The UC San Diego Shiley-Marcos Alzheimer’s Disease Research Center (ADRC) has been at the forefront of identifying the earliest changes in brain function, thinking, and memory that occur in someone who is developing Alzheimer’s disease (AD). Our founding director, the late Dr. Robert Katzman, was one of the first physician-scientists to describe AD as a condition where brain pathology slowly accumulates without causing significant symptoms until some threshold level of disease is approached and crossed.

[CONTINUED ON PAGE 2]

Announcing the UC San Diego Comprehensive Alzheimer’s Program
BY MICHAEL RAFII, MD, PhD AND DOUGLAS GALASKO, MD

We are pleased to inform you about the establishment of the Comprehensive Alzheimer’s Program (CAP) within the Department of Neurosciences at UC San Diego. CAP is dedicated to both state-of-the-art patient care and therapeutic research, and is focused on translating discoveries made in the laboratory into new methods for the prevention, diagnosis, and treatment of Alzheimer’s disease. UC San Diego’s Neurosciences Department is at the forefront of such research, and CAP brings together a large cadre of researchers and clinicians devoted to better understanding and treating Alzheimer’s disease. [CONTINUED ON PAGE 4]
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Once the pathology becomes severe enough, symptoms of memory loss or other deficits in thinking gradually become apparent. As these symptoms worsen and begin to interfere with everyday functions such as work activities, household tasks, or hobbies, AD can be clinically diagnosed. Through research at UC San Diego and elsewhere, we now know that a subtle decline in memory often precedes the emergence of more substantial cognitive and functional decline that marks clinical AD. This condition is known as Mild Cognitive Impairment (MCI). MCI is identified in elderly people who feel that their memory has significantly declined and perform poorly on formal memory tests, but who have little or no change in their ability to perform their usual everyday functions. MCI is often an early stage of AD (approximately 8 to 15% of people with MCI progress to AD each year). However, some people with MCI do not progress and others have a disease other than AD.

Research scientists affiliated with the Shiley-Marcos ADRC are conducting studies using neuropsychological, neuroimaging, and electrophysiological techniques to improve the ability to detect MCI and better predict who will progress to dementia. To date, our neuropsychological studies of the earliest cognitive changes to occur in those who are developing MCI show that the ability to remember new information over a delay steadily and rapidly declines in the period immediately preceding the diagnosis of AD. The ability to retain information over a delay steadily and rapidly declines in the period immediately preceding the diagnosis of AD.

Thus, the rate of change in this aspect of memory may be a more important marker of impending dementia than the absolute level of memory ability.

Although research on cognitive changes in MCI at the ADRC has largely focused on memory, recent studies suggest that cognitive changes during MCI may be more global in nature and can involve language, attention, executive functions, and visuospatial abilities.

To demonstrate this effect, Dr. Laura Mickes and her colleagues examined the results of annual cognitive evaluations of ADRC participants who began the study as cognitively normal but developed MCI and AD over the subsequent three to six years. The results showed that performance falls off rapidly in all areas of cognitive functioning prior to the time a diagnosis of dementia can be made, although memory abilities are particularly vulnerable.

In related studies, ADRC investigators showed that subtle cognitive changes can be detected as an asymmetric profile of performance across cognitive domains in cognitively normal elderly people who are destined to develop MCI or dementia. That is, people who perform better on visual than language tests, or vice versa, are more likely to decline than those who perform at a similar level on both kinds of tests. These and related findings led Dr. Amy Jak, Dr. Mark Bondi, and their ADRC colleagues to propose new MCI diagnostic criteria that rely on detailed testing of all major aspects of cognition and not
just memory. The new criteria provide a diagnosis that is much more stable than the typical definition of MCI, and more accurate in predicting who will decline further and develop dementia.

Several neuroimaging studies of patients with MCI were carried out by ADRC affiliated investigators over the past several years. In one of these studies, Dr. Lisa Delano-Wood, Dr. Mark Bondi, and their colleagues used a newly developed neuroimaging technique called diffusion tensor imaging to show that white matter in the brain (i.e., the tissue made up of fibers that connect various regions of the brain) was significantly reduced in patients with MCI compared to cognitively normal elderly people, particularly in portions of the corpus callosum, the fiber tract that connects the left and right brain hemispheres. The degree of white matter abnormalities predicted the severity of memory impairment. In addition, the degree of white matter abnormality was higher in MCI patients who also had risk factors for stroke than in those who did not have this additional risk.

Using a different technique known as functional MRI (fMRI), Dr. Christina Wienerga and other ADRC investigators showed that patients with higher risk of developing MCI and AD due to a genetic risk factor required more widespread brain activation than those without the risk factor when naming various types of animals, tools, or vehicles. In addition to these local studies, many ADRC participants with MCI have volunteered for a large national study known as the Alzheimer’s Disease Neuroimaging Initiative (ADNI). The ADNI study is using state-of-the-art neuroimaging techniques and biological markers of AD in cerebrospinal fluid to identify those patients with MCI who will go on to develop AD dementia.

**A Series of Recent Studies by Dr. Guerry Peavy and Her Colleagues Showed that Stressful Life Events and the Elevation of Certain Hormones Related to Stress (e.g., Cortisol) Accelerate the Development of Dementia in Those with MCI, and May Increase the Odds of Developing MCI in Cognitively Normal Elderly People.**

Electrophysiology (i.e., brain waves) studies in patients with MCI recently carried out at the UC San Diego ADRC showed that changes in the pattern of brain waves that occurs when new information is encountered (also known as event-related potentials) is altered in patients with MCI and can accurately predict the likelihood of progression from MCI to dementia. A study led by Dr. John Olichney, for example, showed that the degree of alteration in certain event-related potentials is highly correlated with verbal memory test performance. Furthermore, patients with MCI with abnormal potentials had 87 to 88% likelihood of dementia within three years while those with normal potentials had an 11 to 27% likelihood. These important findings suggest that electrophysiological measures may be useful biomarkers for the detection and staging of MCI and very early AD.

Finally, it is important to note that the Shiley-Marcos ADRC is also carrying out studies that involve the development of potential new treatments for MCI and early AD. A number of ADRC investigators played key roles in the first treatment trial that evaluated the usefulness of vitamin E in slowing the progression of cognitive decline in patients with MCI, and they will be involved in new drug trials that are on the horizon. In addition, a series of recent studies by Dr. Guerry Peavy and her colleagues showed that stressful life events and the elevation of certain hormones related to stress (e.g., cortisol) accelerate the development of dementia in those with MCI, and may increase the odds of developing MCI in cognitively normal elderly people. This ground-breaking research is continuing and now focusing on the possibility that stress reduction therapies may slow the development of MCI.

**Shiley-Marcos ADRC and CAP programs are designed to assist in the accurate identification and diagnosis of MCI in seniors with memory concerns:**

1) **The Memory in Aging Project (MAP)** provides seniors who have memory concerns and are eligible for research participation with a no-cost cognitive assessment. Contact Cecily Jenkins, PhD at 858-822-4800 for an assessment.

2) **Our Memory Screening Day provides seniors with a no-cost memory evaluation with feedback that they can share with their physician.** Contact Cecily Jenkins at 858-822-4800.

3) **CAP provides no-cost, 30-minute memory screenings on an ongoing basis.** Contact Kacie Smith at 858-246-1404 or Kts001@ucsd.edu.
Comprehensive Alzheimer’s Program (CAP)

The overall goal of the program is to lessen the burden of Alzheimer’s disease for patients and their families, and provide new treatment options that are not available elsewhere. At CAP, patients will have access to a team of highly skilled clinicians who specialize in memory disorders and neurodegenerative diseases, supported by nurse practitioners and other staff to provide excellent care as well as opportunities for research, in particular clinical trials that test novel treatments. CAP has grown out of the close relationship between the Shiley-Marcos Alzheimer’s Disease Research Center (founded in 1984), and the Alzheimer’s Disease Cooperative Study (the largest academic Alzheimer’s clinical trials program in the world, active since 1991). The leaders of these research organizations have planned and implemented CAP so that patients in the greater San Diego region can benefit from the latest research discoveries. CAP builds on the Memory Disorders Clinic at UC San Diego, which was created in 1987, and has integrated and expanded this with a comprehensive clinical trials program.

The Shiley-Marcos Alzheimer's Disease Research Center (ADRC)
The Shiley-Marcos Alzheimer’s Disease Research Center conducts a wide variety of research studies dedicated to understanding the causes, clinical features, and neuropathological basis for Alzheimer’s disease (AD) and related memory disorders. The ADRC follows over 350 seniors with AD or a related dementia, and over 100 age-matched participants with no memory problems. Participants undergo an annual comprehensive clinical and neuropsychological examination, and are offered participation in additional research studies. The ADRC supports research into accurate diagnosis of AD and other dementing disorders, early diagnosis of Mild Cognitive Impairment (MCI) and the transition to AD in very mildly impaired subjects, and studies of healthy cognitive aging. The ADRC also participates in local, national, and international research initiatives. Education of the community and of healthcare professionals is a key part of the ADRC mission. The ADRC also provides a number of socially and cognitively stimulating Quality of Life programs for persons with dementia and their families including a variety of support groups and community-based programs.

The Memory Disorders Clinic (MDC)
The Memory Disorders Clinic at UC San Diego specializes in diagnosis and management of disorders of memory and thinking. In particular, the clinic emphasizes treatment and care of patients with dementia such as Alzheimer’s disease. In addition, the clinic covers other disorders that cause deterioration of thinking, language, and memory, including Lewy Body dementia, Frontotemporal dementia, and Vascular dementia. The Memory Disorders Clinic is staffed by expert clinicians who identify and diagnose these disorders, and provide medical treatment, comprehensive care, and support to caregivers and their families; state-of-the-art brain imaging techniques and neurocognitive evaluations are available.

The Alzheimer’s Disease Cooperative Study (ADCS)
The Alzheimer's Disease Cooperative Study was formed in 1991 as an agreement between the National Institute on Aging (NIA) and UC San Diego. The ADCS was developed to accelerate research into the development of drugs that might be useful for treating patients with AD and to improve the design and measurement of outcomes in clinical trials. The ADCS focuses on evaluating compounds that will benefit the general good of AD patients, improve cognition, slow the rate of decline, or delay the appearance of AD, and also studies agents designed to ameliorate behavioral symptoms. The ADCS, as part of large-scale studies such as the Alzheimer’s Disease Neuroimaging Initiative (ADNI), has helped to implement advances such as using MRI and other brain imaging methods as outcome measures in clinical trials.

Therefore, the overarching mission of CAP is to:
• Diagnose, treat, and manage patients with cognitive problems that may be due to AD or related disorders
• Provide access to and conduct the latest clinical trials for AD
• Educate professionals and the community regarding AD
• Provide outreach to the San Diego community regarding diagnosis, treatment, and care for persons with AD

By bringing these resources at UC San Diego together to develop a unified clinical team, we hope to make great strides towards improving care and finding a cure for Alzheimer’s and related disorders. CAP has obtained space adjacent to the ADRC to support an extensive clinical trials program that will offer the latest and most hopeful new treatment approaches as clinical trials for Alzheimer’s and related disorders.

For more information about CAP, call 858–246-1300 and ask for a study coordinator or nurse practitioner.
Colorful quilts are stacked up in piles and on top of bookshelves and desks in the Alzheimer’s Disease Cooperative Study located in the offices above the Shiley-Marcos Alzheimer’s Disease Research Center. The quilts come from as far as Hawaii, Alaska, and Maine. They’re headed for more than 70 research centers throughout the nation where they will be handed out to patients taking part in a variety of clinical trials coordinated nationwide through the federally-funded Alzheimer’s Disease Cooperative Study (ADCS). Wherever the quilts come from and wherever they’re headed, they first find a temporary home in the office of Jeffree Itrich, a communications specialist for the ADCS who came up with the idea of donating quilts to patients in clinical trials. The quilt project is meaningful to Itrich because she is a quilter who also lost her mother to dementia.

The project began when Itrich wanted to thank the patients who take the time to participate in clinical trials that sometimes involve sitting in an MRI, receiving infusions, or other time-consuming procedures. Quilts are perfect comfort objects for patients and their families. “It’s about giving back and trying to do the right thing,” Itrich says. She has contacted fellow quilters, blogs, and websites with the project proposal. As a quilter, she knows those who share her hobby are generous, but she didn’t anticipate the deluge of blankets that have come pouring into her office. When the AARP got wind of her efforts and featured the quilt donation program in their bulletin, the phone started ringing off the hook. So far, Itrich has collected nearly 1500 quilts. The patients’ responses are very moving. “The quilts are making a difference,” she says.

Quilts are perfect comfort objects for patients and their families. ‘It’s about giving back and trying to do the right thing,’ Itrich says.

One clinical trial coordinator told the story of a woman who came with her daughters to a research center to undergo an MRI. The coordinator realized the patient was going to get cold during the procedure, so she gave her one of the quilts. The woman’s daughters were deeply moved and astounded that a complete stranger would take time to make a quilt for their mother.

Meanwhile, Itrich didn’t anticipate the emotional response from the quilters who gave their work. Some had lost a parent or friend to Alzheimer’s. Some feared they were next. All said they felt compelled to do something to thank the patients who are helping to find a cure. “Most people have been touched by Alzheimer’s but have not been able to work through their grief,” Itrich says. “It’s been a catharsis for them.” Many quilters have sent notes along with their work, some three to four pages long. “Thank you for all you are doing to study Alzheimer’s,” one quilter wrote. “With the knowledge of the researchers and the courage of the volunteers, hopefully one day there will be a cure.”

For anyone interested in donating a handmade quilt to the project, quilts should be new and lap-sized, approximately 40 inches wide and 45 to 50 inches long, and made of 100% cotton or flannel. A little larger or smaller is fine. You can use any design or pattern. The study participants are both men and women so a variety of colors work best, or you can make a “themed” quilt specifically for a woman or a man. There is no deadline. Whenever you can make and send a quilt is fine. Some quilters put labels on the back with their name and city or thanking the recipient for participating in Alzheimer’s research but that is optional.

For more information on the quilt project see:  http://adcs.org/ResearchQuilts.aspx
Scientific advancement and discovery in clinical research would not be possible without the volunteerism of individuals who are willing to participate in research studies. Most people are aware that persons with a given health condition may participate in research studies designed to better diagnose and treat their condition. While participants give many reasons for volunteering in research, including the desire to help future generations, many also hope that they will gain access to state-of-the-art technologies and treatments that may not yet be FDA approved and hence publicly available.

Fewer people however, are aware that healthy persons (those without any major medical conditions) are also needed to participate in research studies devoted to better understanding a multitude of diseases and their potential treatments. More specifically, in the study of neurodegenerative disorders such as Parkinson’s disease (PD), Alzheimer’s disease (AD), and related dementias, healthy control groups are extensively used in a wide variety of clinical studies, many of which are observational in nature (they do not involve experimental medications or interventions).

There are several reasons why it is essential to include healthy persons in research studies designed to better understand and treat PD, AD, and related dementias. These neurodegenerative conditions impact the human brain, which is an incredibly complex organ that we do not yet completely understand. The brain, like any other organ in the body, does undergo some normal age-related changes, but as people continue to live longer lives, we must continue to learn more about what characterizes normal age-related processes and what characterizes the presentation and progression of specific diseases that affect the brain. Objectively characterizing and comparing the structural and biochemical changes that occur in two groups of participants, those with and those without a neurodegenerative disease, enables scientists to better understand what is “normal” and what is alternatively, the function of a specific disease process.

In addition, when scientists are able to follow persons in a longitudinal study (one that occurs over a prolonged period of time) a percentage of the group that enrolls in the normal/healthy control cohort will ultimately develop the conditions being studied. Having the opportunity to systematically evaluate this subgroup of individuals, who convert from the normal control group to the group with neurodegenerative symptoms, provides researchers with information about which structural and biochemical changes occur earliest in the disease process. This information or identification of key biomarkers may be able to replace the current medical model, which relies on the development of observable symptoms before a diagnosis can be determined. Identifying the presence of these disease-related changes earlier enhances the likelihood that treatments designed to stop the progression will be effective.

"The brain, like any other organ in the body, does undergo some normal age-related changes, but as people continue to live longer lives, we must continue to learn more about what characterizes normal age-related processes and what characterizes the presentation and progression of specific diseases that affect the brain."

Finally, in the earliest phase of clinical trials, new drugs and treatments must often be tested on healthy volunteers first. Researchers need the participa-
tion of older people in their clinical trials so that scientists can learn more about how the new drugs, therapies, medical devices, surgical procedures, or tests will work. Many older people have special health needs that are different from those of younger people. For example, as people age, their bodies may react differently to drugs. Older adults may need different dosages (or amounts) of a drug to have the right result. Also, some drugs may have different side effects in older people than younger people. Having seniors enrolled in drug trials enables researchers to obtain the information they need to develop the right treatment for older people, the group most likely to be impacted by a dementia disorder.

Healthy controls contribute to a wide array of clinical studies at the Shiley-Marcos Alzheimer’s Disease Research Center (ADRC). In our Longitudinal Study, we follow approximately 100 healthy controls and 350 persons with a dementia diagnosis to enhance the detection, diagnosis, and treatment of Alzheimer’s and related dementias. Participants receive an annual evaluation that consists of a physical and neurologic exam, as well as a detailed cognitive assessment. In addition, in the first year of the study, participants provide valuable biomarker data in the form of blood, cerebral spinal fluid, and volumetric MRI scans. Participants also agree to brain donation at the end of life. Participants in this longitudinal study receive annual feedback about their cognitive status and diagnosis, and how that changes or remains stable from one year to the next. Many participants in this study are also invited to participate in other studies, including those that simply involve additional cognitive assessments.

Healthy persons who seek to advance knowledge about causes, progress, and treatment of disease play a valuable role in clinical research at our Shiley-Marcos ADRC. Eligible participants may personally benefit by receiving a range of detailed and cutting-edge medical assessments by expert clinicians.

Healthy controls can also volunteer to participate in The Alzheimer’s Disease Neuroimaging Initiative (ADNI) 2 study. ADNI is a landmark study that began in 2004 as a public-private research partnership tasked with identifying biomarkers to detect AD. The study has gathered and analyzed thousands of brain scans, genetic profiles, and biomarkers in blood and cerebrospinal fluid (CSF). The study was designed to enable researchers to follow AD as it progresses in an individual, from various points in the disease process. Researchers are seeking new volunteers to join those already participating in the study as it enters the ADNI 2 phase. The study participants will be followed for several years to define any changes in brain structure and function as people transition from normal cognitive aging to Mild Cognitive Impairment (MCI) to AD. Like the previous phases of the study, researchers will use imaging techniques and biomarker measures in blood and CSF specially developed to track changes in the living brain.

Healthy persons who do not have a first degree relative with PD can also volunteer to participate in the Parkinson’s Progression Markers Initiative (PPMI). PPMI is an observational research study to identify biomarkers of PD progression. The discovery of a biomarker of PD is critical to the development of new and better treatments, particularly those that could ultimately slow or stop the progression of the disease. PPMI is the first clinical study to assemble a population of sufficient size to collect this information, draw meaningful scientific conclusions over time, and try to develop better ways to measure the progression of PD. Participants will be followed over a 3 year period and will undergo a multitude of assessments including cognitive testing, brain imaging via MRI and DaTScan, and cerebral spinal fluid draw (CSF).

Healthy persons who seek to advance knowledge about causes, progress, and treatment of disease play a valuable role in clinical research at our Shiley-Marcos ADRC. Eligible participants may personally benefit by receiving a range of detailed and cutting-edge medical assessments by expert clinicians. In addition, some studies compensate participants for their willingness to undergo particular procedures such as brain scans or CSF draws. If you or someone you know is 65-85 years old, in good general health, and interested in participating in clinical research at the Shiley-Marcos ADRC, call Christina Gigliotti, PhD, 858-822-4800 to receive more information and determine your eligibility.
### Nerve Growth Factor

**PRINCIPAL INVESTIGATOR:** Michael Rafii, MD, PhD  
**TIME INVOLVED:** 24 Months  
**CONTACT:** Christina Gigliotti, PhD - (858) 822-4800

Nerve Growth Factor (NGF) research is a phase 2 double-blind placebo controlled study to test the safety, tolerability, and effectiveness of a gene transfer drug called Cere-110 in those with mild-to-moderate AD. Studies suggest that NGF may help increase the survival of neurons that degenerate in AD. In this study NGF is delivered by surgical insertion into the region of the brain where cell death occurs.

**REQUIREMENTS:**
- 55-80 years old and in general good health  
- On stable AD medication for 3 months  
- Have a study partner for all visits  
- Fluent in English

### Genentech ABE4869g (ABBY)

**PRINCIPAL INVESTIGATOR:** Michael Rafii, MD, PhD; Judith Rivera, NP  
**TIME INVOLVED:** 22 Months  
**CONTACT:** Michelle Herman - 858-246-1305

Phase II drug trial with a monoclonal beta-amyloid antibody. Subjects will receive either subcutaneous injections every two weeks or an IV infusion monthly for 69 weeks. MRIs required. Optional CSF and DNA repository studies.

**REQUIREMENTS:**
- 50-80 years old  
- Mild-to-moderate AD with MMSE score 18-26  
- Have a study partner for all visits

### Effects of Intravenous Ibuprofen on Amyloid-Beta Protein Production

**PRINCIPAL INVESTIGATOR:** Doug Galasko, MD  
**TIME INVOLVED:** Two visits over 3-4 weeks  
**CONTACT:** Helen Vanderswag, RN - (858) 822-4800

Participants will undergo screening to qualify for the study. Those who qualify will receive a single dose of 800 mg of ibuprofen or placebo, and will undergo repeated blood draws through an intravenous line.

**REQUIREMENTS:**
- 20-40 years old and in general good health  
- People with certain medical conditions and allergies will not be eligible

**COMPENSATION:**  
$100 for people who complete the study

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### Your Questions Answered

**Why are you still investigating non-steroidal antiinflammatory drugs (NSAIDS) when prior research has suggested they aren’t helpful in treating Alzheimer’s?**

Epidemiological studies suggested that chronic users of nonsteroidal antiinflammatory drugs (NSAIDs) have a lower risk of developing Alzheimer’s disease (AD), indicating a role in possibly preventing or delaying the onset of AD. Whether this is a true “cause and effect” of NSAIDs is unknown and even if so, the underlying mechanisms of action are not clear. Treatment trials with various NSAIDs in AD subjects have not shown any benefit and as a result, have failed to confirm the predictions from epidemiological studies. However, this negative outcome could be due to selecting patients who are too advanced in the disease course and not representative of a preventive study. Further, “ineffective” NSAIDs may have been used in the various trials.

Our own research studies here at UC San Diego suggested that some but not all of NSAIDs have additional activities in lowering the longer and possibly more pathogenic amyloid β-protein (Aβ) species. It may be that this Aβ42-lowering property of NSAID is necessary for any beneficial effects in AD. Of the commonly used NSAIDs, ibuprofen and indomethacin are Aβ42 lowering but not naproxen or celecoxib. We are currently conducting this study to test whether a single intravenous dose of ibuprofen will lower the levels of Aβ42 in blood as predicted from our laboratory studies. If we can demonstrate this Aβ42-lowering property in healthy controls, we will proceed to ask whether this can also be seen in the cerebrospinal fluid of AD subjects as a prelude to a small treatment trial.

I’ve recently heard about a cancer drug that can treat Alzheimer’s. Is this true?

Researchers at Case Western Reserve recently reported on the ability of a cancer drug, bexarotene, to dramatically
Alzheimer’s Disease Neuroimaging Initiative 2 (ADNI 2)

PRINCIPAL INVESTIGATOR: James Brewer, MD, PhD
TIME INVOLVED: 4 Years | CONTACT: Helen Vanderswag, RN - (858) 822-4800

The purpose of the study is to examine how brain imaging technology and biomarker tests, along with measurements of memory and daily functioning, can be used in the future conduct of studies that focus on the identification and treatment of AD at an early stage.

REQUIREMENTS:
- Early memory problems, a diagnosis of MCI or AD, and those without memory changes
- 55-90 years old; 65-90 for normal controls
- Have a study partner for all visits
- Able and willing to undergo MRI, PET scans, and lumbar puncture procedure (LP)
- MMSE score of 20 or above

Roche WN25203B (SCarlet RoAD)

PRINCIPAL INVESTIGATOR: Michael Rafii, MD, PhD; Judith Rivera, NP
TIME INVOLVED: 24 Months | CONTACT: Kacie Smith - (858) 246-1303

Randomized, double-blind, placebo-controlled, parallel-group two-year study to evaluate the effect on cognition and function in prodromal Alzheimer’s disease of subcutaneous gantenerumab.

REQUIREMENTS:
- 50-85 years old
- Prodromal AD with MMSE greater than 24
- Have a study partner for all visits
- On no memory medications

Resveratrol (ADC-037-1.ES)

PRINCIPAL INVESTIGATOR: Michael Rafii, MD, PhD; Judith Rivera, NP
TIME INVOLVED: 12 Months | Jennifer Foster - (858) 246-1306

Phase II, double-blind, placebo-controlled, parallel arm drug trial to evaluate the safety, tolerability, and effectiveness of resveratrol when given to people with mild-to-moderate AD. All participants will undergo CSF collection (lumbar puncture) and volumetric MRI.

REQUIREMENTS:
- Age 50 or older with mild-to-moderate AD
- MMSE score 14-26 (inclusive);
- Have a study partner for all visits
- Able to abstain from eating large quantities of resveratrol containing foods or resveratrol dietary supplements

Reduce beta-amyloid and improve functioning in Alzheimer mice. Since the drug is already approved to treat a rare form of cancer, some may be tempted to try to obtain it for AD. We strongly recommend against this. First, mouse models of Alzheimer’s don’t fully replicate the human condition; treatments that work in mice have often failed to work in humans. Bexarotene also has known side effects and has rarely been used in the elderly. Although someone could manage to obtain this drug on his or her own, issues such as what dose to take, how often to take it, and what side-effects to look out for are not well understood, and results could be more harmful than beneficial. The findings from this study are novel and very interesting, and relevance will rapidly be determined by carefully conducted human clinical trials. Stayed tuned!

My daughter bought me resveratrol supplements from the health food store because she heard Resveratrol can treat Alzheimer’s disease. Is it worth taking?

Resveratrol comes from plants and is found in the skin of red grapes and in red wine. Some research has suggested that limited consumption of red wine may lower the risk of developing AD, and researchers hope that beneficial compounds in resveratrol may also help to treat persons who have the disease. Many people are interested in “natural” treatments for Alzheimer’s and will spend a great deal of money on supplements that claim to treat the disease. Thus it is important to test any potential benefit of a natural supplement through well-designed clinical trials.

The Alzheimer’s Disease Cooperative Study (ADCS) will soon begin enrolling 120 participants with mild-to-moderate Alzheimer’s from 26 sites across the United States in a clinical trial of resveratrol. Participants must consent to blood draws, magnetic resonance imaging (MRI), and lumbar puncture (LP) during the course of the 12-month study.

See above for more information on the resveratrol clinical trial.
Exciting Advances in Alzheimer’s Research Using Stem Cells

Researchers and scientists at UC San Diego School of Medicine have, for the first time, created stem cell-derived, in vitro (made in a laboratory) models of sporadic and hereditary Alzheimer’s disease (AD) using induced pluripotent stem cells from patients with AD. These stem cell-derived neurons provide a new tool for unraveling the mechanisms underlying the complex disease.

“Creating highly purified and functional human Alzheimer’s neurons in a dish – this has never been done before,” said senior study author Lawrence Goldstein, PhD, professor in the Department of Cellular and Molecular Medicine, Howard Hughes Medical Institute Investigator and Director of the UC San Diego Stem Cell Program. “It’s a first step. These aren’t perfect models. They’re proof of concept. But now we know how to make them. It requires extraordinary care and diligence, really rigorous quality controls to induce consistent behavior, but we can do it.” Goldstein and his postdoctoral researcher, Mason Israel, PhD, worked together to develop the project and he and Goldstein now have a patent pending on their technology.

Living cells provide an unprecedented tool for developing and testing drugs to treat the disorder. “We’re dealing with the human brain. You can’t just do a biopsy on living patients,” said Goldstein. “Instead, researchers have had to work around, mimicking some aspects of the disease in non-neuronal human cells or using limited animal models. Neither approach is really satisfactory.”

The stem cell breakthrough, published in the January 25 online edition of the journal Nature, represents a new and much-needed method for studying the causes of AD. Dr. Edward Koo, co-director of the Shiley-Marcos Alzheimer’s Disease Research Center (ADRC) is one of 17 co-authors on the paper. Shiley-Marcos ADRC director Douglas Galasko, MD; nurse practitioners Deborah Fontaine, NP, and Judith Rivera, NP; and community health program supervisor, Christina Gigliotti, PhD, were gratefully acknowledged in the paper for their assistance in recruiting ADRC research participants for the study and for doing the participants’ skin biopsies.

Goldstein and colleagues extracted primary fibroblasts from skin tissues taken from two patients with familial AD (a rare genetic early-onset form of the disease), two patients with sporadic AD (the common form whose cause is not known), and two persons with no known neurological problems. They reprogrammed the fibroblasts into induced pluripotent stem cells (iPSCs) that then differentiated into working neurons. The iPSC-derived neurons from the Alzheimer’s patients exhibited normal electrophysiological activity, formed functional synaptic contacts and displayed tell-tale indicators of AD. Specifically, they possessed higher-than-normal levels of proteins associated with the disorder.

With the in vitro Alzheimer’s neurons, scientists can more deeply investigate how AD begins and chart the biochemical processes that eventually destroy brain cells associated with memory and other cognitive functions. “The differences between a healthy neuron and an Alzheimer’s neuron are subtle,” said Goldstein. “It basically comes down to low-level mischief accumulating over a very long time, with catastrophic results. In this work, we show that one of the early changes in Alzheimer’s neurons thought to be an initiating event in the course of the disease turns out not to be that significant.” Goldstein adds that they discovered a different early event plays a bigger role. The scientists also found that neurons derived from one of the two patients with sporadic AD showed biochemical changes possibly linked to the disease. The discovery suggests that there may be sub-categories of the disorder and that, in the future, potential therapies might be targeted to specific groups of AD patients.

Though just a beginning, Goldstein emphasized the iPSC-derived Alzheimer’s neurons present a huge opportunity in a desperate fight. “At the end of the day, we need to use cells like these to better understand Alzheimer’s and find drugs to treat it. We need to do everything we can because the cost of this disease is just too heavy and horrible to contemplate. Without solutions, it will bankrupt us – emotionally and financially.”

Revised and reprinted with permission from LeFee, Scott. Researchers Induce Alzheimer’s Neurons From Pluripotent Stem Cells. UC San Diego News Center, January 25th, 2012.
Helpful and Informative New Resources

Latest Alzheimer's Research Progress Report Released

2010 Alzheimer's Disease Progress Report: A Deeper Understanding, highlights important developments and directions in federally funded research. The booklet is prepared by the National Institute on Aging (NIA), which leads the effort supporting Alzheimer's research. The Shiley-Marcos ADRC and 28 other university-based research centers in the US are funded primarily through the NIA.


Biology of Aging

What is aging? Can we live long and well? Is aging in our genes? How does our metabolism relate to aging? Can your immune system still defend you as you age? Learn the answer to these questions and more. Biology of Aging: Research Today for a Healthier Tomorrow describes some of NIA's exciting findings about the basic biology of aging and points to directions for future investigation.


What's On Your Plate? Smart Food Choices for Healthy Aging

Making wise decisions about what you eat as you get older is important. This 80-page guide to healthy eating, written especially for older adults, describes what you need to know about food groups, serving sizes, food labels, and more. The entire booklet is available to read online or to download in PDF format.


Contents of this publication include:
- Risk for developing Alzheimer's including genetics
- Neuroimaging and biomarkers that detect and track the disease
- Research into new treatments
- Lifestyle factors that may worsen or protect against the disease
- Help for caregivers
- Animation showing the progression of Alzheimer's in the brain
- Video interviews highlighting new insights into the disease

Contents of this publication include:
- Aging under the microscope
- Genetics of aging
- Does stress really shorten your life?
- Immune system: Can your immune system still defend you as you age?
- What happens when DNA becomes damaged?
- Does how much you eat affect how long you live?
- The promise of research: past, present, and future

Contents of this publication include:
- Plans for healthy eating
- Important nutrients to know
- Healthy lifestyle
- Food shopping—making the trip easier, saving on the cost
- Making sure your food is safe
- Everyday healthy eating—sample menus and recipes
- Roadblocks to healthy eating
- A healthier future
- Storing cold food
- Practical appendices
**Shiley-Marcos Alzheimer’s Disease Research Center**

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**2012 SERIES**

**Memories at the Museums**

**San Diego Museum of Art**  
January 13, May 11, September 14

**Mingei International Museum**  
February 10, June 8, October 12

**Timken Museum of Art**  
March 9, July 13, November 9

**Museum of Photographic Arts**  
April 13, August 10, December 14

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 required. Please call Lisa Snyder, LCSW at the Shiley-Marcos Alzheimer’s Disease Research Center at (858) 822-4800 to register for a tour.