

LEADING  
**TRANSFORMATIVE CHANGE**  
AT MEDICINE'S  
**ULTIMATE FRONTIER**

**UTSouthwestern**

Peter O'Donnell Jr.  
Brain Institute

CAMPAIGN FOR THE BRAIN



# EXPEDITION: THE BRAIN



DESPITE GREAT PROGRESS IN UNCOVERING THE UNDERLYING MECHANISMS OF MANY DISEASES OVER THE LAST SEVERAL DECADES, MODERN MEDICINE HAS JUST BEGUN TO UNDERSTAND THE HUMAN BRAIN—THE BODY’S MOST COMPLEX SYSTEM AND MEDICINE’S GREATEST MYSTERY.

More than just an organ or part of the physical body, the brain is a vast complex of interconnected circuits encompassing 86 billion neurons. It is where our intellect, memories, identities, and seat of consciousness reside. That personal, private self is at stake for those who suffer from brain diseases and disorders. Cures are what patients want; precision treatments are what they need.

However, a comprehensive model of the human brain in health and disease remains incomplete. A lack of cures for Alzheimer’s, Parkinson’s, ALS, and a number of rare, debilitating neurological diseases are but one aspect of the bigger picture.

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*Brain fiber images on the outside cover and this page are both courtesy of Joseph Maldjian, M.D., Professor, Radiology and Advanced Imaging Research Center. Recent advancements in neuroimaging now make it possible for our researchers to map and understand how information between different areas in the brain is relayed. This exciting work will ultimately improve how we prevent, diagnose, and treat brain injury due to sports or other trauma.*

Mental illness, including depression, affects up to 27% of the American population, and it is estimated that by 2020 depression will be the second leading cause of disability throughout the world. And millions of Americans suffer from migraines, chronic pain, and sleep disorders. Just treating the symptoms is not sufficient.

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## FINDING THE UNDERLYING CAUSES OF BRAIN DISEASES WILL PROVIDE THE FOUNDATION FOR PREVENTION AND CURES.

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Brain disease in its various forms—whether developmental, traumatic, psychiatric, or degenerative—looms as one of the greatest challenges of our time. It is estimated that 50 million Americans suffer from brain-related diseases, with debilitating effects that may continue for years or even decades. On its current trajectory, the devastating impact of brain disorders on our society will only grow, causing untold suffering and a staggering economic burden that is approaching \$1 trillion. **The toll of brain disorders is more than just financial. It's the human cost—a patient's loss of self magnified by the emotional strain experienced by family members as caregivers—that cannot be quantified.**

While the obstacles on the path to recovery from brain disorders may seem insurmountable, humankind has overcome challenges of similar scale with every great advance in history: human flight, walking on the moon, and treatments for AIDS. Teams of individuals with laser focus and unrelenting drive accomplish feats that transform the world. With so much groundbreaking research and development in neuroscientific technologies like imaging, brain stimulation, bioengineering, artificial intelligence, and integrative, translational research methods, the time to focus our attention on the brain is now. Recent advances have opened the door to limitless new discoveries and treatments, all within reach in our lifetime.

Despite the underlying causes and processes of brain injuries and disorders varying, the fundamental challenge is cross-cutting—the need to identify the basic mechanism of brain function and the means to promote repair and functional recovery. An undertaking of this magnitude requires a concerted approach at every level, including basic and applied research, and clinical innovation. It requires a new paradigm built on scientific rigor, interdisciplinary collaboration, and open innovation to ensure that advances in science and technology move with maximum speed to reduce human suffering.



## OUR VISION

IMAGINE A DAY WHEN ALZHEIMER'S DISEASE IS A PREVENTABLE CONDITION, WHEN A PHARMACOLOGICAL THERAPY PROMOTES REPAIR AFTER A BRAIN INJURY, WHEN BRAIN STIMULATION SPEEDS RECOVERY AFTER A STROKE, AND WHEN DEPRESSION CAN BE HALTED IN ITS EARLIEST STAGES BY SELECTING THERAPIES BASED ON A PATIENT'S SPECIFIC BIOSIGNATURE. TO REALIZE THIS FUTURE, WE MUST UNDERSTAND THE GENES, MOLECULES, AND PATHWAYS THAT ARE ALTERED IN DISEASE IN ORDER TO DISCOVER NEW TARGETS FOR THERAPY.

At UT Southwestern, we believe that the next decade will be as burgeoning in brain science as the 1980s were for cardiovascular research. That scientific revolution led to the discovery of statins—cholesterol lowering drugs that have helped tens of millions of people around the world—as well as to UT Southwestern's first two Nobel Prizes. North Texas will be the seat of scientific discovery, as it was 30 years ago, but this time it will be for unraveling the mysteries of the brain.

**OUR GOALS FOR THE O'DONNELL BRAIN INSTITUTE ARE AMBITIOUS.  
UT SOUTHWESTERN SEEKS TO:**

**1. Understand how the nervous system functions and how it generates integrative behavior and cognition.**

At the forefront of biology, neuroscience represents a vast frontier for exploration of some of the most profound questions concerning living systems. Understanding how the nervous system functions and how it generates integrative behavior and cognition remain among the most difficult challenges in science today.

**2. Apply advanced imaging tools and analytics.**

For years, one of the great challenges in diagnosing and treating brain injury was that conventional imaging tools often failed to show abnormalities even when clinical manifestations of brain injury are apparent. New technologies developed at UT Southwestern's Advanced Imaging Research Center offer opportunities to directly visualize disruption of brain function and structure.

**3. Understand the causes and mechanisms of major forms of brain disease and develop new therapies.**

Our clinical fields have suffered from a lack of drugs and treatments that can actually restore and improve brain function. Based on our improved understanding of brain circuit properties, critical areas for breakthroughs are in the development of drug and molecular therapies for neurologic disease, as well as in the development of neuromodulation (brain stimulation) therapies.

**4. Leverage UT Southwestern's clinical expertise across multiple specialties to provide the nation's best acute and restorative care.**

UT Southwestern will become a national center for excellence in the precise diagnosis and treatment of the full spectrum of brain disorders and facilitate collaborative care for our patients. Seamless coordination for patients from the point of access throughout the continuum of care will help drive outstanding patient satisfaction, safety, and clinical quality.



# WHAT IS AT STAKE?



For those suffering from brain diseases ranging from Alzheimer's to aggressive brain tumors, "there is no cure" is heard all too often. Effective treatments are severely limited for many diseases of the brain. Particularly in the case of neurodegenerative disorders, no therapies have been able to slow disease progression.

Even for treatable conditions such as depression, patients' responsiveness to therapies varies widely. A trial-and-error approach to treatment and lack of targeted treatments mean that some patients improve dramatically, while others show little response.

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*Rachel, Michael, and baby Caedmon Creed were served by siblings Drs. Shivani and Toral Patel (left, right). In her first trimester of pregnancy, Rachel suffered three seizures and was diagnosed with a malignant brain tumor. UT Southwestern was able to remove the tumor in a complex operation performed while she was still pregnant. Our cutting-edge science and expert medical care are changing, extending, and saving lives.*

## IN THE U.S. ALONE . . . THE NUMBERS ARE STAGGERING

### ■ ALZHEIMER'S DISEASE

By 2050, it is estimated that a new case of Alzheimer's disease will be diagnosed every 33 seconds.

### ■ AUTISM

Autism and autism spectrum disorders are now estimated to affect 1 in 68 children.

### ■ DEPRESSION

More than 25% of Americans have suffered from depression. Last year in the DFW metroplex alone, almost one million adults experienced a mental illness, and more than 190,000 had thoughts of suicide.

### ■ MULTIPLE SCLEROSIS (MS)

MS is the second most common cause of acquired neurological disability in young and middle-aged adults.

### ■ PARKINSON'S DISEASE

More than 500,000 people are suffering with Parkinson's disease, and about 50,000 new cases are diagnosed each year.

### ■ SPINAL CORD INJURY (SCI)

The incidence of SCI is highest among persons age 16-30, meaning that young people who are affected live for many decades with SCI's debilitating consequences.

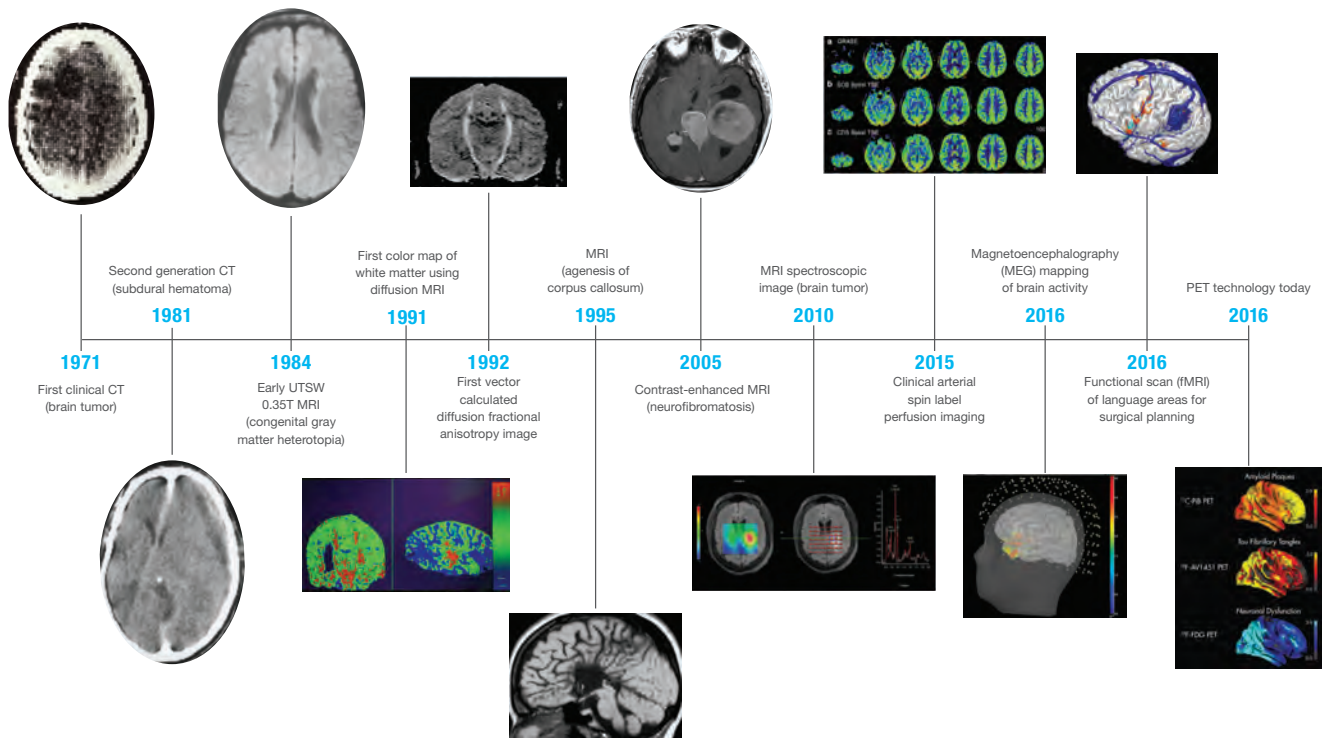
### ■ STROKE

130,000 people die from stroke each year.

### ■ TRAUMATIC BRAIN INJURY (TBI)

80,000 Americans live with varying degrees of disability due to traumatic brain injury.

## EVOLUTION OF NEUROIMAGING



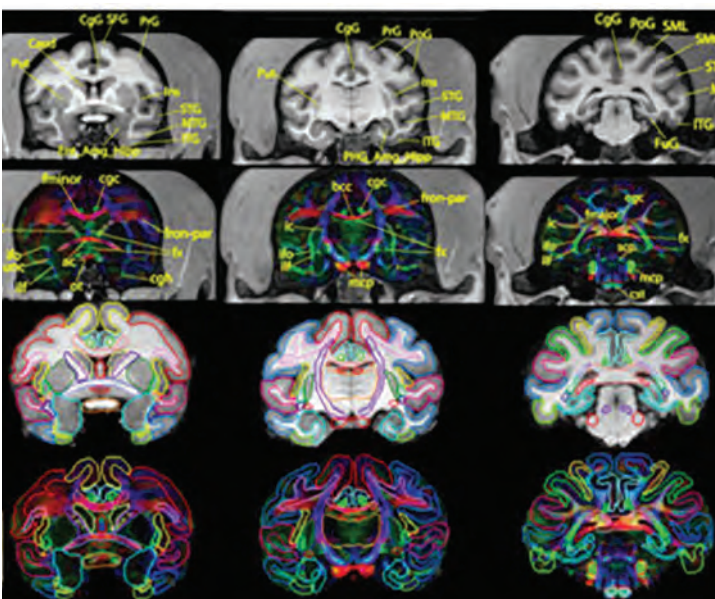
## OPPORTUNITIES FOR BREAKTHROUGHS

# HAVE NEVER BEEN GREATER

For years, medical science faced a dark wilderness with little more than a flashlight and curiosity to probe the vast, uncharted territory of the brain. Today, a wealth of recent breakthroughs in chemistry, biophysics, genetics, genomics, imaging, and informatics provide new opportunities to answer important questions. What are the genes, molecules, and pathways that underlie neurogenesis, neuronal signaling, circuit formation, and complex behaviors? How are these pathways altered in disease, and can we discover new targets for therapies?

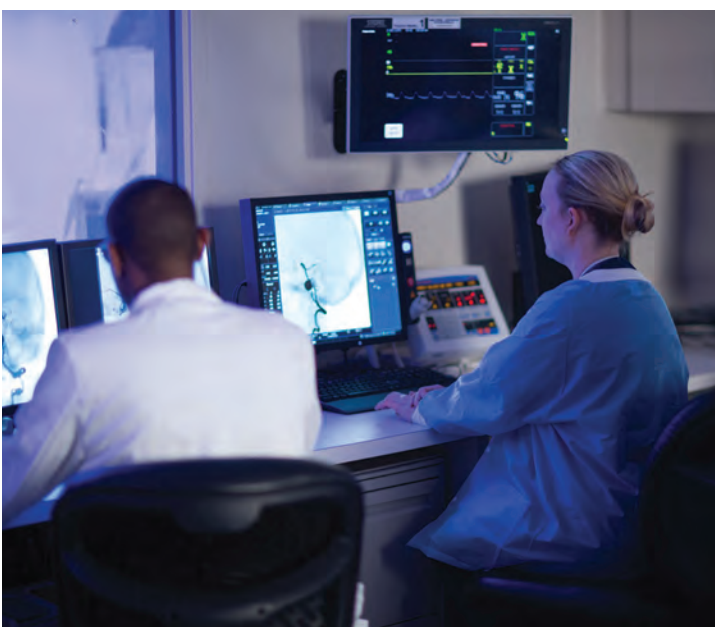
Neuroscience is entering a new era of innovation where fundamental discoveries will be made that will be ripe for translation to clinical practice. Building on this foundation, the availability of new imaging technologies, research breakthroughs related to the basic mechanisms of brain disease, and the ability to analyze massive amounts of data are paving the way for transformative advances.





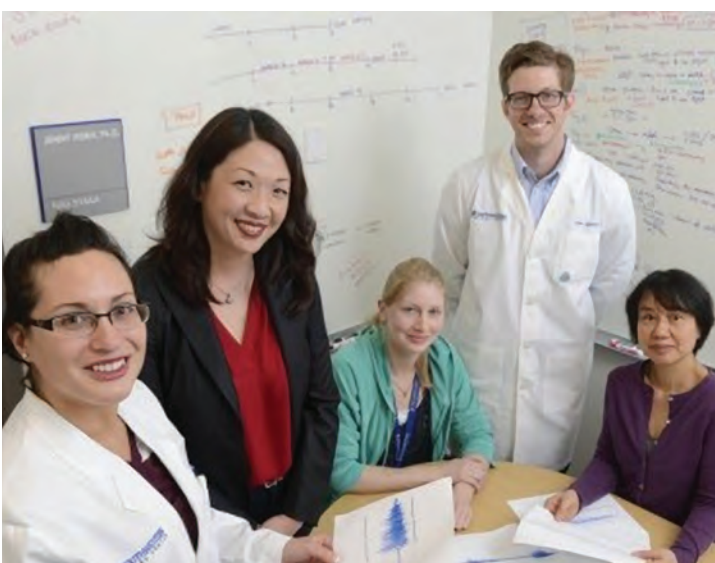
## ADVANCES IN BRAIN IMAGING

Rapid progress in brain imaging, more than any other technology, is transforming the field of neuroscience research and clinical care. Modern management of stroke, brain malignancies, multiple sclerosis, and trauma would otherwise be impossible. Although progress in brain imaging over the last 20 years is impressive, the opportunities now are even more exciting. For example, methods to image regions of brain activation, termed functional magnetic resonance imaging or fMRI, have matured and are now the foundation of most neuroscience studies in patients. New methods to image fluxes in metabolic pathways, image specific chemicals and neurotransmitters in the brain, and image specific ligands—notably molecules associated with Alzheimer’s disease—are now emerging.



## PROMISING BREAKTHROUGHS IN UNDERSTANDING BASIC MECHANISMS OF BRAIN DISEASE

Until recently, scientists have not known how to identify and block the molecular events that lead to brain dysfunction in neurodegenerative disorders. But through a recent breakthrough discovery by a researcher at UT Southwestern, we now know how neurodegenerative diseases spread from cell to cell, mediated by a protein called tau that is a normal part of brain cells. When a few brain cells begin to die, they release toxic tau that invades neighboring brain cells, creating a chain reaction that soon destroys large parts of the brain. The tau discovery creates an enormous therapeutic opportunity: if we can stop the spread of tau, we may prevent a whole panorama of degenerative brain diseases.



## SOPHISTICATED DATA ANALYSIS

Biomedicine has become an information science. Mining large, multidimensional data sets for meaningful patterns is critical to translating research discoveries into innovative therapies. UT Southwestern is poised to lead discovery efforts in neurosciences through the application of new bioinformatics approaches to exploring both normal brain function, as well as brain injury and repair. The challenges are significant, and include imaging and modeling brain morphology, signal processing in neural networks, neurogenetics of disease and injury, and artificial intelligence and deep learning. However, eminent success in these domains will propel the next great leap forward in neurosciences, which will permit both new approaches to learning and recovery from injury.

# WHY UT SOUTHWESTERN?

Few places in the world are as primed for discovery and development as UT Southwestern is right now. Major strengths include the scientific caliber of our investigators, coupled with our collaborative and interactive environment. With six faculty having received Nobel Prizes, 22 members of the National Academy of Sciences, and 14 Howard Hughes Medical Institute Investigators, UT Southwestern is internationally recognized as a biomedical research powerhouse.

UT Southwestern's faculty includes many of the nation's top neurosurgeons, neurologists, psychiatrists, radiologists, and specialists in rehabilitation medicine working together to deliver coordinated care for patients. This collaborative talent and expertise enables UT Southwestern to lead the way in treating the most complex and rare neurologic conditions of the brain with superior outcomes.

With a goal of bringing together these leading minds in science and medicine and recruiting additional faculty in key areas to focus on UT Southwestern's top priority—finding cures for disorders of the brain—the medical center has recently established the **Peter O'Donnell Jr. Brain Institute**. This multi-disciplinary, multi-dimensional initiative leverages the institution's demonstrated expertise in fundamental neuroscience, clinical and translational medicine, and brain imaging to rapidly advance research discoveries to new therapies for those suffering from disorders of the brain.

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**THE WORK OF THE O'DONNELL BRAIN INSTITUTE  
IS SINGULARLY AIMED AT FINDING INNOVATIVE  
SOLUTIONS THAT GIVE PATIENTS BACK THEIR LIVES.**

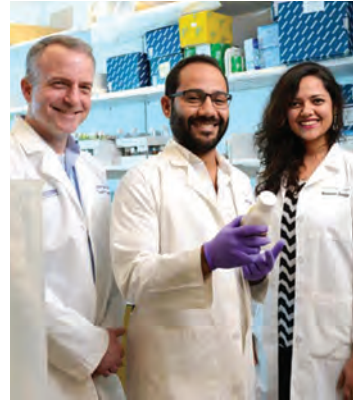
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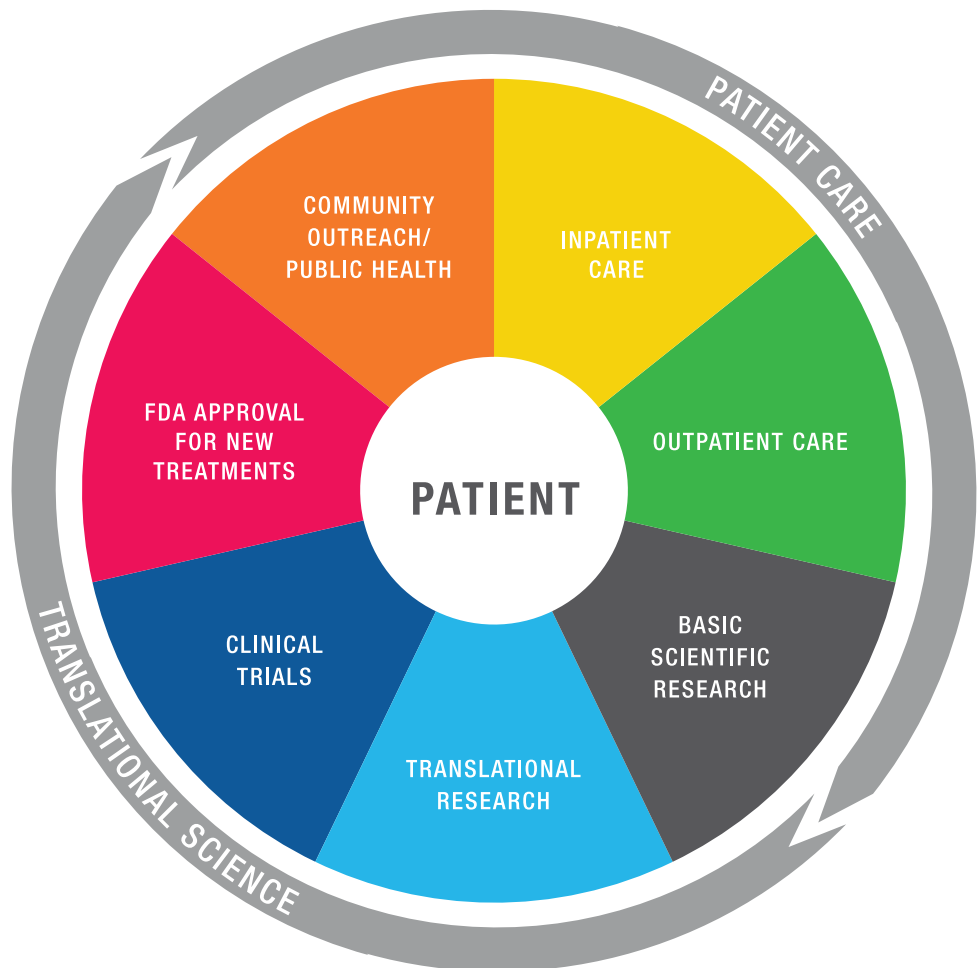
**EDUCATION**



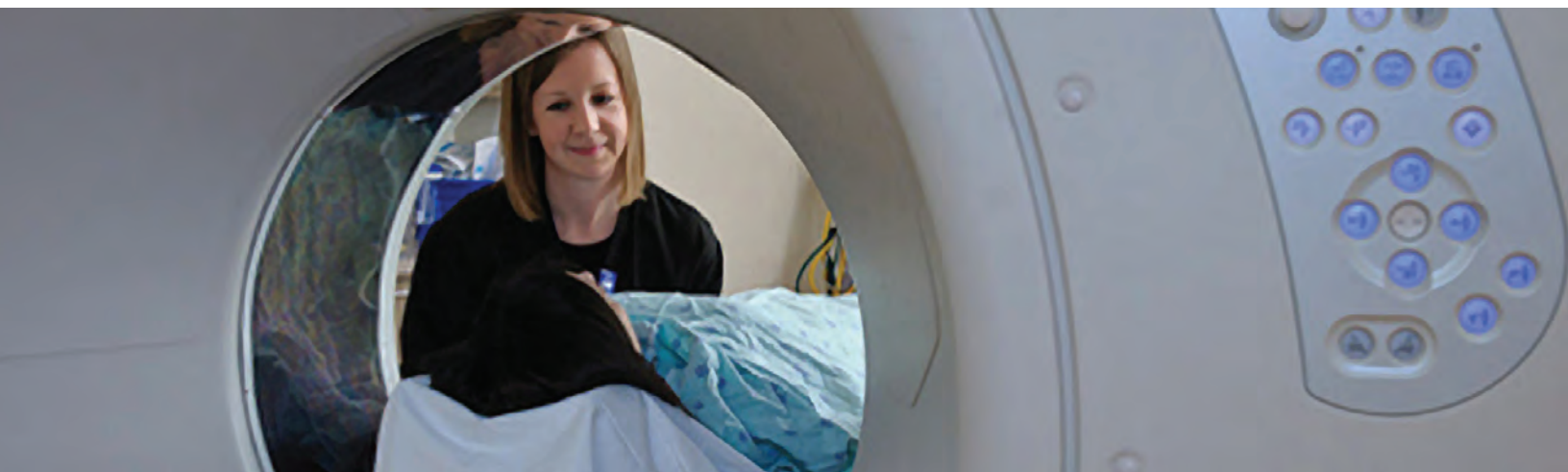
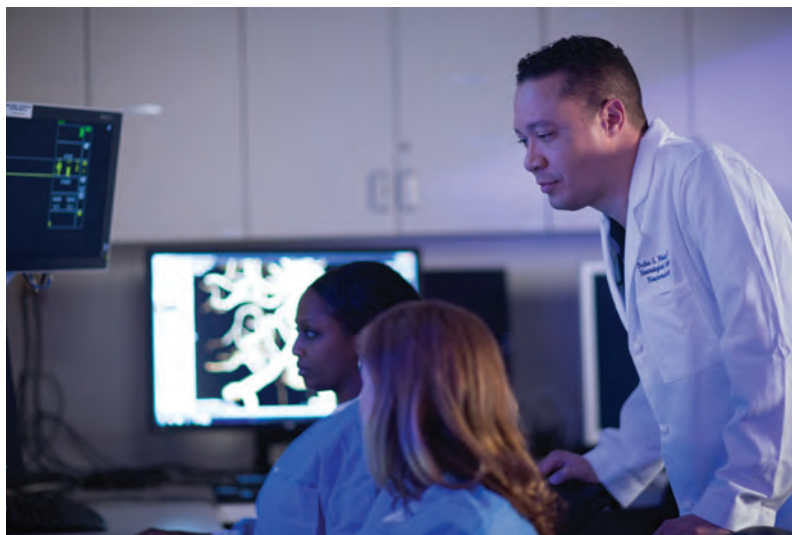
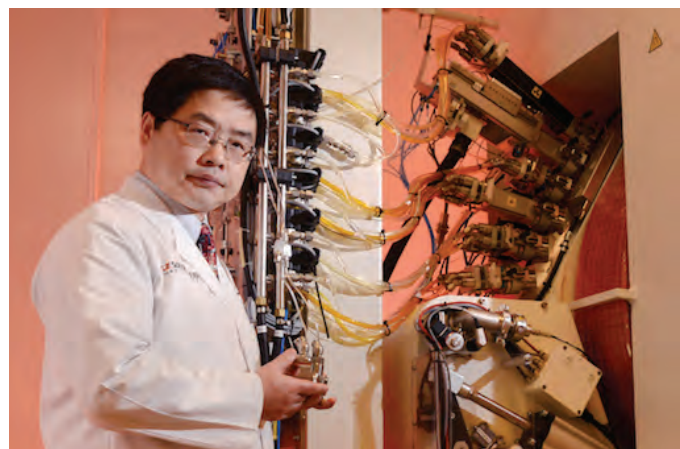
**PATIENT CARE**



**SCIENCE**







## **ALREADY, WORK AT UT SOUTHWESTERN IS LEADING TO PROMISING NEW THERAPIES . . .**

### **A THERAPEUTIC AGENT PRESERVES BRAIN FUNCTION AFTER INJURY**

Investigators in the Department of Biochemistry are working on novel agents that in preliminary studies have been shown to mitigate the cascade of brain deterioration that occurs in the days and weeks after traumatic brain injury.

### **NEUROMODULATION SHOWS PROMISE FOR TARGETED RECOVERY FROM BRAIN DISEASES AND INJURIES**

Neuromodulation therapies such as deep-brain stimulation—used in the treatment of Parkinson’s disease, epilepsy, pain, and depression—show promise for targeted recovery in traumatic brain injury, stroke, and other acquired, neurodegenerative, and developmental brain diseases.

### **THE REGENERATION OF NEURONS PROVIDES HOPE FOR TREATING ALS**

At our Hamon Center for Regenerative Science and Medicine, researchers have taken one kind of cell and, through various manipulations, turned it into a motor neuron—the cell from the spinal cord that is involved in directing muscle movement. Someday it may be possible to regenerate neurons from the body’s own cells to treat conditions such as Lou Gehrig’s disease or multiple sclerosis.

### **A DISCOVERY ABOUT NEURODEGENERATION COULD REVOLUTIONIZE THERAPY**

Researchers in our Center for Alzheimer’s and Neurodegenerative Diseases have developed a new therapeutic antibody for common disorders such as Alzheimer’s disease that traps pathological protein aggregates as they move between cells, leading to their clearance from the brain. This therapeutic antibody is the first of its kind in clinical trials for patients with neurodegenerative diseases.





*Brad Lega, M.D., Assistant Professor of Neurological Surgery and of Neurology and Neurotherapeutics, has begun performing a minimally-invasive procedure with the assistance of a Robotized Stereotactic Assistant (ROSA). UT Southwestern is one of the leaders in the use of this advanced tool, which allows our surgeons to pinpoint the source of seizures and then expertly place laser probes used for thermal ablation of brain tumors or abnormal areas that generate seizures. For patients this means the utmost in personalized treatment with more effective and longer lasting results.*



*The Team Based Learning (TBL) Center launched with members of UT Southwestern Medical School's Class of 2019 as part of their annual orientation. The facility offers the latest in technology and supports the framework of the TBL program, which incorporates an active small-group strategy to replace lectures medical students have received for many years. TBL is a longtime educational strategy in business and science, and has only recently been introduced into medical education. The new curriculum is designed to foster problem solving, teamwork, and long-term acquisition and retention of medical skills.*



# FUNDING PRIORITIES

Unraveling the mysteries of the brain depends on our ability to bring together the best and brightest physicians and researchers, provide them with the resources they need, and allow them to flourish.

## **PRIORITY ONE: RECRUIT AND RETAIN WORLD-RENOWNED FACULTY**

With six Nobel Prizes awarded to its faculty over the last three decades, UT Southwestern's research prowess is unmatched. Early on, civic leaders realized UT Southwestern could be elevated from good to great by nurturing exceptional talent, supporting their work, and maintaining their loyalty in the face of highly attractive offers from other prestigious institutions. Augmenting UT Southwestern's basic research and clinical expertise through the recruitment and retention of the best clinician scientists in the country will be critical to the Medical Center's ability to tackle the biggest challenges in brain science and medicine.

## **PRIORITY TWO: ENHANCE COLLABORATION THROUGH CENTERS OF EXCELLENCE**

Novel experimental design and new technologies result from the intersections of disciplines. With a focus on bringing together researchers and clinicians to eliminate disciplinary and occupational divides that can stunt targeted research efforts, Centers of Excellence in targeted areas—ranging from autism to depression—will provide infrastructure for collaboration on the most important and challenging problems in brain science and clinical care. The goal of these new centers will be to rapidly translate research discoveries into new therapies for patients.

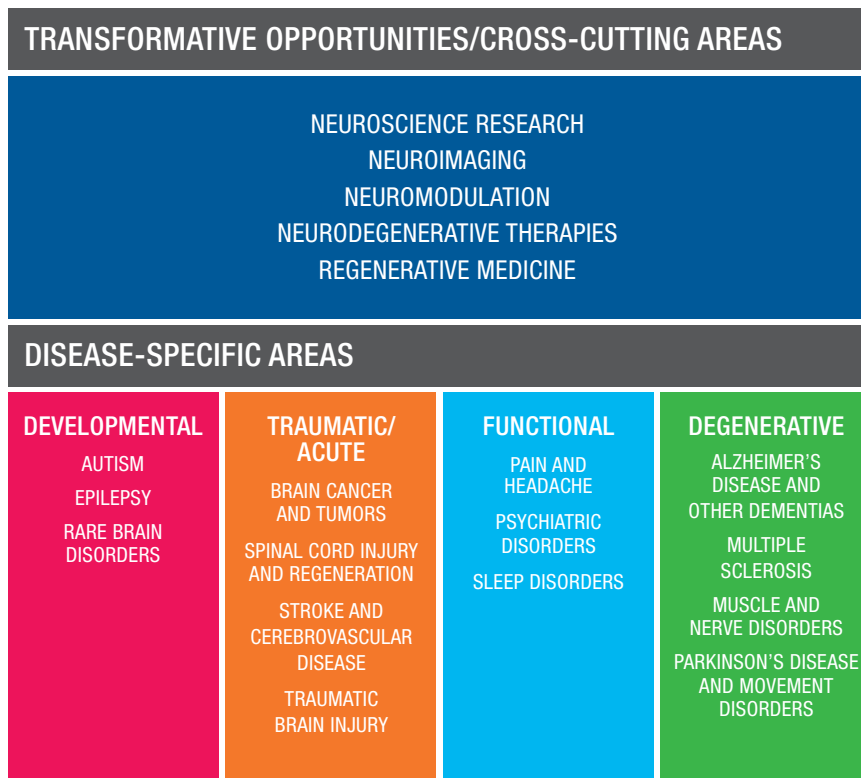
## **PRIORITY THREE: FUND PROMISING AND BOLD NEW RESEARCH**

Asking bold questions and taking intrepid risks today will have a profound impact on how we will treat brain disorders tomorrow. Both current-use and endowed research funds will enable us to expand annual support for innovative research initiatives that show promise in treating brain-related diseases, but that might be too preliminary to be funded by traditional funding mechanisms. This investment would provide researchers with the stability and flexibility needed to take advantage of important opportunities for innovation, research, and improved treatment.

## **PRIORITY FOUR: ENHANCE RESEARCH AND PATIENT CARE THROUGH STATE-OF-THE-ART FACILITIES**

The best minds in science and medicine must be supported by state-of-the-art facilities and next generation equipment. Funds are being sought for advanced equipment, clinical enhancements of UT Southwestern's existing facilities, and strategic new construction, including a third tower to be added to Clements University Hospital for inpatient care of brain-related illnesses and a nearby building for the O'Donnell Brain Institute's transformative research.

# FOCUS AREAS



## MAKING IT HAPPEN

The total cost for UT Southwestern's O'Donnell Brain Institute over the next five years is estimated at \$1 billion, which will be financed through a combination of clinical revenues, federal and state funds for research, and philanthropy.

A project of this magnitude requires a constellation of philanthropic partners. Already leaders in our community—including Peter O'Donnell Jr., Lyda Hill, the Hamon Charitable Foundation, Southwestern Medical Foundation, The Hersh Foundation, and the W.W. Caruth, Jr. Foundation—have made critical invest

ments in research, bioinformatics, and brain imaging, the nexus of which fuels opportunities for transformative change.

UT Southwestern seeks to raise \$500 million in philanthropic support to enable advances in brain research and care that cross UT Southwestern's basic science laboratories, clinical and research centers, and our University Hospitals and Clinics. These funds will fuel the next generation of discoveries that will improve the lives of people in North Texas and around the world.

**WILL YOU JOIN US?**