

Alzheimer's

D I S E A S E C E N T E R N E W S

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



The Alzheimer's Disease Center (ADC) held a symposium on Friday, February 10, titled "Translational Research in Mechanisms of Neurodegeneration." We believed it was an area of potential collaboration among the research community at UT Southwestern. The response was overwhelming, with audience representation from all of our basic science departments and strong inclusion from psychiatry and neurology members.

We tapped into a deep reservoir of collaborative research into neurodegenerative disease. Three hundred and thirty people registered for the symposium, mainly predoctoral students, postdoctoral fellows, neurology and psychiatry residents and fellows, and junior faculty. They represent the future of research in neurodegenerative disease and were exactly whom we had hoped to target.

The response to the symposium clearly reveals great enthusiasm about the opportunities for research on neurodegenerative diseases at UT Southwestern and particularly the resources that the ADC provides, including clinical and neuropathology databases, patient tissues and fluids, and the opportunity to apply for Pilot Project or Friends of the ADC grants.

Gregory Fitz, M.D., Dean and Provost of UT Southwestern Medical School, expressed his plans to develop neuroscience and neurodegenerative disease research at UT Southwestern in his opening address.

The keynote address was given by Bruce Beutler, M.D., Nobel Laureate in Physiology or Medicine, who spoke on "How Inflammation Begins." It is a topic of central importance to understanding Alzheimer's disease since inflammation is an early and major factor in the causation of disease onset and progression.

The morning session, chaired by Mark Goldberg, M.D., Chairman of Neurology and Neurotherapeutics, emphasized therapeutics being developed by UT Southwestern faculty and included talks by Andrew Pieper, M.D., Ph.D., on "Neuroprotective Therapy for Neurodegenerative Disease"; myself, on "DNA Vaccine as Preventive Therapy for Alzheimer's Disease"; Craig Powell, M.D., Ph.D., Associate Professor of Neurology, on "Autism and Degeneration of Synaptic Function: Molecules to Potential Therapies";

and Joachim Herz, M.D., Director of the Center for Alzheimer's and Neurodegenerative Diseases, on "Therapeutics for Neurodegenerative Disease."

The afternoon session was led by Joseph Takahashi, Ph.D., Chairman of Neuroscience. Speakers were James Malter, M.D., Chairman of Pathology, who spoke on "Amyloid Precursor Protein Gene Regulation at the Synapse"; Philipp Scherer, Ph.D., Director of the Touchstone Center for Diabetes Research, on "Role of Peripheral Amyloid-beta in Mitochondrial Dysfunction"; Ilya Bezprozvanny, Ph.D., Professor of Physiology, on "Presenilins, Calcium Signaling, and Alzheimer's Disease"; Gang Yu, Ph.D., Associate Professor of Neuroscience, on "Biology and Therapy of Alzheimer's Disease and Frontotemporal Dementia"; and Weichun Lin, Ph.D., Associate Professor of Neuroscience, on "Regulation of Synapse Formation by ApoE Receptors and Amyloid Precursor Protein."

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Research Studies



STATEWIDE CONSORTIUM STRIVES TO MAKE TEXAS A GLOBAL LEADER IN ALZHEIMER'S DISEASE RESEARCH

By C. Munro Cullum, Ph.D.

The Texas Alzheimer's Research & Care Consortium (TARCC) is a statewide collaborative research effort that includes UT Southwestern Medical Center, the University of North Texas Health Science Center, Baylor College of Medicine, Texas Tech University Health Science Center, and the UT Health Science Center at San Antonio. TARCC was established in 2005 to improve diagnosis, treatment, and prevention of Alzheimer's disease.

Each site recruits individuals who are diagnosed with Alzheimer's disease (AD) or Mild Cognitive Impairment (MCI), or who are healthy aging controls. Participants undergo advanced analyses of blood proteins, clinical histories, neuropsychological functioning, and metabolic and genetic data in conjunction with demographic information. More than 2000 participants have been enrolled, and more than 1,500 have returned for annual follow-up visits to provide longitudinal data that will aid in understanding the course of the disease.

Striving to make Texas a global leader in Alzheimer's disease research, TARCC investigators have analyzed more than 26 million genetic markers in more than 700 participants using state-of-the-art genetic technology. Preliminary analyses have discovered genes that affect disease risk and may lead to the development of new drugs and therapies to improve the quality of life of Alzheimer's patients. In addition, TARCC is collaborating with the Alzheimer's Disease Genetics Consortium in the largest study of Alzheimer's genetics to date.

In 2010, TARCC researchers created a serum-protein blood test for Alzheimer's disease that has shown promise in terms of diagnostic accuracy. Although further validation is required, the blood test, as part of a multi-tiered screening approach, holds the potential to advance geriatric medicine globally. In addition, TARCC is evaluating links between heart disease, cholesterol, and insulin metabolism in the development of Alzheimer's disease. TARCC investigators also have developed new ways of measuring cognitive functioning and analyzing neuropsychological data that have shown promise in disease staging, differential diagnosis, and enhancing the efficiency of neuropsychological assessment in individuals with known or suspected dementia.

The resulting relational database of clinical, neurocognitive, and biological data that is housed at UT Southwestern provides a rich platform that allows for unique, multimodal investigations into the biology and clinical aspects of Alzheimer's disease, helping to propel Texas into the forefront of neurodegenerative disease research. *



Photo: Mark Matson

New Fund Promotes Statewide Collaboration as Texas 'Game-Changer'

The Darrell K Royal Research Fund for Alzheimer's Research was launched February 28 at a Texas Senate Interim Joint Committee hearing on Alzheimer's disease. Named after legendary UT football coach Darrell Royal, who is now living with Alzheimer's disease, the fund will focus both on research and care for Texans dealing with Alzheimer's.

The fund will support a collaborative effort throughout the State of Texas in developing new treatment strategies and methods of prevention. In her testimony before the committee, Mr. Royal's wife, Edith, stressed the need for sharing research discoveries to more quickly advance the fight against Alzheimer's disease and related dementias.

Lance Armstrong (left), Edith and Darrell Royal, and Matthew McConaughey address a joint legislative committee in Austin.

Cutting-edge research into mechanisms of neurodegenerative diseases took center stage at the Alzheimer's Disease Center's February symposium.

From left, Gregory Fitz, M.D., Bruce Beutler, M.D., Roger Rosenberg, M.D., Mary Quiceno, M.D., and Joachim Herz, M.D.



FRIENDS GRANT SUPPORTS RESEARCH ON THE ROLE OF INFLAMMATION IN ALZHEIMER'S DISEASE

By Amanda Billings

The Friends of the Alzheimer's Disease Center awarded \$65,000 to Chantelle F. Sephton, Ph.D., a post-doctoral fellow in the Department of Neuroscience.

The impetus for Dr. Sephton's research is the knowledge that inflammation contributes to the pathology of several age-related neurodegenerative diseases, including Alzheimer's disease. Identifying drugs that stop inflammation may be a good approach to treating these diseases. Currently, there are no effective drugs that stop the inflammation that leads to neurodegeneration.

Dr. Sephton believes that knowing more about how inflammatory responses are regulated could lead to the development of better therapeutics for neurodegenerative diseases.

New studies suggest that the protein—fused in sarcoma (FUS)—is a key regulator of inflammation. Moreover, FUS aggregation is a pathological marker for several neurodegenerative diseases. Questions still remain about how FUS regulates inflammation and how it causes neurodegeneration.

Dr. Sephton's research will examine the role FUS has in regulating inflammation and its involvement in neurodegeneration. Once the FUS-regulated inflammatory pathway is identified, Dr. Sephton will select FDA-approved drugs that are known to modulate the molecular components of that pathway and test their efficacy in reducing inflammation.

"This generous grant from the Friends will let us expand our research efforts in an area in which we have just barely scratched the surface," said Dr. Sephton. "We believe that our work will lead to new and better targeted therapies for preventing neurodegenerative diseases such as Alzheimer's."

Chantelle F. Sephton, Ph.D.



THE MANY BENEFITS OF EARLY INTERVENTION

By Kristin Martin-Cook



The face of Alzheimer’s disease (AD) is changing. Gone are the days when it can be said that if you have enough awareness to seek medical help for your memory loss, then you must not have a real memory problem. The most rapidly growing segment of those seeking diagnosis and participation in research trials are those who recognize their risk for Alzheimer’s disease and their struggle with memory failures, which they often notice before anyone around them.

It is exciting to imagine that a person at risk for Alzheimer’s disease might be able to change the trajectory of their cognitive loss by exercising.

For these persons, it isn’t the inability to remember or to function, but a consistent need to work harder to keep up with the same information or function—tasks that were so automatic and took little effort just a few years before.

This group of individuals has a strong voice, advocating for earlier detection, early treatment, and more attention to what can be done to help them successfully live with the cognitive changes they are experiencing. Based on wide demand, a support group in Plano was established to address the issues faced by people with early/young onset of Mild Cognitive Impairment (MCI) and early AD. This is a group where people with memory disorders

discuss their issues—how to continue living, working, and making the most of their abilities.

This change in the people who refer themselves to the UT Southwestern Memory Research Unit and Alzheimer’s Disease Center (ADC) is all the more important since recent research suggests that the disease starts even more silently than was thought in the past, perhaps a decade before the dementia

of AD can be recognized and diagnosed by most physicians. It is also during this early phase of MCI, or even before, that treatments are most likely to have real benefit, according to leading researchers at UT Southwestern.

Studies at the ADC and world-wide are beginning to make a shift by moving the timeline back in terms of qualifying study participants—meeting these subjects where they are rather than waiting until symptoms become more severe. The hope is that earlier detection and treatments aimed at the very earliest biology of the disease in the brain will offer a more positive long-term result to patients than treatment after the onset of dementia. It is important to understand that dementia is not a disease, but rather a descriptive term meaning that a person’s thinking and day-to-day activities are significantly impaired.

While waiting for “the cure,” it is imperative that we study and employ interventions that offer a way to maximize cognitive function and quality of life of those living with cognitive impairments that may or may not progress to AD or a related dementia. Clinicians at UT Southwestern are making every effort to translate research findings into best practices with patients in the clinic, as well as helping patients find the right studies for them to contribute to the research that will support further growth of the field.

One study currently under way at the ADC includes a study of the efficacy of exercise on improving cognitive function, quality of life, and emotional stability—all important issues to address even in early MCI. There is mounting evidence that exercise is not only helpful for our vascular system and for increasing brain blood flow, but that exercise actually acts on beta amyloid, a protein thought to be a significant player in the cascade of events that leads to AD. Whereas more research is needed, it is exciting to imagine that a person at risk for Alzheimer’s disease might be able to change the trajectory of their cognitive loss by exercising.

Another ADC study is searching for a biomarker that may identify who is at greatest risk before significant cognitive loss occurs. This study, funded by the Alzheimer’s Association and conducted in collaboration with UT Dallas, will attempt to measure and better understand early changes in brain connections and how they work or fail while a person is engaged in a challenging mental task. A related study will provide cognitive retraining in an attempt to alter failing brain connections,

which may enhance cognitive performance. Another new investigation will utilize a combination of biochemical, neuroimaging, and neuropsychological findings in an attempt to identify subjects who may be at greatest risk for more rapid decline.

Although they are sometimes frustrated by memory deficits or word-finding challenges, persons with MCI are not just sitting around waiting to decline cognitively. They are participating in research, engaged in hobbies, travelling, and

deciding how to best spend their retirement. Sometimes they are still working a full schedule. Mostly, they are focused on living life to the fullest and not giving up. As one participant said, “I may have some problems, but now let’s see how well I can learn to dance.” Researchers and clinicians are not giving up either. ❄

FORUM SPEAKER TO DISCUSS POTENTIAL BLOOD TEST FOR ALZHEIMER’S DISEASE

By Betsy Lewis

A novel technology discovered by UT Southwestern researchers could one day help physicians diagnose Alzheimer’s disease in patients long before symptoms ever appear. Dwight German, Ph.D., Professor of Psychiatry, will describe his work on an experimental new blood test for Alzheimer’s disease in a talk at a Spring Public Forum on April 30, presented by the Friends of the Alzheimer’s Disease Center.

“One of the great challenges in treating patients with Alzheimer’s disease is that once symptoms appear, it is too late,” said Dr. German. “If we can find a way to detect the disease in its earliest stages and before cognitive impairment begins, we might be able to stop it in its tracks.”



The 7 p.m. forum, titled “What’s Next: A Blood Test for Alzheimer’s Disease,” will be held in the Simmons/Hamon Biomedical Research Buildings on the UT Southwestern North Campus, 6000 Harry Hines Blvd. Complimentary valet parking is available.

The public forum is one of many programs sponsored by the Friends of the Alzheimer’s Disease Center, which was established in 1996 to provide financial support for Alzheimer’s research at UT Southwestern. Contributions from the Friends 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. To attend the free forum on April 30, please call 214-648-2344 to make a reservation.

Dwight German, Ph.D.

FROM THE DIRECTOR

Continued from page 1

Discussions were vigorous and spirited, and the speakers inspired great interest in their presentations. The goal now is to develop interdisciplinary research ideas for grant submissions to the National Institutes of Health, the Alzheimer’s Association, and foundations. Consilience and crystallization of these ideas have already started among several faculty members in the writing of a com-

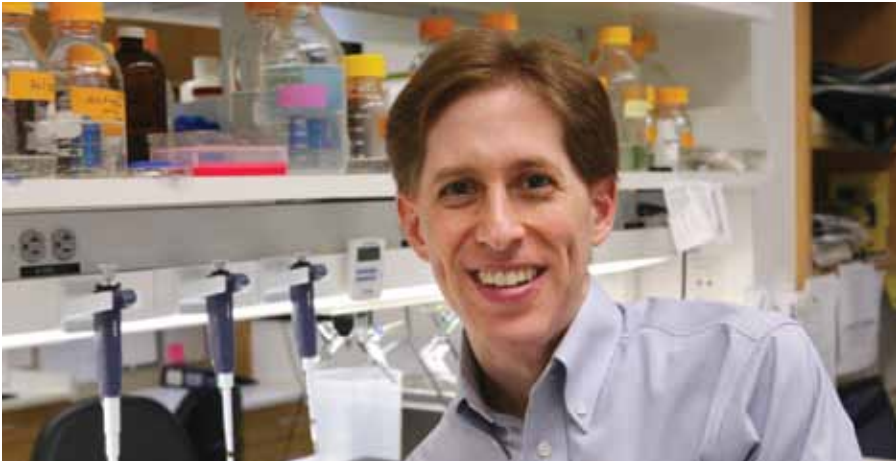
prehensive program project grant, which will involve multiple scientific disciplines in investigating specific molecular targets that have a probability to develop a new therapy for Alzheimer’s disease. The time is now and no greater need exists.

Major credit for the success of the symposium goes to Mary Quiceno, M.D., ADC Education Core Leader, and to Barb Davis, ADC

Education Core Coordinator, for their dedicated leadership and perseverance to make all of the essential arrangements. *

DR. MATT GOLDBERG AWARDED SPECIAL GRANT FROM THE FRIENDS OF THE ALZHEIMER’S DISEASE CENTER

By Betsy Lewis



Matthew S. Goldberg, Ph.D.

To crack an inscrutable health mystery, Matthew S. Goldberg, Ph.D., is going to the cutting-edge. Dr. Goldberg, Assistant Professor of Neurology, was awarded a special grant funded by several members of the steering committee for the Friends of the Alzheimer’s Disease Center. The group generously decided to collaborate on supporting Dr. Goldberg’s proposal based on its merits when available funding for the 2011 Friends grant was insufficient for a second grant in a competitive pool of applicants. His work focuses on the use of “next generation sequencing” (NGS) to search for distinct molecular flags

in brain tissue and blood cells that could indicate a high risk of developing Alzheimer’s disease. These flags, called biomarkers, are cell mutations that can be identified and studied in the postmortem brain cells of patients who suffered from Alzheimer’s disease. Confident that state-of-the-art NGS technology allows a more precise and rigorous analysis of the Alzheimer’s brain, Dr. Goldberg’s work includes comparisons between biomarkers and cells that, though from the same individual, were not part of the central nervous system. He also plans to look at postmortem brain cells from control subjects who did not have Alzheimer’s disease.

Dr. Goldberg believes the biomarkers are a key to understanding the cellular and molecular basis of neurodegeneration, and once that insight is gained, rapid diagnosis, early intervention, and more effective therapies are likely to follow. Next generation sequencing was brought to public attention in the 1990s when the Human Genome Project, an international research endeavor to map the approximately 23,000 human protein-coding genes, began. Since then, the technology has continued to expand, enabling intensive disease-specific research like that conducted by Dr. Goldberg’s laboratory. In modern molecular biology and genetics, the genome is defined as the entirety of an organism’s hereditary information. Dr. Goldberg’s project, titled “Rapid Screen for Alzheimer’s Disease Diagnostic Tests and Therapeutic Targets,” builds on previous research into genomic abnormalities in brain cells that became impaired from Alzheimer’s disease. *

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.

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.



Myron F. Weiner, M.D., Professor of Psychiatry, prepares for a teleconference.

COMING SOON

Two new clinical trials: Resveratrol and Intravenous Immunoglobulin (IGIV). Watch our website for more details.

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, or 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.

CORE AND TARCC 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.

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.

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STRATEGIES CAN HELP EASE EFFECTS OF MILD MEMORY LOSS

"Senior moments" may be the stuff of jokes, but for people with mild cognitive impairment or Alzheimer's disease, memory loss is a frustrating reality. Some simple strategies can help, however.

"Small changes in everyday life can minimize the impact of memory problems," says Kristin Martin-Cook, Clinical Research Coordinator for the Alzheimer's Disease Center at UT Southwestern Medical Center.

Ms. Martin-Cook suggests some of the following memory aids:

- Use medication dispensers, whether something as simple as a plastic pill organizer or as complex as an electronic dispenser with alarms.
- Keep a calendar, with enough details that can cue memory, in a prominent location.
- Keep a summary of medical history, current medications and allergies, emergency contacts, and doctors' phone numbers on the refrigerator at home and in one's wallet.
- Register with the Alzheimer's Association's Safe Return program, which provides a medical alert bracelet.
- Rely on routine and familiarity. "New learning is difficult when short-term memory is a weakness, so stick with the same phone, same car, same appliances whenever possible," Ms. Martin-Cook says.

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