integrated picture that can be mapped onto human pathology, and more recently onto tau PET imaging in the brain.

His talk was entitled 'Factors Underlying Progression in Alzheimer's Disease.' Dr. Hyman discussed how abnormally aggregated forms of the tau protein form tangles in the brain in Alzheimer's disease, initially in highly vulnerable areas within the hippocampus, then involving nearby areas in the temporal lobe and then the cortex. Tau pathology is used as a staging system for Alzheimer's disease in autopsy studies. Dr Hyman has developed a transgenic mouse model that expresses an abnormal form of tau selectively in the hippocampus. Over time, tau pathology spreads to involve nearby regions and eventually the cortex, resembling the tangles of Alzheimer's (this mouse model does not develop amyloid pathology). Dr Hyman has found that abnormal forms of tau may be released from nerve cells and taken up by nearby nerve cells, and that this mechanism may be important in the progression of tau pathology. He is working to characterize the abnormal forms of tau that may be responsible for this, which could serve as a target for treatment.

We are grateful for Darlene Shiley's donation that will allow us to provide this annual Shiley lecture as a means of advancing knowledge to our own UCSD scientists, as well and the larger San Diego community.

Continuing to Plant Seeds: Outreach Efforts in the South Bay Latino Community

By Sara Espinoza

The Shiley-Marcos ADRC's commitment to the Latino Community in San Diego has been firm for over 20 years. As we continue to strengthen our efforts to engage and support Latinos coping with dementia, researchers and staff are developing innovative culturally sensitive programs to reach out to the Latino Community. One of our most recent events was a community presentation at Bonita Library. The Bonita Library provided an intimate, familiar, and local setting to the South Bay attendees for this bilingual presentation and discussion about our dementia research efforts.

The attendees were multiracial and multigenerational, ranging in age from early 40's to late 70's. They were daughters caring for parents, community health professionals, seniors with memory concerns, and their spouses. Memory, aging, and dementia were the topics of the presentation and the audience was inquisitive, engaged, and demonstrated much more than a concern about brain health; they were also knowledgeable about the progression of dementia, the lack of resources to get diagnosed, the challenges faced by a person affected by the disease and their family, and how this also impacts their community. Their questions were poignant regarding preventive steps, diagnostic process, genetic predisposition, and new scientific developments in the fight against Alzheimer's and related disorders. Some attendees were also interested in research participation and are currently being followed up with enrollment into our Longitudinal Study.

At present, there is little known about whether there are differences and/or similarities in the effects of Alzheimer's on Latinos versus non-Latinos. What we do know is thanks to Latinos who have participated in our studies and other similar studies. Culturally sensitive development of treatments, medication, or diagnostic tools can only be created or improved when Latinos participate in this important research.

The ADRC continues its commitment to the Latino community providing a variety of resources including educational presentations. San Diego's population is over 28% Latino and our outreach to Latinos and their inclusion in research is of great importance. Our collaborative efforts with community health professionals have strengthened outreach efforts in South Bay and we will continue to work towards building on these invaluable partnerships.

Introducing Our New Partner in Development: Laura Adler



Hello! I am a new Director of Development for UC San Diego Health Sciences, specifically focused on building philanthropic support for Alzheimer's disease and related dementias. I feel honored and privileged to be working with the UC San Diego Shiley-Marcos Alzheimer's Disease Research Center (ADRC) and all the related areas working to discover effective treatments and a cure for the disease. Alzheimer's disease remains one of the most critical public health issues in America and is the 6th leading cause of death in the United States. The ADRC is dedicated to translating advances in research into improved diagnosis and care for individuals with Alzheimer's and related disorders and their caregivers, while focusing on finding ways to prevent, treat and ultimately cure the disease.

I have been a development officer for over 13 years, most recently at UCLA, focused on raising funds for scholarships and student support initiatives such as former foster youth, veteran students, and students with disabilities to name a few. I chose to make the move to San Diego not only for the incredible professional opportunity, but primarily because I have two amazing nieces (2 ½ and 6 weeks old!) that I knew I wanted to be closer to. I also knew that San Diego is where I wanted to be long-term!

I am fully dedicated to understanding Alzheimer's disease, the individuals and families affected by it, and to building relationships within the community. I love connecting people with one another, understanding their motivations, and working with them to discover opportunities to philanthropically support research and programs that are personal and meaningful to them. I feel in my own small way I am giving back and making a difference. One breakthrough can change the landscape of prevention, treatment, and a cure for Alzheimer's. I feel that UC San Diego has all of the components to be the place where that will happen. That is exciting to me! Philanthropy – gifts of all sizes - has the power to propel the institution to new levels of achievement that would not be possible otherwise.

Your support funds:

- Vital research to better understand Alzheimer's disease and related dementias
- Development of new medications and treatments for Alzheimer's disease
- Advances in clinical interventions, including prevention
- Programs aimed at improving the quality of lives for patients and caregivers

Gifts of every size make a significant impact. Make a gift by check made payable to "UC San Diego Foundation" with Shiley-Marcos Alzheimer's Disease Research Center indicated in the memo. Please mail to:

UC San Diego Foundation Attn: Laura Adler 9500 Gilman Drive #0937 La Jolla, CA 92093-0937

Also, did you know that there is more than one way for you to support the ADRC? From a bequest in your will or trust, to a beneficiary designation in your retirement account, to a donation of appreciated securities, there are many types of non-cash gifts that will help us achieve our goals.

If you are interested in learning more about how you can support the Shiley-Marcos Alzheimer's Disease Research Center, I can be reached by email at: Imadler@ucsd.edu or by phone at 858-246-1141. I would love to hear from you!



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