

Alzheimer's

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



Edith and Peter O'Donnell Jr.

UT Southwestern establishes Peter O'Donnell Jr. Brain Institute

UT Southwestern has established the Peter O'Donnell Jr. Brain Institute, a comprehensive center that will be dedicated to better understanding the molecular workings of the brain and applying these discoveries to the prevention and treatment of brain diseases and injuries.

A \$36 million gift from the O'Donnell Foundation funded establishment of the Institute, which the UT System Board of Regents recently approved.

The Institute will support the recruitment of world leaders in science and medicine. Already, Dr. Marc Diamond, who was recently recruited to be Professor of Neurology and Neurotherapeutics, and his team are rapidly advancing basic

knowledge of debilitating brain diseases.

Simultaneously, investments in advanced technology and multidisciplinary clinical programs are positioning Zale Lipshy University Hospital to enhance its excellent care for patients with a variety of brain disorders.

"The support of the O'Donnell Foundation recognizes that one of the greatest challenges of our time is brain injury in its various forms. The gift enables UT Southwestern to accelerate progress in injury prevention, novel brain preservation strategies, and restoring brain function lost by injury and disease," said Dr. Daniel K. Podolsky, President of UT Southwestern, who holds

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Dallas man supports Alzheimer's research in wife's memory

When Alzheimer's disease started its devastating spiral of progression in Guinevere Blackstone, her husband Edward searched the country for the best treatment facility. Her doctor had one recommendation: UT Southwestern Medical Center.

"She said the Alzheimer's Disease Center at UT Southwestern was tops in both research and treatment," said Mr. Blackstone "Now that I've seen it in action, I agree."

Dr. Myron Weiner, Professor Emeritus of Psychiatry, initially treated Mrs. Blackstone. Her care team eventually expanded to include Dr. Roger Rosenberg, Director of the Alzheimer's Disease Center, Professor of Neurology and Neurotherapeutics, and Physiology, and holder of the Abe (Brunky), Morris and William Zale Distinguished Chair in Neurology; and Dr. Mary Quiceno, Associate Professor of Neurology and Neurotherapeutics.

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FROM THE DIRECTOR |

Roger N. Rosenberg, M.D.

We have some great news from our friends at the Alzheimer's Women's Association for Resources and Education, or AWARE.

This outstanding Dallas-based organization has been on the front lines of the battle to beat Alzheimer's disease since 1989, and to date has raised and donated more than \$12 million for related research and education.

This year, AWARE has given the Alzheimer's Disease Center at UT Southwestern Medical Center \$50,000 to advance our development of a potential Alzheimer's vaccine.

In animal models, our amyloid beta 42 (A β 42) vaccine stimulates antibodies that bind to and eliminate beta-amyloid, a protein whose buildup in the brain has been linked to Alzheimer's disease. This patented

DNA vaccine eliminates problems with brain inflammation that derailed earlier clinical trials of another proposed Alzheimer's vaccine.

The DNA A β 42 vaccine has the potential be a safe therapy to delay or prevent Alzheimer's disease, as compared with the A β 42 peptide vaccination. DNA A β 42 immunization has shown a 50 percent reduction in the level of amyloid-containing plaques in the brains of Alzheimer's disease-model mice.

We hope to complete animal testing in the next few years, analyze the results, and then by the end of the decade submit an application to the FDA to initiate human clinical trials.

With the donation from AWARE and the generous support of the Friends of the Alzheimer's Disease



Center and other donors, we will continue this important research toward finding better treatments, and hopefully a cure for Alzheimer's.

If you would like to learn more about the vaccine, I invite you to be my guest at the President's Lecture Series, Thursday, Oct. 29, at 4 p.m., in the Tom and Lula Gooch Auditorium here at UT Southwestern. A reception will follow the presentation.

Thank you for your continued support. ✱

UT Southwestern joins national consortium working to develop implantable device to treat memory loss



Dr. Bradley Lega

UT Southwestern Medical Center has joined a consortium of eight leading universities to develop new technologies to restore and improve lost memory in people with Alzheimer's disease or traumatic brain injuries.

Specifically, UT Southwestern is part of a study with the goal of developing an implantable neural monitoring and stimulation system to treat memory loss by the end of the four-year program in 2018.

Researchers plan to use safe levels of electrical stimulation in neurosurgery patients who already receive brain stimulation as part of their therapy for epilepsy or Parkinson's disease. Researchers hope to determine whether giving brain stimulation as these individuals play memory games improves their memory function.

"If memory can be improved in patients who have electrodes implanted to treat epilepsy and Parkinson's disease – and who frequently have mild memory impairment – then we will have gained extremely valuable information on how to restore memory function in patients with traumatic brain injury or Alzheimer's disease," said Dr. Bradley Lega, Assistant Professor of Neurological Surgery, Neurology and Neurotherapeutics, and Psychiatry at UT Southwestern, who will lead the Dallas arm of the study.

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FALL FORUM:

Leading-edge Alzheimer's researcher to speak



Dr. Tony Wyss-Coray

What if we could give Alzheimer's disease patients an infusion of blood elements from young people, rejuvenating their brains?

Studies by Dr. Tony Wyss-Coray of Stanford University School of Medicine point in this direction. Dr. Wyss-Coray is Professor of Neurology and Neurological Sciences at Stanford.

Dr. Wyss-Coray will discuss his research as the keynote speaker for the Friends of the Alzheimer's Disease Center's Fall Public Forum on Oct. 8. The presentation begins at 7 p.m. in the Simmons Biomedical Research Building, 6000 Harry Hines Blvd. Reservations are requested by calling 214-648-2344.

In his Stanford lab in California, Dr. Wyss-Coray and his colleagues

injected blood plasma from younger mice into older mice. The results were breathtaking, he said. The aged mice showed numerous important molecular, neuroanatomical, and neurophysiological changes, and outperformed their control group on standard spatial-memory tests.

"This could have been done 20 years ago," said Dr. Wyss-Coray, who is also a senior research career scientist for the Veterans Affairs Palo Alto Health Care System. "You don't need to know anything about how the brain works. You just give an old mouse young blood and see if the animal is smarter than before. It's just that nobody did it."

Earlier research by Dr. Wyss-Coray's team revealed that key regions in the brains of older mice

exposed to the blood of younger mice produced more nerve cells. When younger mice were exposed to the blood of older mice, fewer nerve cells were produced.

His research team is now trying to isolate the blood factors responsible for that phenomenon, and is at work on plasma-based therapies that use the same principle to potentially treat disorders of the central nervous system.

Dr. Wyss-Coray is the recipient of an NIH Director's Transformative Research Award, a Zenith Award from the Alzheimer's Association, and a Distinguished Research Scholar Award from the John Douglas French Alzheimer's Foundation. He also is an inventor and has multiple patents. *

WHO: Dr. Tony Wyss-Coray, Professor of Neurology and Neurological Sciences at Stanford University School of Medicine

WHAT: 2015 Alzheimer's Fall Public Forum

WHEN: 7 p.m., Thursday, Oct. 8

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

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

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The effort is part of a national "Restoring Active Memory" (RAM) program sponsored by the Defense Advanced Research Projects Agency and supported by the National Institutes of Health's Brain Research through Advancing Innovative Neurotechnologies (BRAIN). The NIH has allocated \$127.4 million

to the BRAIN Initiative during 2014 and 2015. The initiative is designed to improve understanding of the brain and cognitive function by accelerating the development and application of innovative technologies to find new ways to treat, cure, and even prevent brain disorders. Currently, some 5.3 million Americans have been diagnosed with Alzheimer's disease,

and 1 million have been diagnosed with Parkinson's disease.

The data gathered at UT Southwestern will be combined with data from the University of Pennsylvania, Thomas Jefferson University in Philadelphia, the Mayo Clinic, Dartmouth University, Emory University and Boston University to develop and test new theories. *

FUNDING THE FIGHT

Friends group awards \$130,000 to two UTSW researchers

Since its inception in 1996, the Friends of the Alzheimer's Disease Center has donated more than \$1 million toward UT Southwestern Medical Center-led investigations into Alzheimer's and other neurodegenerative diseases. These critical gifts help early-career researchers get started on important projects and attract additional funding from governmental groups and supporters. Earlier this year, the Friends awarded two \$65,000 grants to UT Southwestern researchers.

2015 Grant Recipient

ANDREY KARAMYSHEV, PH.D.

Dr. Andrey Karamyshev, Assistant Professor of Physiology, was awarded a grant to investigate "Modulation of proteins associated with Alzheimer's disease by a novel pathway of translational regulation." He joined the UT Southwestern faculty in 2009.

Alzheimer's disease is associated with the accumulation of misfolded proteins in the brain. Dr. Karamyshev and colleagues recently discovered a mechanism of protein quality control involved in protein production, which the researchers coined Regulation of Aberrant Protein Production, or "RAPP."

RAPP appears to be able to decrease aberrant protein production, interfere with protein misfolding, and prevent accumulation of misfolded proteins. This grant will be used to explore use of this mechanism to modulate proteins associated with Alzheimer's and to prevent toxic protein accumulation. It could potentially lead to discovery of drugs to treat Alzheimer's disease in the future.

"This is a very interesting proposal and is different from the traditional directions of Alzheimer's disease research," said Dr. James Stull, Chairman of Physiology and holder of the Fouad A. and Val Imm Bashour Distinguished Chair in Physiology.



Grant recipients Dr. Genevieve Konopka, left, and Dr. Andrey Karamyshev, right, meet with Friends Chair Charron Denker at the last Friends of the Alzheimer's Disease Center forum.

2015 Grant Recipient

GENEVIEVE KONOPKA, PH.D.

Dr. Genevieve Konopka, Assistant Professor of Neuroscience, was awarded a grant to investigate "Identification of alternative splicing networks relevant to Alzheimer's disease." She joined the UT Southwestern faculty in 2011.

Alzheimer's disease is a brain disorder characterized by severe memory impairment. There is a strong genetic component to Alzheimer's disease, but researchers still do not know all of the genes responsible for development of the disorder.

Dr. Konopka is studying a class of proteins called splicing factors that regulate which parts of genes are expressed, or switched on. In particular, she is examining the role of two splicing factors (RBFOX1

and ELAVL2) that appear to be regulatory genes involved in Alzheimer's development.

Using human neurons, Dr. Konopka will manipulate the expression of these splicing factors and assess where these proteins bind in the human genome. She will then assess whether this binding is affected in Alzheimer's disease by examining brain tissue. These experiments will provide new candidate genes and molecular mechanisms for therapeutic targets in the treatment of Alzheimer's.

"Dr. Konopka is a rising star in the field of neurogenomics and her project will be a novel way to identify new candidate gene targets for Alzheimer's disease," said Dr. Joseph Takahashi, Chairman of Neuroscience and holder of the Loyd B. Sands Distinguished Chair in Neuroscience. ❁

Mr. Blackstone hopes the research will one day lead to new treatments for others with Alzheimer's disease.

BLACKSTONE

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The signs of Mrs. Blackstone's Alzheimer's disease began in 1998, with her frequently getting lost. She also had several risk factors for developing Alzheimer's disease:

- Women have a 35 percent higher risk of developing the disease;
- As an African-American, her risk of developing Alzheimer's disease was twice as high as Caucasians; and
- She had a family history of the disease.

Mrs. Blackstone's physicians in San Francisco first diagnosed Alzheimer's, which the UT Southwestern Alzheimer's Disease Center later confirmed. In 1999, the couple moved from San Francisco to Dallas for her treatment here.

In addition to regular treatment, Mrs. Blackstone participated in the early trials of anti-Alzheimer's drugs. "I guess it had some good effect," said Mr. Blackstone. "She lived with Alzheimer's for 14 years."

Sadly, Mrs. Blackstone died in 2013.

In her memory, Mr. Blackstone carries on the fight against Alzheimer's disease by participating in clinical trials. He currently volunteers for two Alzheimer's studies at UT Southwestern, serving as a control study subject among a group of healthy seniors who experienced many of the same environmental factors as his wife.

"Once you look around and see people, and how



Kathryn Gaylord, clinical data specialist, conducts a neuropsychological test with Edward Blackstone, who serves as a control subject in two ADC studies.

desperate the situation is, how can you sit still?" Mr. Blackstone questioned. "Any little bit anyone can do, they should do it. Anything I can do, I'd do it."

Mr. Blackstone participates in the Center's Neurobiology of Alzheimer's Disease and Aging study, as well as a Texas Alzheimer's Research and Care Consortium study. These studies involve annual visits to the UT Southwestern campus for neuropsychological testing, physical and neurological exams, blood sampling, and possibly brain imaging. The data collected from these visits are used by many investigators studying the aging brain and disorders of cognitive function.

Healthy seniors, as well as those suffering from mild cognitive impairment or early Alzheimer's disease, are needed for these studies. For more information, please contact Sarah Brisebois at 214-648-0563.

Looking ahead, Mr. Blackstone hopes that the research in which he is participating will one day lead to new treatments for others with Alzheimer's disease.

"After helplessly watching your loved one fade away from life, it gives you much pleasure to finally be helpful in some way by participating in research," Mr. Blackstone said. *

O'DONNELL

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the Philip O'Bryan Montgomery, Jr., M.D. Distinguished Presidential Chair in Academic Administration and the Doris and Bryan Wildenthal Distinguished Chair in Medical Science.

"UT Southwestern's enormous talent in neuroscience and neuro-

technology provides an important opportunity to invest in this critical field," said Mr. O'Donnell. "The medical school consistently tackles some of the most difficult scientific challenges with enormous success, benefiting patients today and patients for generations to come. I have every confidence that the field of neuroscience will make great strides at UT Southwestern. I look forward to seeing the next discover-

ies that are made, and meeting the next extraordinary scientists and researchers who will be recruited to the Brain Institute."

The new Institute will further UT Southwestern's well-established foothold in neuroscience, including both basic and translational science, as well as clinical care, supported by its unique expertise in affiliated fields. *

Brain changes in ex-NFL players who lost consciousness from concussion may shed light on Alzheimer's progression

In the first study of its kind, former National Football League (NFL) players who lost consciousness due to concussion during their playing days showed key differences in brain structure and function later in life. The hippocampus, a part of the brain involved in memory, was found to be smaller in 28 former NFL players as compared with a control group of men of similar age and education.

The findings, reported in a recent edition of *JAMA Neurology*, represent the first study to compare the relationship between hippocampal volume, memory performance, and concussion severity.

Some of the retired NFL players



Dr. Munro Cullum

also met criteria for mild cognitive impairment (MCI), a condition that typically affects memory and may lead to dementia.

“Since MCI is often a precursor to Alzheimer’s disease, our results may have a direct implication for the development of Alzheimer’s pathology,” said study co-author Dr.

Munro Cullum, Professor of Psychiatry, and Neurology and Neurotherapeutics at UT Southwestern Medical Center, who holds the Pam Blumenthal Distinguished Professorship in Clinical Psychology.

“In particular, our finding of greater hippocampal atrophy among those with a history of loss of cognition has implications for Alzheimer’s disease insofar as

hippocampal impairment and structural change are some of the earliest changes seen in Alzheimer’s as well,” Dr. Cullum added.

The former players ranged in age from 36 to 79, with a mean age of 58. Twenty-one healthy men of similar age, educational level, and intelligence with no history of concussion or professional football experience served as control subjects.

The results do not explain why the hippocampus was smaller in the athletes who suffered more serious concussions. Some shrinkage is a part of the normal aging process, but the reduction is accentuated in MCI and was even more notable in those MCI subjects with a history of concussion accompanied by loss of consciousness. Thus, there appears to be a cumulative effect of concussion history and MCI on hippocampal size and function. *

MEET THE DOCTOR: Laura Lacritz, Ph.D.

Dr. Laura Lacritz, Professor of Psychiatry, and of Neurology and Neurotherapeutics, is a member of UT Southwestern’s Alzheimer’s Disease Center team who sees patients early in the assessment process to diagnose mild cognitive impairment or Alzheimer’s disease.

Dr. Lacritz’s clinical expertise is in the area of neuropsychological assessment, with particular interest in working with individuals who have dementia, epilepsy, movement disorders, brain tumors, and head injury.

Her research interests include early detection of Alzheimer’s disease, mild cognitive impairment, movement disorders, epilepsy, and other cognitive disorders through use of advanced cognitive assessment and other diagnostic techniques. She also researches predicted declines of patients with these disorders.



Dr. Laura Lacritz

“Our challenge is determining how we can best use our diagnostic tests to help with early detection,” Dr. Lacritz said.

Dr. Lacritz, who is board certified by the Association of Postdoctoral Programs in Clinical Neuropsychology, has authored or been a significant contributor to 38 major papers in leading scientific and medical journals. In 2016, she will become President of the National Academy of Neuropsychology.

At UT Southwestern, Dr. Lacritz also is responsible for admissions in the Clinical Psychology Graduate Program.

She was recently elected to the UT Southwestern Academy of Teachers in recognition of excellence as an educator.

“I love the clinical work,” she said, “but I really enjoy training – seeing people develop.” *

MEET A FRIEND | Mike Breard

My late wife, Gayle, was diagnosed with Alzheimer's disease through a brain biopsy in 1990 at the age of 47. I took care of her at home for the next 15 years until her death.

She participated in several clinical trials for drugs tested to alleviate her symptoms. Soon after she became sick, I joined the Friends of the Alzheimer's Disease Center at UT Southwestern Medical Center to learn more about the disease. I also wanted to keep up with trends in research to see if there was any hope for a cure. Back then, there was no hope.

Now, it is so encouraging to go to meetings of the Friends to hear researchers talk about advances that could lead to cures. I have been particularly impressed with the lab tours, during which the research grantees demonstrate their work. The use of modern computer technology allows them to do many things not possible just a few years ago. It also is very encouraging to be able to visit with the faculty at UT Southwestern and see their dedication to finding new



Mike Breard and his wife, Angie

treatments. Anyone who is interested in learning more about Alzheimer's and helping to fund research should certainly join the Friends.

Several years after my wife passed away, I was fortunate to marry Angie, and now we regularly attend the

*Forums and lab tours together. It is a real comfort that because of the efforts of UT Southwestern and the Friends of the ADC, current research and progress in defeating this disease may help future generations, such as my grandchildren. **

STUDY: Evaluating dementia patients by teleconference is valid

Assessment of patients with known or suspected dementia through teleconference was proved to be relatively comparable to in-person consultation, according to a new study from UT Southwestern Medical Center.

Six standard tests to evaluate dementia were given twice to 202 test subjects, once face-to-face with a clinician, and once in front of a television displaying the clinician and test materials. The results of the two tests closely matched, confirming the value of teleneuropsychology.

Use of telemedicine has grown rapidly in recent years, with consultations and even some traditional services being provided in psychiatry, neurology, and radiology. This can be particularly valuable when such services are not readily available to the patient, who may live far from specialized care.

The UT Southwestern study is the largest of its kind. Previous studies focused on healthy control subjects or small samples of patients with a variety of neuropsychiatric diagno-

ses, with little emphasis on traditional and detailed neuropsychological assessments.

The findings were reported in a recent issue of the *Journal of the International Neuropsychological Society*. UT Southwestern authors included Dr. Munro Cullum, Professor of Psychiatry, and of Neurology and Neurotherapeutics, who holds the Pam Blumenthal Distinguished Professorship in Clinical Psychology; Dr. Linda Hynan, Professor of Clinical Science and Psychiatry; and Dr. Myron Weiner, Professor Emeritus of Psychiatry.

Study participants were recruited through the Alzheimer's Disease Center at UT Southwestern, as well as its satellite clinic in Talihina, Oklahoma, which serves the Choctaw Nation. Eighty-three of the study participants had some form of cognitive impairment or Alzheimer's disease. The study recommended that additional testing of videoconference assessment in different populations be conducted to fully explore the value of this approach. *

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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