

Alzheimer's

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

HELPING OTHERS

Clinical trials patient's participation is a pillar of study's strength



Jeff and Jules Rushing

Alzheimer's research cannot happen without brilliant scientists or generous donors, but another virtue is needed for real breakthroughs – the selflessness of Alzheimer's patients and their families who step forward to participate in trials and make research meaningful.

Jeff Rushing is one of those people. The 59-year-old Denton County resident was diagnosed with Alzheimer's disease two years ago. He frequently participates in research at UT Southwestern and says he will volunteer for any research that helps.

"I want to be part of fixing the problem, and research is where it comes from. If you don't have willing participants who have the disease, it's going to slow the research down," he said. "When I meet people that have the disease, I ask them, 'Are you going to help? I want you to participate. You're the people who can help. You know what's happening to you. You can help others by helping the doctors.'" Rushing said his participation in the research has been rewarded with a sense of contributing – and with compassionate treatment by UT Southwestern doctors and staff.

"They're a lot of fun. They're not the typical stick-in-the-mud doctor. They're real. You ask a question, and you get an answer; they don't put you off. They understand what I am going through," he said.

Mr. Rushing's wife, Jules, said the compassionate, respectful treatment given by Dr. Mary Quiceno, Assistant Professor of Neurology and Neurotherapeutics, and Physician Assistant Natalie Martinez has helped make the Alzheimer's diagnosis a little less painful.

Dr. Quiceno said the participation of people like Mr. Rushing is crucial in making progress against the disease.

"We need people to be involved in research because that's how we're going to learn more about the disease," she said. "That's how eventually we're going to put an end to this."

As a student, Jeff Rushing studied economics at Texas Christian University and later worked as a Vice President of Sales for an air conditioning company for 30 years.

"I was the phone book for the company. Before we had smart phones, they would say, 'What is so-and-so's number?' and I would spit it out. I could remember a job I did 20 years ago and every detail about it," he said.

But after many years witnessing his solid work, co-workers became puzzled by changes in Mr. Rushing's performance.

"I couldn't bring stuff back from my memory, and then I couldn't

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DEVELOPING DIAGNOSIS: Alzheimer's speaker appreciates broad-based disease examination



Dr. Sid E. O'Bryant

A researcher known for developing a blood test to diagnose Alzheimer's disease believes a much broader look at the disease is still warranted. Dr. Sid E. O'Bryant will elaborate on his views during the Friends of the Alzheimer's Disease Center Spring Public Forum, scheduled for March 25 at UT Southwestern Medical Center.

Dr. O'Bryant's presentation, titled "Blood-Based Tools in Diagnosis and Novel Treatments for Alzheimer's Disease: Another Hope for the Future," begins at 7 p.m. in the Simmons/Hamon Biomedical Research Building. Reservations are available by calling 214-648-2344 or by emailing rsvp@utsouthwestern.edu.

Dr. O'Bryant, the Interim Director of the University of North Texas Health Science Center's Institute on Aging and Alzheimer's Disease Research and a psychologist by training, believes scientists should look at the disease more holistically.

"Alzheimer's is a very complex disease. It's not one thing. It's not one pathology," said Dr. O'Bryant, who is also an Associate Professor of Internal Medicine at the UNT Health Science Center.

UT Southwestern's participation in major anti-amyloid drug trials represents the institution's decades-long focus on amyloid buildup as the main cause of Alzheimer's disease. Dr. O'Bryant's presentation acknowledges UT Southwestern's vigor in considering all possible breakthroughs in disease research while still playing a prominent role in some of the world's most important research and drug trials.

Dr. O'Bryant said Alzheimer's disease researchers should model what has been done with great success by scientists studying cancer and heart disease. He said treatment for those diseases break down along the lines of what type of cancer and heart disease patients have – but such breakdowns are not happening in Alzheimer's research.

"I'm hoping that others will embrace this notion that Alzheimer's is very, very complex. It's not as straightforward as we initially thought it would be, and, because it's so complex, we need to take a different view on it," he said.

Dr. O'Bryant has developed a highly accurate blood test for diagnosing Alzheimer's disease. In 2012, he received a \$600,000 grant from the National Institutes of Health to continue his work on the tests, first reported in *JAMA Neurology* in 2010. In January, Dr. O'Bryant was awarded an Early Career Impact Award by

the Federation of Associations in Behavioral & Brain Sciences Foundation.

Dr. O'Bryant majored in psychology at Louisiana State University before earning a master's degree and a doctorate in clinical psychology from the University of Albany. He joined the UNT Health Science Center in 2012 after six years with the Texas Tech University Health Science Center. ✱

WHAT: 2014 Alzheimer's Spring Public Forum

WHEN: 7 p.m., Tuesday, March 25

WHERE: Simmons/Hamon Biomedical Research Building,
6000 Harry Hines Blvd.

LECTURE: "Blood-Based Tools in Diagnosis and Novel Treatments for Alzheimer's Disease: Another Hope for the Future"

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

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



We are excited about what spring 2014 has in store for the UT Southwestern Alzheimer's Disease Center. First, the Spring Public Forum on March 25 will feature Sid O'Bryant, Ph.D., Interim Director of the University of North Texas Health Science Center's Institute on Aging and Alzheimer's Disease Research. Dr. O'Bryant is an expert on thinking and behavior during the aging process and will discuss his innovative research into the development of new therapies for treating and preventing Alzheimer's disease. I invite all of you to join us at the Forum.

Then, on March 28, the Center will host its annual symposium, which will feature presentations and discussions about "Emerging New Therapies for Neurodegenerative Diseases" from some of the best minds in our field. The symposium's keynote speaker is Dr. Beth Levine, Professor of Internal Medicine and

Microbiology at UT Southwestern and a member of the National Academy of Sciences. Her ongoing research focuses on the emerging field of autophagy, a natural process in which cells metabolize and remove damaged proteins and organelles. Dr. Levine will discuss its role in neurodegenerative diseases, which provide the basis for considering potential new therapeutic approaches for Alzheimer's disease.

Other speakers at the symposium will cover various topics, including the use of genetic biomarkers called endophenotypes in the development of new therapeutic approaches; immunotherapies; the effects of sildenafil, commonly known as Viagra, on brain blood flow; APOE and A 42 lipidation states; and dietary-dependent therapeutics. The symposium will also share some information about the Food and Drug Administration-approved clinical trials at our Center

using a monoclonal antibody or intranasal insulin to prevent Alzheimer's disease in at-risk, asymptomatic individuals. It will be an exciting and insightful set of lectures by authorities in neurodegenerative diseases and will provide a window of opportunity to learn about the next generation of therapies now being implemented.

Thank you for your continual support of the scientific research and therapeutic interventions that take place through the Alzheimer's Disease Center – we look forward to seeing you this spring. ✱

EMERGING NEW THERAPIES FOR NEURODEGENERATIVE DISEASES

A Symposium sponsored by the Alzheimer's Disease Center of UT Southwestern Medical Center

Friday, March 28, 2014 | 8 a.m. to 4 p.m. T. Boone Pickens Auditorium | 6001 Forest Park Road | Dallas, TX 75390

SPEAKERS

KEYNOTE: BETH LEVINE, M.D.

Professor of Internal Medicine and Microbiology
Charles Cameron Sprague Distinguished Chair
in Biomedical Medicine
UT Southwestern
"Autophagy and Neurodegenerative Diseases"

SID O'BRYANT, PH.D.

Associate Professor of Internal Medicine
Interim Director, Institute on Aging
and Alzheimer's Disease Research
University of North Texas Health Science Center
"Using Endophenotypes for Novel Therapeutic Approaches in Alzheimer's Disease"

NANCY MONSON, PH.D.

Associate Professor of Neurology and
Neurotherapeutics and Immunology
UT Southwestern
"What Can Immunophenotyping Tell Us About Alzheimer's Disease?"

KYLE WOMACK, M.D.

Assistant Professor of Neurology and Neurotherapeutics
and Psychiatry
UT Southwestern
"Effect of Sildenafil, a phosphodiesterase inhibitor, on brain blood flow"

ANGELA HANSON, M.D.

Research Fellow/Acting Instructor, Geriatric Medicine
VA Puget Sound Health Care System
"Will APOE Lipidation Become a Viable AD Therapy?"

MARY QUICENO, M.D.

Assistant Professor of Neurology and Neurotherapeutics
Director, Cognitive Memory Disorders Clinic
Leader, Education & Information Core
of the Alzheimer's Disease Center
UT Southwestern
"Alzheimer's Disease Center Update"

TRIALS AND TRIUMPH

UT Southwestern at the forefront of promising clinical trials

UT Southwestern Medical Center is part of important drug trials for Alzheimer's disease that may eventually lead to effective treatment or even a vaccine for people likely to develop it.

The two trials build on lessons from past research and make use of new technologies for medicine delivery and brain scans to monitor progress. Both trials target one of the main instigators of Alzheimer's disease – a protein buildup that interferes with brain function.

“Our Alzheimer's Disease Center is at the forefront of developing these two potential therapies, and it is hoped that significant positive results will be obtained in less than two years,” said Dr. Roger Rosenberg, Director of the Center and Professor of Neurology and Neurotherapeutics and Physiology.

It is estimated that more than 5 million Americans have Alzheimer's disease, according to the Alzheimer's Foundation of America, and the number of cases is expected to more than double to 12 million by 2030. More than \$200 billion is spent on care for Alzheimer's patients annually, far more than what is spent on research.

New gains against the disease may be made with these drug trials, which are focused on sophisticated, pinpoint strikes at what Alzheimer's researchers see as one of the main culprits: amyloid. Amyloid is a protein crucial to making memories and learning. But for people with Alzheimer's, there's far too much amyloid accumulation, and the buildup disrupts connections between brain cells.

The Expedition 3 trial will evaluate whether monthly infusions of antibodies can help clear excessive

amyloid. The drug under investigation is from Eli Lilly, a pharmaceutical company based in Indianapolis.

The SNIFF trial is so named because it involves an insulin nasal spray that researchers speculate may spur a process to clear amyloid buildup. SNIFF stands for Study of Nasal Insulin to Fight Forgetfulness. Twenty-nine other sites are involved in the SNIFF trial, which is led by the Alzheimer's Disease Cooperative Study, a partnership with the National Institute on Aging and research institutions studying Alzheimer's. UT Southwestern's participation in the trial shows its prominence as one of the NIA's Alzheimer's Disease Centers. UT Southwestern's Center was established in 1988 and has a \$9 million grant from the NIA.

Dr. Mary Quiceno, Assistant Professor of Neurology and Neurotherapeutics and Director of UT Southwestern's Cognitive and Memory Disorders Clinic, described the Expedition 3 trial as an ambitious strike at amyloid buildup.

“I hope this will eventually lead to primary prevention in which we will help people never develop any signs or symptoms,” she said.

The clinical trials break new ground by taking advantage of new technologies and important lessons from past trials.

In 2012, the Food and Drug Administration approved the first amyloid imaging agent that enables scientists to see amyloid buildup in the brain in Positron Emission Tomography scans, which are similar to the better known CAT scans. Using amyloid buildup as a biomarker is so new it is not yet covered by Medicare, Dr. Quiceno said.



Dr. Mary Quiceno

“I hope this will eventually lead to primary prevention in which we will help people never develop any signs or symptoms.”

— Dr. Mary Quiceno

She and Dr. Rosenberg said they hope an additional benefit of this study will be proof that amyloid buildup is a major factor in developing Alzheimer's.

The SNIFF trial evaluates the effectiveness of a nasal spray that delivers insulin straight to patients' brains without affecting insulin blood levels. The UT Southwestern section of the trial is led by Dr. Kyle Womack, Assistant Professor of Neurology and Neurotherapeutics and Psychiatry.

He said insulin in the brain – which is very low in Alzheimer's patients – increases an insulin-degrading enzyme that also clears amyloid. Scientists hope to conjure up this enzyme as an ally to chip away at amyloid.

Dr. Womack described the delivery mechanism as a clever maneuver to breach the blood-brain barrier that has proved insurmountable for many other drugs. He said molecules can pass through tiny openings around the nerve twigs and vessels at the top of the nose directly into the brain, and the nasal spray has been designed for exactly that.

“Molecules of a certain size will actually track up those little tiny spaces and get directly into the spinal fluid that the brain is bathed in so it doesn't have to cross the blood-brain barrier. They actually have some really interesting special technology that's been developed especially for this trial in the applicators,” Dr. Womack said. “It's a carefully engineered delivery system that makes very precisely sized droplets that will reliably track right up that part of the nose, giving consistent delivery of insulin to the central nervous system.”

Dr. Quiceno said family members of Alzheimer's patients often express their fear to her that they, too, will someday get the disease. She said these trials are a hope that they might not.

“They don't want this to happen to them. Research will stop this from happening to them,” she said. *

Faculty Profile

DR. JAMES BIBB

Associate Professor of Psychiatry and Neurology and Neurotherapeutics



Dr. James Bibb

A group of UT Southwestern researchers led by Dr. James Bibb has discovered a brain mechanism that can be targeted to enhance memory.

The findings of their study, published in the March online edition of *Neuron*, may provide a new path for treating cognitive disorders. Dr. Bibb and his colleagues first determined that the mechanism in the brain critical for memory formation involved the control of a neurotransmitter receptor called NR2B. They then found that its movement to the surface during synaptic remodeling was controlled by a protein kinase called Cdk5. The researchers developed a small drug-like peptide that specifically disrupted Cdk5 and NR2B interactions so that more NR2B found its way to the surface of synapses. The delivery of this peptide to a part of the brain associated with learning and memory dramatically enhanced cognitive function in adult and aged mouse models.

“This exciting new finding shows that synaptic remodeling mechanisms may be specifically targeted to develop novel therapeutic drugs for patients with cognitive impairments such as Alzheimer's disease,” said Dr. Bibb.

“This exciting new finding shows that synaptic remodeling mechanisms may be specifically targeted to develop novel therapeutic drugs for patients with cognitive impairments such as Alzheimer's disease.”

— Dr. James Bibb

Dr. Bibb's ongoing research focuses on the discovery of memory enhancement drugs to treat cognitive deficits, as well as addiction, depression, neuronal injury, and cancer research. *

MEET A FRIEND | Chair Charron Denker

Q: Why did you join the Friends of the Alzheimer's Disease Center?

A: I joined the Friends of the Alzheimer's Disease Center because of my direct interest in the disease of Alzheimer's. My mother died of this disease in 2009 after suffering for many years. Because I knew so little about this disease, it was several years before I recognized that it was Alzheimer's disease that was causing my mother's problems. I initially learned about the Friends of Alzheimer's Disease Center by way of their public fora and learned much from attending those lectures.

Q: What would you like to accomplish as Chair?

A: My goal as chair of the Steering Committee of the Friends is to increase membership in the Friends. It is through our membership dues that we are able to fund the research projects developed by our own UT Southwestern researchers. Alzheimer's disease is a progressive disease affecting problems with memory, thinking, and behavior, leading to deterioration in all areas of daily living and often ultimately to death. It is only through research will we be able to

discover ways of early detection to either slow or halt the disease's progression. For this reason, I believe it is critical to address the lack of necessary funding to conduct research. The Friends are in the position to make possible important research through the grants we offer to UT Southwestern researchers.

Q: What achievement of the Friends has made you most proud?

A: Last year, the Friends granted funding for four research projects. Because the Friends had only enough money from our dues to fund two grants, two interested parties came forward and asked to fund the remaining two projects. This year, the Friends were able to fund two projects and again, others stepped up to fund a third one. It is my hope that others will be interested in following suit to memorialize or honor a family member or friend.

Q: What would you say to inspire others to join the Friends?

A: To encourage others to join the Friends, I would say that it is a wonderful way to be a part of exciting new research into finding a cure for Alzheimer's Disease.



Charron Denker

Q: Outside of finding a cure for Alzheimer's disease, what are your interests and passions?

A: My interests are centered on our family ranch. I am in partnership to sell hay raised on our ranch. In the fall, we have limited success with our dove hunting, and consistently better luck hunting for quail, chukar and pheasant at a local hunting resort. While I love riding, I have been accused of spending more time playing "beauty-parlor" with my two palominos' manes and tails. I enjoy my vegetable garden and am in the process of starting it at this time. I love the outdoors and country life. *

HELPING OTHERS

Continued from page 1

keep up with technology changes as quickly as other people could. It was getting to me, and it was frustrating me, and so that's why we went to the doctors," he said.

Mr. Rushing, a father of two and grandfather of six, was diagnosed with Alzheimer's at age 56. He had to retire from his job a few months after the diagnosis, and the Rushings had to change the plans they had envisioned for the rest of their lives.

"It was the diagnosis I feared the most," Mrs. Rushing said.

The couple acknowledged that

they went through an emotionally devastating period, grappling with the fact that Alzheimer's was now a dominant part of their lives. But they rebuilt a sense of hope by taking any positive action they could and becoming advocates for Alzheimer's research and awareness.

Mr. Rushing set out to prove that Alzheimer's may have eroded some of his memory but none of his spirit. He works in the yard and at friends' workshops to keep active. He works out with a personal trainer two or three times a week, and volunteers with the Alzheimer's

Association of Greater Dallas. He spoke at the Alzheimer's Promise Garden Ceremony at last year's Walk to End Alzheimer's, and he and his wife were recently made co-chairs of the Early Stage Advisory Group for the Alzheimer's Association of Greater Dallas.

He said a pillar of his work in Alzheimer's is his constant participation in research studies at UT Southwestern.

"If I can make it better for the next person, I am going to do it," he said. "If I can be some part of the solution, I'm happy."*

Research Studies

CLINICAL TRIALS

SOLANEZUMAB

This 18-month clinical trial is for individuals ages 55 to 90 with mild Alzheimer's disease. The trial will examine the investigational drug Solanezumab. Solanezumab is being studied as a neuroprotective agent for persons with Alzheimer's disease, and UT Southwestern researchers are seeking to determine whether or not it will slow the cognitive and functional decline of Alzheimer's disease as compared with a placebo. Participants will be assigned at random to receive the investigational drug or a placebo and will be monitored over the period of the trial. For more information, please contact Kathy Koch, 214-648-9343.

ARICEPT STUDY

Individuals between 50 and 90 years of age with a diagnosis of mild cognitive impairment or Alzheimer's disease

who have received a new prescription for Aricept/Donpezil are needed for an imaging study. This study will measure magnetic resonance imaging changes in patients before and after a two-month treatment of the acetylcholinesterase inhibitor Aricept. Please contact Zohre German, 214-648-2952, for more information.

EXERCISE

This one-year study is seeking people ages 55 to 80 with mild cognitive impairment who do not currently adhere to a regular fitness program. The study will compare individually tailored, supervised aerobic exercise training with flexibility and stretching. The trial researchers 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. For more information, please contact Zohre

German, 214-648-2952, or Candace Hill, 214-345-4665.

COGNITIVE TRAINING FOR MILD MEMORY COMPLAINTS

This study is seeking people 60 years of age or older who are in overall good health but who are noticing more "senior moments" or who have been diagnosed with mild cognitive impairment. The study will evaluate the effects of cognitive training on brain function, and a brief 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. For more information, please contact Audette Rackley, 214-905-3007. *

OBSERVATIONAL AND BIOMARKER DEVELOPMENT

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

CORE AND TARCC RESEARCH STUDIES

People with no memory complaints, mild cognitive impairment, or early Alzheimer's disease 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 may involve financial compensation. For more information, please contact Sarah Brisebois, 214-648-0563.

LOAD (LATE-ONSET ALZHEIMER'S DISEASE) GENETICS INITIATIVE

The LOAD study began enrolling subjects in 2002, with more than 500 subjects enrolled through UT Southwestern. A new grant, based on previous findings

from that study, is facilitating a phone follow-up for subjects from the first study as well as enrolling new subjects.

The goal of this national study is to expand upon the scope of data gathered from subjects already enrolled in the first phase of LOAD as well as to enroll new large families (with three or more living siblings 60 years of age or older) diagnosed with Alzheimer's disease. The focus of the study is to learn more about the genetic, environmental, and health risks that may contribute to the development of Alzheimer's. For all subjects previously enrolled in the LOAD study, the coordinator will contact each person for phone follow-up only. People who have participated in previous family studies and are now ages 60 and older may also enroll in this study. For more information, please contact Barb Davis, 214-648-9367.

COMING SOON

A4 – ANTI-AMYLOID TREATMENT IN ASYMPTOMATIC AD

The A4 study will be a clinical trial for individuals ages 65 to 85 who have normal thinking and memory function, but who have evidence of amyloid plaque buildup in their brains and who may be at risk for developing Alzheimer's disease in the future. A4 is a groundbreaking trial that will test an anti-amyloid investigational drug with the aim of delaying or preventing memory and cognitive decline. Although this study is not open to enrollment yet, please check our website for updates (www.utsouthwestern.edu/ad), as well as www.clinicaltrials.gov (search identifier NCT02008357). For more information, please contact Kathy Koch, 214-648-9343. *

For more information about approved new studies, please visit www.utsouthwestern.edu/ad.

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 provides 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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