UT SOUTHWESTERN MEDICAL CENTER

Fall 2011

Alzheimer's

DISEASE CENTER NEWS

FROM THE DIRECTOR | *Roger N. Rosenberg, M.D.*

NIH RENEWS ADC's FUNDING

Our Alzheimer's Disease Center grant has been renewed for the fifth consecutive time by the National Institutes of Health's (NIH) National Institute on Aging, representing 28 years of continuous support.

The $9 million award will allow us to continue our research on vascular risk factors and inflammation that help cause the dementia of Alzheimer's disease. It also will help us develop new research efforts into the genetics and genomics of Alzheimer's.

We are a stable and effective team. In 1988, the principal leaders of the first successful NIH grant we received included Dr. Perrie Adams, deputy director; Dr. Myron Weiner, clinical core leader; Doris Svetlik, nurse manager; Dr. Joan Reisch, statistics and data management core leader; and Dr. Charles White III, neuropathology core leader. Twenty-three years later, we are still together and coordinating our clinical and research efforts.

We are fortunate indeed to be joined now by Dr. Munro Cullum, newly appointed as the clinical core leader, and Dr. Mary Quiceno, the new education and information transfer core leader. Dr. Cullum has been an investigator in the center's clinical core and also serves at UT Southwestern as chief of psychology. He brings great clinical and research experience to the ADC and will lead our efforts to develop existing translational research programs related to vascular risk factors and inflammation and their role in affecting the process of dementia, as well as beginning new programs investigating the genetics and genomics of dementia.

Dr. Quiceno was a resident and fellow in the Department of Neurology and Neurotherapeutics and is an active clinician in the clinical core. This new position will allow her to merge her two main interests of caring for patients and educating the community about dementia.

Dr. Weiner served with distinction as clinical core leader and will now be core leader for Native American studies, providing diagnostic services and conducting research on dementia in the Choctaw Nation of Oklahoma. Our ADC contributes one-half of all of the clinical data

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FORUM SPEAKER TO DISCUSS PROSPECTS FOR NEW THERAPIES

By Rachel Skei Donihoo

Fall Public Forum
7 p.m. • Oct. 25
6000 Harry Hines Blvd.

Advances in our understanding of the neurobiology of Alzheimer's disease over the past few decades have led to modestly effective symptomatic treatments, as well as many promising targets for disease-modifying interventions. Nevertheless, no new treatment has been approved since 2003.

In a talk at the Fall Public Forum presented by the Friends of the Alzheimer's Disease Center on Oct. 25, Dr. Paul Aisen of the University of California, San Diego, will review the history of Alzheimer's disease research and emphasize recent advances in disease biomarkers and trial design that have renewed optimism about the prospects for major therapeutic advances.

The 7 p.m. lecture, titled "Toward a New Generation of Alzheimer's Disease Therapeutics,"

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WHAT'S INSIDE

Research Studies

FROM PHYSICIAN TO ADVOCATE

AFTER DIAGNOSIS, DOCTOR USES BLOG TO SPREAD THE WORD ABOUT ALZHEIMER'S

By Jeff Carlton

Alzheimer's disease runs in Dr. Dewayne Nash's family, so the Austin-area family physician always worried that one day it would come for him.

Last year, having long ago vowed to participate in a research study to advance understanding of the disease, Dr. Nash took a neuropsychological examination at the Alzheimer's Disease Center at UT Southwestern Medical Center. He thought he would be part of the control group.

"But as I was taking the test," said Dr. Nash, 61, "I realized I had a problem."

He couldn't keep track of 10 words he was supposed to memorize and repeat back every five minutes. Dr. Nash's difficulties with this task, designed to test short-term memory, led to a finding of mild cognitive impairment. The diagnosis was heartbreaking.

"I had to quit practicing medicine, which was what I loved to do," Dr. Nash said. "I enjoyed going to work every day."

Dr. Nash is now part of the Alzheimer's Disease Neuroimaging Initiative – Phase 2, or ADNI 2. This international study began seven years ago and was designed to find the best ways to measure the effects of Alzheimer's treatments. The goal has since expanded to use biomarkers, or proteins found in blood, to identify Alzheimer's before the onset of dementia.

After researching Alzheimer's studies, Dr. Nash initially came to UT Southwestern because of its involvement with ADNI 2."There's going to be a lot of good stuff coming out of this study," he said. "It's the least I can do to help in a small way to find a cure and better treatment for this awful disease."

Dr. Dewayne Nash, who retired after being diagnosed with mild cognitive impairment, meets regularly with Dr. Mary Quiceno at the Alzheimer's Disease Center at UT Southwestern.

"Alzheimer's is a disease everyone is scared of. People don't like to talk about it." - Dewayne Nash, M.D.

Now retired, Dr. Nash said he has found new purpose as an advocate for Alzheimer's. His blog, www.organicgreendoctor.com, is both a journal of green living on his 10-acre property and a personal diary of coping with a devastating disease.

He said his experience as both a physician who treated people with Alzheimer's and now a patient dealing with its symptoms has given him a unique perspective. The revelations on his blog often feel private, but Dr. Nash says he hopes they encourage people to discuss Alzheimer's in an open fashion.

"My goal with the blog is to talk about what's going on with me and to use it as a vehicle for people

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CLINICAL TRIALS

To learn more about studies under way or find out when new studies are added, visit www.utsouthwestern.edu/adc or call the UT Southwestern Memory Research Unit at 214-648-9376.

COGNITIVE TRAINING FOR MILD MEMORY COMPLAINTS

People 60 or older who are in overall good health but noticing more "senior moments" or have been diagnosed with mild cognitive impairment are needed for a study evaluating the effects of cognitive training on brain function. A short cognitive screening will be given to determine eligibility for the study. Those who qualify will receive eight cognitive training sessions, study-related assessments, an electroencephalogram to measure brain waves, and follow-up testing. Call Kristin Martin-Cook, 214-648-9368, or Audette Rackley, 214-905-3007.

DAVUNETIDE

Participants with progressive supranuclear palsy are needed for a study on davunetide. If accepted, they will receive placebo or davunetide nasal spray twice a day for 52 weeks. Participants must be 41 to 85 years old; be able to tolerate magnetic resonance imaging and lumbar punctures; be able to ambulate independently or with limited assistance; have a caregiver willing to attend all study visits and monitor study medication dosing; and have a 12-month history of postural instability or falls. No memory medications are allowed. Call Jackie Rabb, 214-648-9376.

EXERCISE STUDY

People with mild cognitive impairment who do not currently adhere to a regular fitness program are sought for a one-year study that will compare individually tailored, supervised aerobic exercise training with flexibility and stretching training. The study will investigate the effects of exercise on cognitive and cardiovascular health as well as changes in proteins known to damage and/or protect the brain. Call Kristin Martin-Cook, 214-648-9368, or Estee Brunk, 214-345-4665.

OBSERVATIONAL AND BIOMARKER DEVELOPMENT STUDIES

While these studies do not require or offer a new treatment, they are the foundation for future research and therapeutic trials.

ADNI 2 (ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE – PHASE 2)

This study builds on the first ADNI studies and will enroll people ages 55 to 90 with no memory problems, mild cognitive impairment and early Alzheimer's disease. Participants will undergo magnetic resonance imaging (MRI), traditional glucose-based positron emission tomography (PET), new amyloid PET scanning to investigate the formation of beta-amyloid plaque formation, and standard neuropsychological and neurological exams. Participants will be compensated for their time and participation. Call Kristin Martin-Cook, 214-648-9368.

ERK AD-INDEX STUDY

People 50 and older with memory loss or depression, or who have experienced other cognitive decline or impairment, are being sought for a study of the ERK AD-Index, a test that could aid in the diagnosis of Alzheimer's disease in the future. Participants must be available for a one-hour visit that involves consent, medical history, sampling of blood and a skin biopsy, and must agree to a brain autopsy with results contributing to the study. Participants will be compensated for their time. Call Kathy Koch, 214-648-9343.

CORE AND TARC RESEARCH STUDIES

People with mild cognitive impairment, early Alzheimer's disease or frontotemporal dementia are needed for observational studies. The studies usually involve one visit a year for neuropsychological testing, neurological exams, brain imaging and blood sampling. The data collected from these visits are used by many investigators studying the aging brain and disorders of cognitive function. These visits often involve financial compensation. Call Jackie Rabb, 214-648-9376, or Kristin Martin-Cook, 214-648-9368.

TELENEUROLOGY

People with dementia are needed to participate in a videoconferencing study. Two neurological examinations will be performed by a physician, once in person and once via TV screen. This research may help bring new diagnostic services to rural and underserved populations and aid in the development of new examination procedures for patients who need to be seen by a neurologist but cannot visit a doctor's office due to illness or distance. Call Mari "Ife" Madhi, 214-648-0315. ❄

NELSON MAULDIN HONORS LATE MOTHER WITH $200,000 GIFT

By Rachel Skei Donihoo

In honor of his beloved mother whose final years were consumed by Alzheimer's disease, Nelson Mauldin has donated $200,000 to support research at UT Southwestern into the debilitating neurological disorder.

The gift to Southwestern Medical Foundation, which was given in the form of a charitable gift annuity, will create the Katie Nelson Mauldin Fund for Alzheimer's Disease Research.

Dr. Daniel K. Podolsky, president of UT Southwestern, said, "We are on the brink of several significant developments in the fight against Alzheimer's disease, and we're sincerely touched by Nelson Mauldin's desire to honor his mother by supporting the medical center's research programs in such a significant way."

An only child and self-professed "mama's boy," Mr. Mauldin became his mother's caretaker during her seven-year battle with the disease.

"She took care of me as a child, so it became my time to take care of her," said Mr. Mauldin, of Arlington. "She was the love of my life and, as difficult as it was, this experience really allowed me to step up to the plate. Unless you have dealt with Alzheimer's firsthand, it is impossible to know how overwhelmed and hopeless you can feel. When I read about everything UT Southwestern is doing to find a cure and help others with the disease, it inspired me to donate to the cause and, I hope, help others in the process."

Born and raised in Dallas, Mr. Mauldin graduated from Crozier Technical High School in 1948 and attended Texas Tech University until 1950. He launched his own electrical manufacturing sales agency in Dallas, which was sold in 1994. After retirement he relocated to Arlington, where he cared for his mother until her death in 1997.

Mrs. Mauldin, an avid gardener, horsewoman and crochet enthusiast, "walked religiously" and remained active all her life, her son said. Mr. Mauldin's father, Fred, spent his career at Lone Star Gas Co. and died of cancer in 1994.

"This generous gift from Mr. Mauldin supports an area of medical research in which there is great promise and urgency," said Dr. Kern Wildenthal, president of Southwestern Medical Foundation. "We are pleased that he has chosen to pay tribute to Katie Mauldin in such a valuable way, and we are very grateful for his thoughtfulness and confidence." ❊

FROM PHYSICIAN TO ADVOCATE

Continued from page 2

who want to know what to do," he said. "Alzheimer's is a disease everyone is scared of. People don't like to talk about it."

His participation in the ADNI 2 study is especially important, because it's unusual to find patients at such an early stage of the disease, said Dr. Roger Rosenberg, director of the Alzheimer's Disease Center and holder of the Abe (Brunky), Morris and William Zale Distinguished Chair in Neurology. Most people are in denial, feel stigmatized about their potential for Alzheimer's or ignore their "senior moments."

"Finding volunteers like Dr. Nash can be difficult, but it's critical," Dr. Rosenberg said. "The idea is to identify people as early as possible so they can start finding a treatment."

Dr. Nash comes to UT Southwestern every few months for blood tests, neuropsychiatric exams and brain imaging. He meets regularly with Dr. Mary Ellen Quiceno, assistant professor of neurology and neurotherapeutics, in the Cognitive and Memory Disorders Clinic.

The effort is worth it, he said, if it helps provide a better understanding of Alzheimer's.

"I saw what happened to my mom and what's happening to a very close relative," Dr. Nash said. "This is something I want to do." ❊

Dr. Dewayne Nash hopes his blog, www.organicgreendoctor.com, which chronicles his experiences with cognitive impairment and memory loss, encourages people to participate in Alzheimer's research and to discuss the disease more openly.

EXPERIMENTAL BLOOD TEST MAY LEAD TO EARLY DETECTION

By Rachel Skei Donihoo

UT Southwestern scientists have helped develop a novel technology to diagnose Alzheimer's disease from blood samples long before symptoms appear.

This preliminary technology, which uses synthetic molecules to seek out and identify disease-specific antibodies, also could be used eventually in the development of specific biomarkers for a range of other hard-to-diagnose diseases and conditions, including Parkinson's and immune system-related diseases like multiple sclerosis and lupus, the researchers predict.

"One of the great challenges in treating patients with Alzheimer's disease is that once symptoms appear, it's too late. You can't un-ring the bell," said Dr. Dwight German, professor of psychiatry and an author of the paper published in *Cell*. "If we can find a way to detect the disease in its earliest stages – before cognitive impairment begins – we might be able to stop it in its tracks by developing new treatment strategies."

Researchers in the study hypothesized that there may be numerous antibodies in the blood serum of people with Alzheimer's that are specific to the disease and can serve as a biomarker.

Antigens – substances such as protein from a virus or bacteria that triggers an immune response – traditionally have been necessary for the discovery of antibody biomarkers. It has been impossible previously to identify an antibody (a type of targeted immune molecule) without first knowing the antigen that triggers its production.

This study, however, challenges conventional wisdom and uses synthetic molecules (peptoids) rather than antigens to successfully detect signs of disease in patients' blood samples. These peptoids have many advantages: They can be modified easily and can be produced quickly in relatively large amounts at lower cost.

The researchers used a library of several thousand peptoids to screen serum samples from mice with multiple sclerosis-like symptoms as well as from healthy control mice. The particular peptoids that retained more antibodies from the blood samples of the diseased animals were identified as potential agents for capturing diagnostically useful molecules.

Dr. Dwight German

The investigators then examined serum samples from six patients with Alzheimer's disease, six healthy patients and six patients with Parkinson's. Three peptoids were identified that captured six times the IgG antibody levels in all of the Alzheimer's patients when compared to the control group or to the Parkinson's patients. Using an additional set of 16 normal control subjects and 10 subjects at the very early stage of Alzheimer's, the three candidate biomarkers identified the disease with 90 percent accuracy.

"The results of this study, though preliminary, show great potential for becoming a landmark," said Dr. German. ❊

CANCER DRUG HOLDS PROMISE AS DEMENTIA TREATMENT

By Deborah Wormser

A drug already approved for people with cancer shows early potential as a therapy for a common form of dementia, UT Southwestern Medical Center researchers report.

"Suberoylanilide hydroxamic acid (SAHA) holds promise as a first-generation drug for the prevention and treatment of familial frontotemporal dementia (FTD), a progressive, inherited neurodegenerative disease for which there is no treatment," said Dr. Joachim Herz, director of the Center for Alzheimer's and Neurodegenerative Diseases and the study's senior author.

"SAHA is already approved for clinical use in an unrelated condition, which should make it easier to move quickly to human trials," added Dr. Herz, professor of molecular genetics and neuroscience at UT Southwestern and holder of the Thomas O. and Cinda Hicks Family Distinguished Chair in Alzheimer's Disease Research.

UT Southwestern researchers from the Alzheimer's Disease Center, the Harold C. Simmons Comprehensive Cancer Center and the Protein Chemistry Technology Center participated in the study.

Because familial FTD patients inherit one working copy of the cell-signalling protein progranulin (GRN) gene and one mutated one, the researchers wanted to identify a drug that would make the working copy of the gene work harder.

In an attempt to move as quickly as possible from basic science to clinical trials, the team established a method to quickly screen 1,200 drugs that already had Food and Drug Administration approval. SAHA emerged as the most active of the chemicals they screened, said lead author and graduate student Basar Cenik, who works in the laboratories of both Dr. Herz and co-senior author Dr. Gang Yu, associate professor of neuroscience and a Thomas O. Hicks Scholar in Medical Research.

Dr. Joachim Herz

SAHA is in a class of drugs called histone deacetylase inhibitors, and is approved for use in a cancer called cutaneous T-cell lymphoma.

"We found a drug that can overcome the chemical deficiency associated with the condition, and we showed that it worked in cells taken from humans with FTD," Dr. Yu said. ❊

NEW NAME REFLECTS NEW EMPHASIS ON TREATMENTS

By Rachel Skei Donihoo

"Neurology has evolved into a discipline offering an array of treatments to improve symptoms for many conditions, including epilepsy, Parkinson's disease and multiple sclerosis," says Dr. Mark Goldberg, who became chairman of the Department of Neurology and Neurotherapeutics in 2010. He also directs the Beatrice Menne Haggerty Center for Research on Brain Injury and Repair in Strokes.

UT Southwestern's Department of Neurology and Neurotherapeutics has taken on a new name to reflect an expanded role.

"The word 'neurotherapeutic' means treatment for neurological disorders," said Dr. Mark Goldberg, chairman of the department that is the first in the country to be so identified with the dual name. "In the past, physicians could diagnose most brain diseases, but not treat them."

The department is participating in drug and device testing, and faculty members are conducting research on brain disease therapy, in part by using UT Southwestern's historic strengths in molecular biology, genetics and neuroscience.

"Neurology has evolved into a discipline offering an array of treatments to improve symptoms for many conditions, including epilepsy, Parkinson's disease and multiple sclerosis. Still, children and adults remain without cures for these and many other debilitating conditions, such as amyotrophic lateral sclerosis [ALS], autism, traumatic brain and spinal-cord injury, stroke, and Alzheimer's disease," said Dr. Goldberg, who holds the Linda and Mitch Hart Distinguished Chair in Neurology.

The Department of Neurology was established 45 years ago. The initial growth of the department and development of the residency program were under the leadership of Dr. Roger Rosenberg, who also served as chairman for 18 years and is now the director of the Alzheimer's Disease Center and holder of the Abe (Brunky), Morris and William Zale Distinguished Chair in Neurology.

The department has expanded to a faculty of 13 clinicians, 26 clinician-scientists and 15 researchers in basic science – all with primary academic appointments in neurology and neurotherapeutics.

This collaborative team is distributed across clinical and laboratory sites on the medical center campus and at affiliated hospitals, including Parkland Memorial Hospital, Children's Medical Center Dallas, Texas Scottish Rite Hospital for Children, Texas Health Presbyterian Hospital Dallas and the Dallas Veterans Affairs Medical Center.

"Our goal is to accelerate the process of therapy development by providing leading scientists with well-validated animal models and testing methods," Dr. Goldberg said. "At the same time, neurological clinicians will have opportunities to bring the most promising treatment approaches to initial trials in human disease quickly."

The department's research efforts include the National Institutes of Health (NIH)-funded Alzheimer's Disease Center and the National Multiple Sclerosis Training Center, as well as NIH-supported research in neuroimmunology, ALS, risk factors for dementia, spinal muscular atrophy, and disorders of cellular excitability.❊

FROM THE DIRECTOR

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to the National Institute on Aging related to dementia of the American Indian, due to the dedicated efforts of Dr. Weiner, Dr. Quiceno and Ms. Svetlik.

In addition to the NIH grant renewal, the state Legislature re-funded the Texas Alzheimer's Research and Care Consortium for more than $5 million for the next two years. The consortium of five Texas universities, including UT Southwestern, provides the data management and major scientific leadership for research on new serum biomarkers for early diagnosis of Alzheimer's disease and genetic analyses of risk factors for developing the disease.

We are extremely fortunate to have a team of physicians, patient care coordinators and senior staff who are truly dedicated to the goal of providing excellent care to our patients and conducting outstanding research into the biology of Alzheimer's disease and related disorders.

Dr. Kyle Womack is pursuing NIH-funded neuroimaging studies of frontotemporal dementia. Dr. Kimmo Hatanpaa is investigating the role of the hippocampus region of the brain in dementia. Dr. Michael Devous is a national leader in the neuroimaging of Alzheimer's disease and presented his latest results at the International Conference on Alzheimer's Disease in Paris this summer.

The UT Southwestern ADC will continue to be a leading research center for Alzheimer's disease and related disorders, searching for new insights into the biology of dementia that will lead to effective therapies to prevent or delay its progression.

We thank you immensely for your support and encouragement. The Friends of the Alzheimer's Disease Center has been vital to developing effective research on Alzheimer's disease on our campus for more than 13 years. We are most grateful to you. ❊

Dr. Rosenberg holds the Abe (Brunky), Morris and William Zale Distinguished Chair in Neurology.

FORUM SPEAKER WILL DISCUSS PROSPECTS FOR NEW THERAPIES

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will be held in the Simmons/Hamon Biomedical Research Buildings on the North Campus, 6000 Harry Hines Blvd. Complimentary valet parking will be available.

The forum is free to the public, but because seating is limited, attendance should be confirmed by calling UT Southwestern's Office of Development at 214-648-2344.

"Alzheimer's disease was described just over 100 years ago as an uncommon devastating dementia affecting people in middle age," said Dr. Aisen, professor of neurosciences and director of the Alzheimer's Disease Cooperative Study at the UC San Diego School of Medicine. "Since then, it has been demonstrated to be an epidemic of enormous proportions, affecting a substantial segment of the aging population.

"The field of Alzheimer's disease research seems poised to bring to clinic the next generation of treatments, moving beyond symptomatic benefits to modification of the underlying neurobiology of the disease. Despite the difficult pitfalls of past research, a clear path forward is emerging."

In his talk, Dr. Aisen will explore strategies that utilize newly available tools for disease diagnosis, assessment and analysis. He also will discuss ways to facilitate the study of new therapeutic treatments at early stages in the disease process, when they are most likely to yield major clinical benefits.

Dr. Paul Aisen, UC San Diego

Dr. Aisen, who earned his undergraduate degree at Harvard University and his medical degree from the Columbia University College of Physicians and Surgeons, also has served on the faculties of the Mount Sinai School of Medicine and Georgetown University.

The Friends of the Alzheimer's Disease Center was established in 1996 to provide financial support for Alzheimer's research at UT Southwestern. All the group's contributions go directly to support Alzheimer's research at the medical center.

Since its founding, the group has raised more than $1 million for grants to researchers. For information on joining the group, call the Office of Development at 214-648-2344. ❊

Join Us

JOIN THE FRIENDS OF THE ALZHEIMER'S DISEASE CENTER

The Friends of the Alzheimer's Disease Center raises funds to establish yearly grants for promising researchers who are working to unlock the mysteries of Alzheimer's disease. In addition, the Friends sponsor public forums each spring and fall to present the latest scientific information on the disease to the general public. We welcome the community to these sessions.

Fully tax-deductible memberships in the Friends begin at $500 per year per individual or couple. To join the Friends, call 214-648-2344 or visit our website at www.utsouthwestern.edu/donatenow. Honorary or memorial gifts are another meaningful way to make contributions toward research that is under way at UT Southwestern.

The Alzheimer's Disease Center News is published by The University of Texas Southwestern Medical Center. We welcome your comments or suggestions at 214-648-3404 or robin.loveman@utsouthwestern.edu

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Memory Tip

KEEPING CONNECTED

Many people wonder what they can do to help couples dealing with Alzheimer's disease or other memory loss. Often couples feel isolated once they've received a diagnosis, says Kristin Martin-Cook, clinical research coordinator at the Alzheimer's Disease Center. It's important to keep Alzheimer's patients engaged while also giving the couple time apart. Some suggestions:

- Set up a regular schedule to meet for a mutually enjoyable activity like having lunch at a favorite place every week or playing cards once a month.
- Schedule joint hair or nail appointments and bring the person along, or offer to take him or her with you to run errands together.
- If the person with dementia isn't cooking anymore, bring dinner a couple of times a month or share with the new cook of the house a few easy favorite recipes.
- Notice simple repairs that might be needed, and offer to help. Sometimes just climbing a ladder to change a light bulb is a problem for older couples.

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