UT Southwestern Medical Center

Spring 2016

Alzheimer's

DISEASE CENTER NEWS

Alice Warren: Helping researchers unravel the genetics of Alzheimer's disease

Alice Warren knows the tragedy of Alzheimer's disease all too well, with friends and family members experiencing its impact, but she considers it a call to action.

"I'm all about prevention," said the 85-year-old mother and grandmother of three, who participates in two ongoing studies with UT Southwestern's Alzheimer's Disease Center. "I do it because of my family. I do it for my son and grandchildren."

She leads a full and active life from her home in North Dallas, with regular dancing, exercise, yard work, tennis, socializing, and travel. But her dedication to helping find treatments for Alzheimer's disease trumps these other interests. For the last 23 years she's been coming to UT Southwestern for annual evaluations, and participates in two ongoing studies – the LOAD study, and core observational study.

The LOAD (Late-Onset Alzheimer's Disease Genetics Initiative) study tracks families with three or more siblings aged 60 or older who have been diagnosed with Alzheimer's disease. The core observational study tracks seniors who show no symptoms, such as Ms. Warren, along with people who have mild cognitive impairment or early Alzheimer's disease.

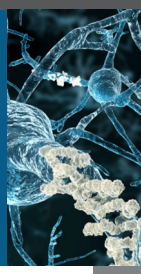
"Our physician-scientists are looking for a specific type of genetic inheritance that might be tied to Alzheimer's disease. The type of inheritance pattern is autosomal dominant (genetic) and results in one-half of the children on average of an affected parent of developing the disease," said Dr. Roger Rosenberg, Professor of Neurology and Neurotherapeutics, and Physiology, and Director of the Alzheimer's Disease Center.

Alice Warren has participated in UT Southwestern Alzheimer's disease studies for the last 23 years.

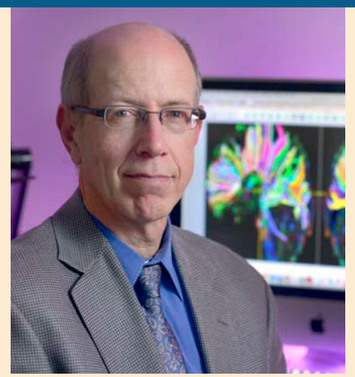
"Determining the inheritance pattern in a family is important to provide the accurate 'at-risk' status for patients who have developed Alzheimer's disease. We pursue obtaining a detailed family history with this objective in mind," said Dr. Rosenberg, holder of The Abe (Brunky), Morris and William Zale Distinguished Chair in Neurology.

Ms. Warren grew up near Ada, Okla., and went on to a career as a fashion director for Bobbie Brooks and a buyer for Neiman Marcus before marrying her late husband of 35 years, Phil Warren. She served as Co-Chair of the Dallas Mental Health Association in the 1960s. Memories of relatives who have Alzheimer's disease continue to inspire her to do her part. ❊

WHAT'S INSIDE



SPRING FORUM: Concussion and aging: What's the risk?



Dr. C. Munro Cullum

Dr. C. Munro Cullum, Professor of Psychiatry, and Neurology and Neurotherapeutics at UT Southwestern, will lead the Alzheimer's Disease Center Friends' Spring Forum on a discussion of concussion and dementia at 7 p.m., March 31.

This presentation will review what is known and not known about concussion: its acute effects, recovery, risks, and association with cognitive disorders later in life.

Dr. Cullum, who holds the Pam Blumenthal Distinguished Professorship in Clinical Psychology, is Chief of the Division of Psychology, directs the Neuropsychology Program at UT Southwestern, and is a Clinical Core Leader in the UTSW Alzheimer's Disease Center. Dr. Cullum is a past-president of the Society for Clinical Neuropsychology and the National Academy of Neuropsychology, and is actively involved in research, teaching, and clinical practice in neuropsychology.

Dr. Cullum is the Principal Investigator on the newly created CON-TEX registry, designed to capture comprehensive, longitudinal data on individuals age 5 and over who have suffered sports-related concussion or other forms of mild traumatic brain injury (TBI).

In recent years Dr. Cullum has done extensive study of the cognitive abilities of veteran National Football League (NFL) players as they age. Findings of those studies have appeared in *JAMA Neurology, Neurology, Clinical Neuropsychology*, and *Current Alzheimer's Research*.

Dr. Cullum's presentation will include a review of recent studies of retired professional athletes with a history of concussion utilizing brain imaging, diagnostic, and neurobehavioral assessment techniques. Additional topics will include traumatic brain injury as a risk factor for the later development of cognitive impairment and dementia. ❊

WHO: Dr. C. Munro Cullum, Professor of Psychiatry, and Neurology and Neurotherapeutics at UT Southwestern

WHAT: 2016 Alzheimer's Disease Center Friends' Spring Forum

WHEN: 7 p.m., Thursday, March 31, 2016

WHERE: Simmons Biomedical Research Building, 6000 Harry Hines Blvd., Dallas, Texas

NOTEWORTHY: The forum is free to the public and there is complimentary valet parking. Please confirm attendance by calling 214-648-2344.

'SNIFF' EXAMINES NASAL INSULIN TO FIGHT FORGETFULNESS

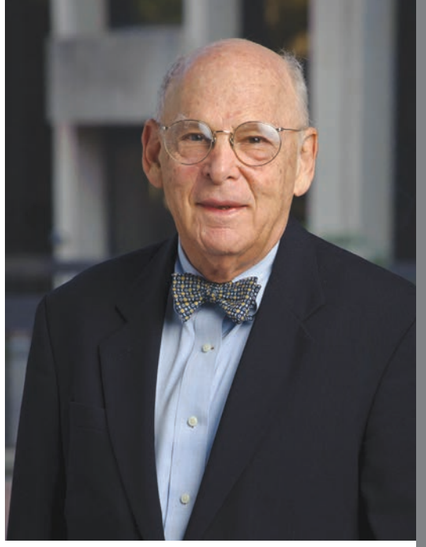
The SNIFF Study (Study of Nasal Insulin to Fight Forgetfulness) will be a clinical study for participants age 55 to 85 with amnestic mild cognitive impairment (aMCI) or mild Alzheimer's disease who do not take drugs for diabetes (type I or II). The purpose of the SNIFF study will be to find out whether a type of insulin, when administered as a nasal spray, improves memory in adults with a mild memory impairment or Alzheimer's disease.

Growing evidence suggests that insulin carries out multiple functions in the brain and that poor regulation of insulin may contribute to the development of Alzheimer's disease. Insulin resistance, reduced cerebrospinal fluid insulin levels, and reduced brain insulin signals have been found in Alzheimer's disease patients, suggesting that a therapy aimed at correcting these deficiencies may be beneficial. Although this study is not open to enrollment yet, please check our website for updates (*utsouthwestern.edu/adc*), as well as *clinicaltrials.gov* (search identifier NCT01767909) or call Sheila Joshi at 214-648-9394, for more information.

New studies are also being considered for 2016, so please check our website (*utsouthwestern.edu/adc*) for updates on current studies available, or call 214-648-0563 for more information. ❊

FROM THE DIRECTOR

Roger N. Rosenberg, M.D.



Neurological research on Alzheimer's disease and related disorders is alive and well throughout Latin America, as I saw at the World Congress of Neurology in Santiago, Chile in November.

I was honored to present my research, "DNA Aβ42 Vaccination as Therapy to Prevent Alzheimer's Disease," in the Presidential Plenary Session, along with Nobel Laureate Dr. Thomas Südhof of Stanford University, Adjunct Professor of Neuroscience and former Chairman of the Department at UT Southwestern.

Vaccinations have started using our DNA Aβ42 vaccine with animal models as required by the Food and Drug Administration for consideration to eventually study it in patients at risk for Alzheimer's disease. The objective is to show that animal models produce good levels of anti-Aβ42 (amyloid) antibodies and that the immune response is non-inflammatory. Similar studies have just been completed with other animal models and the results were positive as the animals did produce high levels of anti-Aβ42 (amyloid) antibody and it was of a non-inflammatory type. They remained healthy during the vaccination period and examinations indicated there was no evidence of encephalitis, which was a major issue with peptide (protein) Aβ42 vaccinations.

Another highlight of the Santiago conference was hearing the research of Dr. Francisco Lopera, Professor and Director of Neuroscience at the University of Antioquia in Medellin, Columbia. His anti-amyloid antibody clinical trial with a large family that has a mutation in a gene important for amyloid metabolism causes half of the children of an affected parent with this mutation to have early onset severe Alzheimer's disease. Latin American neurological research on Alzheimer's disease is excellent with major laboratories investigating amyloid, tau, at-risk gene polymorphisms and potential new therapies in clinical trials. It was important to meet our colleagues there and to develop friendships and collaborations.

We are very pleased that Dr. John Hart, Professor of Neurology and Neurotherapeutics, and Psychiatry at UTSW, and Medical Science Director at the Center for Brain-Health of UT Dallas, has joined us as an investigator in the Alzheimer's Disease Center. Dr. Hart has been a senior investigator in the human dementias for many years with a distinguished record of publications and author of a soon-to-be-published book on the clinical, behavioral, and biological issues in human dementias.

I was pleased to have been invited by Dr. Daniel K. Podolsky, President of UT Southwestern, to present in October for the President's Lecture Series on "The End of Alzheimer's? The Pursuit for a Vaccine." I am most grateful to him for this singular honor.

The faculty and staff of the Alzheimer's Disease Center are most grateful to the members of the Friends of the ADC. You make it possible for us to fund startup grants on dementia-related research for junior faculty to interest them in this field and bring the next generation of investigators into the Center. It has been a very successful program, and we thank you. We wish to express our gratitude to Charron Denker for serving the past two years as Chair of the Friends of the ADC and for her dedication, leadership and efforts to move our agenda in education and research forward. We also thank Bonnie Smith, the new Chair, for her assuming the leadership role of the Friends of the ADC. We know our future is in good hands.

Thank you for your continued support. ❊

STUDY EVALUATES ADUCANUMAB FOR EARLY ALZHEIMER'S DISEASE

The purpose of this study is to evaluate the efficacy of monthly doses of aducanumab in slowing cognitive and functional impairment as compared with placebo, for persons with mild cognitive impairment due to Alzheimer's disease and for persons with mild Alzheimer's disease. Each participant will need a study partner – someone who is close to them, such as a family member or close friend – to attend certain study visits and provide information to the study team. You may be able to take part in this study if you have a study partner, are 50 to 85 years of age and are experiencing symptoms that might be related to mild Alzheimer's disease, such as problems with memory or thinking clearly. Please call Zohre German at 214-648-2952 for more information about this study. ❊

Exercise, reducing cardiovascular risk as Alzheimer's disease prevention studied with $11.7 million NIH grant

The effects of exercise and aggressively reducing cardiovascular risk as a way to ward off or forestall Alzheimer's disease will be the subject of a major study by UT Southwestern's Alzheimer's Disease Center and the Institute for Exercise and Environmental Medicine at Texas Health Presbyterian Hospital Dallas, a partnership between UT Southwestern and Texas Health Resources that studies human physiology. The study is funded by an $11.7 million grant from the National Institutes of Health.

The five-year study will examine the brain function of 640 individuals between ages 65 and 79 who have at least one first-degree relative with Alzheimer's disease. Study participants will begin moderate to vigorous exercise for 30 minutes, three times a week, and build up to about 200 minutes per week. The study will use anti-hypertensive drugs and atorvastatin to treat hypertension and hyperlipidemia following evidence-based national guidelines.

"A sedentary life is a 'disease' and the presence of hypertension and hyperlipidemia increase the risk of Alzheimer's disease," said Dr. Rong Zhang, Associate Professor of Internal Medicine, and Neurology and Neurotherapeutics at UT Southwestern, and Principal Investigator of the study. "Increase in physical activity and using clinically approved drugs to reduce cardiovascular risk factors might be the key to preventing or halting the progression of Alzheimer's disease. We believe improving cardiovascular health plays a pivotal role in preventing cognitive decline, and this study will give us the chance to see just how important that is."

Neuroimaging and blood biomarkers will be taken of study participants to help in the assessment

Dr. Rong Zhang

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IN MEMORIAM: MARGOT WINSPEAR

Philanthropist Margot Winspear, who died Oct. 20, 2015, at age 83, had spent years battling Alzheimer's disease, both personally after her diagnosis in 1994 and through her generous philanthropic efforts.

In 2002, Bill and Margot Winspear donated $2 million to UT Southwestern Medical Center, which established the Winspear Family Special Center for Research on the Neuropathology of Alzheimer's Disease, led by Dr. Charles L. White, III, Professor of Pathology and Director of the Department's Neuropathology Section and the Winspear Center. Through the years, the Center has helped fund numerous studies that have led to better understanding of proteins such as tau and alpha-synuclein and their impact on cognitive function.

Mrs. Winspear received the Alzheimer Association's Civic Award in 2009 amid a standing ovation for her contributions.

She was born March 18, 1932, in Edmonton, Alberta, and attended University High School in Edmonton and the University of Alberta, where she met her husband. The Winspears were married May 30, 1955, in Edmonton, and eventually moved to Dallas in 1975. The couple were staunch supporters of Dallas' fine arts community. Mrs. Winspear served on numerous boards, including the Dallas Opera, Dallas Symphony, Dallas Ballet, and the Women's Council for the Dallas Arboretum and Botanical Garden. The Winspears' support for the opera culminated in the Margot and Bill Winspear Opera House in Dallas, part of the AT&T Performing Arts Center.

Margot Winspear

"Margot Winspear was a delightful woman whose grace and charm overshadowed the ambition and drive behind her selfless contributions to the worlds of art and science," said Dr. White, who holds the Nancy R. McCune Distinguished Chair in Alzheimer's Disease Research. "We will always be grateful for the impact that Margot, her equally charming and generous husband Bill, and their children have had on Alzheimer's disease research at UT Southwestern." ❊

Darrell K Royal Research Fund supports new UTSW research in dementia, TBI

The Darrell K Royal Research Fund for Alzheimer's Disease recently awarded $450,000 for work being done by UT Southwestern researchers.

The Darrell K Royal Research Fund was established to honor legendary former University of Texas football coach Darrell Royal, and fund research into the treatment and cure of Alzheimer's disease and mild cognitive impairment (MCI).

Dr. Yingfei Wang, Assistant Professor of Pathology, and Neurology and Neurotherapeutics, will study the role of a newly identified cell death effector in dementia.

"Neuron injury and neuronal cell death are key features of dementia that cause problems with memory, thinking, and behavior," said Dr. Wang. "In the proposed project, we will study the detailed molecular and cellular mechanisms of neuronal cell death in dementia, which may ultimately lead to an effective therapy."

Dr. Kan Ding, Assistant Professor of Neurology and Neurotherapeutics, was awarded $150,000 over three years for a project titled, "Neurovascular Decoupling and Memory Impairment After Traumatic Brain Injury."

Dr. Ding's group will study cerebral blood supply in TBI patients with forgetfulness, poor concentration, and slow thinking processes. Researchers hope the data obtained will reveal an important vascular mechanism, provide a better understanding of the pathophysiology of TBI-related dementia, and identify early biomarkers for developing effective therapies to improve brain health and prevent post-traumatic dementia in TBI survivors.

This marks the second consecutive year UTSW researchers received DKR Fund awards. Last year, Dr. Steven Patrie, Assistant Professor of Pathology and John L. Roach Scholar in Biomedical Research, Dr. Murat Durakoglugil, Assistant Professor of Molecular Genetics, and Dr. Florian Plattner, Instructor of Psychiatry, received grants.

"We developed small drug-like interfering peptides that facilitate neurotransmission and enhance memory in rodents," wrote Drs. Plattner and Durakoglugil in a recent update report to the fund. Their work will continue to assess if these peptides can rescue or minimize the memory impairment in AD mice.

Debbie S. Hanna, (left) President of the Darrell K Royal Research Fund for Alzheimer's Disease, and Rita Hortenstine, (right) Director of the DKR Fund, present a check for $450,000 to Dr. Daniel K. Podolsky, President of UT Southwestern, to fund work of UTSW researchers.

Drs. Patrie and Plattner have both been recipients of ADC Friends grants, Dr. Patrie in 2013, and Dr. Plattner in 2014.

"The sad fact is that most everyone in our state is touched by this disease and the Darrell Royal family is no exception," said Edith Royal, his widow. "The DKR Research Fund represents a commitment to excellence in Alzheimer's research and care for Texans, the nation, and the world. I am grateful for the opportunity to create this legacy for my husband, and for the incredible group of prominent Texans who want to join us in this endeavor."❊

EXERCISE Continued from page 4

of brain structure and function, and to understand their underlying mechanisms.

Investigators from Washington University in St. Louis, University of Kansas Medical Center, and the Pennington Biomedical Research Center at Baton Rouge, La., will participate in data collection, and Michigan State University will coordinate magnetic resonance imaging.

Dr. C. Munro Cullum, Professor of Psychiatry, and Neurology and Neurotherapeutics, Chief of the Division of Psychology, Clinical Core Leader in the UTSW Alzheimer's Disease Center, who holds the Pam Blumenthal Distinguished Professorship in Clinical Psychology, will be a co-investigator.

"The benefits of exercise and reducing cardiovascular risks are many and well-known," said Dr. Zhang, "and some participants get a free health club membership to boot."

If you are interested in participating in the study or want to learn more, contact the study coordinator, Marcel Turner, at 214-345-4973 or *MarcelTurner@texashealth.org* ❊

Barb Davis, Manager of Clinical Research in Neurology and Neurotherapeutics, explains ongoing research underway in the Alzheimer's Disease Center to participants of the Brain Smart University, held at Shiloh Road Baptist Church in Plano.

Dr. Mary Quiceno, Associate Professor of Neurology and Neurotherapeutics, and Pat Knowles, Clinical Research Coordinator, participate in Brain Smart University, an educational program that reaches out to the black community, a demographic group that is at an elevated risk for Alzheimer's disease.

Advances in drug to treat Alzheimer's disease

Three UT Southwestern faculty members reported promising results on a drug to potentially treat Alzheimer's disease and other central nervous system diseases in a recent study appearing in *Neurodegenerative Diseases*.

The drug, ANAVEX 3-71, formerly AF710B, appeared to enhance neuroprotection and cognition in Alzheimer's disease models, the researchers said.

Dr. Ilya Bezprozvanny, Professor of Physiology, Dr. Lili Wu, former senior research scientist, and Dr. Daniel Ryskamp, postdoctoral research fellow, authored the paper, "AF710B, a Novel M1/Sigma-1 Agonist with Therapeutic Efficacy in Animal Models of Alzheimer's Disease," along with Dr. Abraham Fisher of the Israel Institute for Biological Research, who developed the compound.

"Our preclinical findings for ANAVEX 3-71 demonstrate its significant potential to enhance neuroprotection and cognition through activation of sigma-1 and muscarinic acetylcholine receptors," said Dr. Bezprozvanny, who holds the Carl J. and Hortense M. Thomsen Chair in Alzheimer's Disease Research. "This could be a highly effective treatment for Alzheimer's when compared with competing drugs, including donepezil (Aricept)."

Dr. Ilya Bezprozvanny

The Bezprozvanny laboratory demonstrated that ANAVEX 3-71 was able to reverse synaptic loss in hippocampal neurons from mouse models of Alzheimer's disease. The actions of this compound at the synapse may explain its ability to mitigate cognitive impairments and lessen Alzheimer's-like pathologies in mouse models of Alzheimer's disease, the researchers concluded. Now the team will study the target and the mechanism of the compound to better understand how it acts. ❊

MEET A FRIEND | *Bonnie Smith*

Bonnie Smith

Q: How did you become involved with the Friends of the Alzheimer's Disease Center?

A: *Like many other Friends, I have a close family member who has Alzheimer's disease. So when asked to join in 2011, I said yes and then quickly became part of the steering committee.*

Q: Why have you continued to support the Friends?

A: *My generation is experiencing widespread neurodegenerative disease with our parents, as many of them are living well into their 80s. Right now there is no cure for Alzheimer's and it's only going to get worse. Alzheimer's takes a huge emotional and financial toll on families. It impacts the quality of life of people living with the disease, as well as their loved ones and caregivers. We have to find solutions.*

Q: Why should others support the Friends?

A: *I'm very impressed with how UT Southwestern is confronting diseases of the brain, considered the "last frontier" of medical science. The establishment of UTSW's Peter O'Donnell Jr. Brain Institute makes the study of the entire brain a top priority and will change how we understand and treat brain-related diseases and disorders, including Alzheimer's.*

Supporting the Friends is an important investment in the future; it continues the momentum of incredible visionaries in the field like Dr. Roger Rosenberg, who is testing a possible Alzheimer's vaccine. Just imagine the potential impact.

I also like the fact that becoming a Friend is accessible to many; it's an easy way to get informed and participate, without a huge financial or time commitment. Because of this collective effort, I strongly believe that we will see major breakthroughs in my lifetime or my children's lifetimes.

Q: What do you hope for the future of the Friends?

A: *I'd like us to continue to broaden the base of our membership and cultivate the next generation of Friends.*

Q: What would you like to share with your fellow Friends?

A: *Thanks to Friends like you, brilliant and deserving young investigators receive the seed funding they need to kick-start novel research, which, in turn, could be just the spark that ignites the next major breakthrough in neuroscience.* ❊

SAVE THE DATE: Saturday, Oct. 1, 2016

WHAT: The 2016 Greater Dallas Walk to End Alzheimer's, sponsored by the Alzheimer's Association

WHERE: The Lawn at Reunion Tower, 300 Reunion Blvd. E, Dallas

WHEN: Registration at 7 a.m., walk begins at 9 a.m.

WHY: The world's largest event to raise awareness and funds for Alzheimer's disease care, support and research. More than 600 communities nationwide participate.

HOW: For more information, contact Marchetta Miller at 214-648-0563 or email *Marchetta.Miller@utsouthwestern.edu*. You also can join the UT Southwestern Brainiacs team.

Photo courtesy of the Alzheimer's Association

Join Us

SUPPORT THE QUEST FOR PREVENTION, TREATMENT, AND A CURE

JOIN THE FRIENDS OF THE ALZHEIMER'S DISEASE CENTER

The Friends of the Alzheimer's Disease Center provide crucial support to UT Southwestern Medical Center's most promising and passionate researchers working to unlock the mysteries of Alzheimer's disease.

In addition to funding research through generous annual grants, the Friends sponsor a community-wide public forum every fall and spring where the latest breakthroughs and best information on Alzheimer's disease are presented by leading experts from UT Southwestern and major medical centers nationwide.

Membership begins at $500 per year, per individual or couple. Your donation is tax deductible and truly makes a difference in the fight against Alzheimer's disease.

To join the Friends of the Alzheimer's Disease Center, call 214-648-2344. Your support safeguards vital research into enhancing quality of life through early detection and improving the lives of patients and their families who live courageously each day with Alzheimer's disease.

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