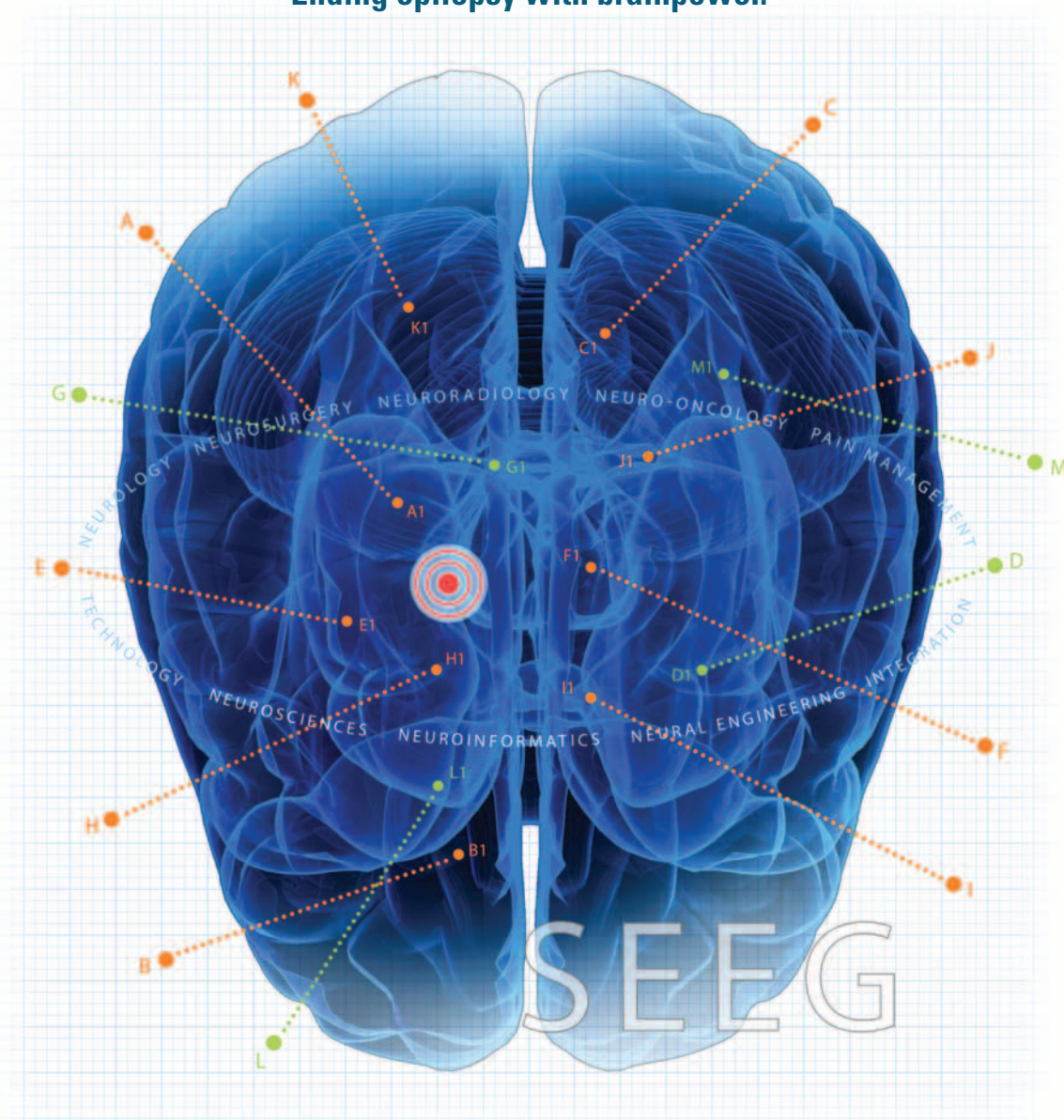


JOURNAL

A publication of The University of Texas Health Science Center at Houston

Ending epilepsy with brainpower.



UTHealth®
Neurosciences

The University of Texas Health Science Center at Houston

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Moving Forward Together

We are excited to highlight the many facets of our program in this issue of the Journal. As a comprehensive neuroscience provider, UTHealth Neurosciences provides expert neurological evaluation and treatment at 18 locations across the Greater Houston area. We are a national destination for neuroscience care, recognized among the top research centers in the United States.

In this issue we highlight the achievements of the Texas Comprehensive Epilepsy Program and welcome internationally renowned neurologist Dr. Samden Lhatoo as the program's new director. Dr. Lhatoo is also co-director of the new UTHealth Texas Institute for Restorative Neurotechnologies, which aims to advance care for epilepsy and other functional neurological disorders.

In the 2019-20 academic year, research funding for the Department of Neurology is more than \$28.5 million. Research funding for the Department of Neurosurgery exceeds \$17.4 million. In a special section on Research and Innovation, we highlight several ongoing studies in neurology and neurosurgery. We're excited to announce that our neurosurgery department was recently ranked eighth in National Institutes of Health rankings of grants to academic neurosurgery departments in the country. Our own Dr. Georgene Hergenroeder is the seventh-ranked individual neurosurgery researcher, and Dr. Claudio Soto is ranked No. 6 among principal investigators of NIH-funded clinical science research studies in neurology. We are also proud to report that our neurology and neurosurgery departments have joined the elite group of American academic programs offering residents and fellows protected research time through an R25 Research Education Program grant from the National Institute of Neurological Disorders and Stroke.

We would like to congratulate Dr. Arthur Day for being awarded the prestigious Distinguished Service Award from the Society of Neurological Surgeons, Dr. David Sandberg for receiving the American Association of Neurological Surgeons 2019 Humanitarian Award, and Dr. Rachael Sirianni, who received the UTHealth Women Faculty Forum 2019 Rising Star Award.

We continue our work together to provide the best in clinical care and to advance research. If you would like to learn more about our services, research, and programs, please contact us directly.

With best wishes,



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UTHealth's New Texas Institute for Restorative Neurotechnologies Seeks Cures for Brain Disorders



Functional disorders are characterized by disordered operations of brain networks with minimal or no discernible structural abnormalities. They have an enormous social and economic impact. Epilepsy alone affects more than 3 million Americans.

A new initiative integrates efforts across specialties and schools at UTHealth to advance clinical care for epilepsy and other functional neurological disorders.

The UTHealth Texas Institute for Restorative Neurotechnologies (TIRN) brings together the imagination and energy of three leaders in the fields of neurology, neurosurgery, neuromodulation, and neurodata to create a transformative force whose impact will extend beyond the Texas Medical Center. The Institute's co-directors are neurosurgeon Nitin Tandon, MD, FAANS; neurologist and big-data neuroscientist Samden Lhatoo, MD, FRCP (Lon); and computer scientist GQ Zhang, PhD, who aim to leverage systems of neuroscience, neurotechnology, and neuroinformatics to create a clinical and research institute for the treatment of functional disorders of the brain.

"Functional disorders are characterized by disordered operations of brain networks with minimal or no discernible structural abnormalities. They have an enormous social and economic impact. Epilepsy alone affects more than 3 million Americans," says Tandon. "Similarly, movement disorders, intractable psychiatric illnesses, and chronic pain disorders lead to untold suffering and economic impact. Successful management and treatment of these conditions requires large multidisciplinary teams, but the typical program offered at tertiary centers is made up of fragmented groups of physicians working across departments. What we aim to accomplish at TIRN is to integrate these groups with computational and engineering efforts to develop new insights and technologies."

The Institute is currently focused on epilepsy management. "The new Institute is a key

strategic asset to our university, and will lead to productive collaborations among all six of our schools and with partner institutions across the Texas Medical Center," says UTHealth President Giuseppe N. Colasurdo, MD.

TIRN integrates expertise and research across UTHealth to provide innovative therapies for pharmaco-resistant epilepsy; uses big data to elaborate risk profiles and optimize therapies; provides unique insights into brain function in health and disease; develops neural technologies for brain-machine interfaces; and develops wearable technologies to establish brain-body communication.

"We're harnessing the power of computer science and bioinformatics to enable delivery of precision medical care to patients," says Lhatoo, co-director of TIRN and director of the Texas Comprehensive Epilepsy Program. "We're creating a world-class clinical neural engineering program in conjunction with Rice University, one that will leverage knowledge gained from data-driven approaches, combined with areas of specific clinical need, particularly epilepsy and related functional disorders. We are also working with industry partners to develop wearable technology for patients with Parkinson's disease, autonomic disorders and multiple sclerosis. We're starting off with a strong focus on epilepsy because those are the patients Dr. Tandon and I have worked with the longest. Our long-term goal is to leverage the epilepsy exemplar to find new treatments and possibly even cures for other functional disorders." ■

Neurosurgeon Nitin Tandon, MD, FAANS, and neurologist Samden Lhatoo, MD, FRCP, are harnessing the power of computer science and bioinformatics to deliver precision medical care.



Donna Merrill Finds Freedom from Epilepsy



Donna Merrill in Kuranda, Australia, at Kuranda Koala Gardens and Birdworld

Like every other person diagnosed with epilepsy and managed medically, Donna Merrill dreamed of being drug-free. “People with epilepsy don’t talk about it because of the risk of discrimination,” says Merrill, who is retired and splits her time between Colorado and Georgia. “I worked in special education my entire life, and no one I worked with knew about my epilepsy. My first neurologist advised me not to tell anyone. I don’t believe I would have come as far professionally if people had known.”

Merrill, 66, had two grand mal seizures at the age of 21, just before she started graduate school. The

side effects of her phenobarbital prescription caused her to miss the first three weeks of class. A year later, she suffered a Jacksonian seizure, a type of focal partial seizure caused by unusual electrical activity in a small area of the brain. She thought she was having a stroke.

“It’s a horrible thing to know you have this disorder and can’t come out,” she says. “Even my mother asked me if I was sure it wasn’t my blood sugar, and I didn’t tell my husband I had epilepsy until we were serious. It was a shock for him, but he accepted it. There are people, even in the education field, who still associate epilepsy with mental retardation. I had to think hard before agreeing to this article.”

Later, another neurologist prescribed Dilantin®, which Merrill took for 44 years without a problem. Then in October 2013, she and her husband were reconciling accounts at the small business they own in Fort Collins,

when her right leg suddenly jumped up about four inches from the floor. “I turned to my husband and asked if he saw it,” she recalls. “It jumped up again while he was watching, and then my arm started jerking. Again, I thought I was having a stroke. Epilepsy was way in the back of my mind.”

By the time they reached the ER, her arm was jerking wildly and her signature looked like an EEG. “That really scared me,” she says. “It turned out that my Dilantin level was low, and the MRI showed a large lesion on the left side of my brain.”

Under the care of a Denver neurologist, she learned that the lesion was a mass of capillaries. A neurosurgeon evaluated her and told her that surgery would be too risky.

“We trialed eight different anticonvulsive medications with side effects that ranged from double vision to being so sedated that my husband had to help me walk. I could no longer go to the supermarket without someone accompanying me, because I couldn’t find my way back to the car. It was horrible,” says Merrill, then 62. “Every time I had to go

to Denver to see the doctor, I had to hire a driver because my husband had to work. Our house is in the country, so without the ability to drive, I was living a terribly restricted life.”

She also suffered a loss of identity. “I had worked in special education since 1974,” she says. “I started off teaching and then became an educational diagnostician. Along the way I was a school principal. I was working on a contract with the Wyoming Department of Education. Driving was a requirement, and I had to give up my job.”

Merrill was on five different medications from August to October 2018. “The last one was very costly. I knew I couldn’t live like that and was considering ending my life, but I decided to give it one more try. I went on the internet and looked at clinics around the country. I was impressed with the Texas Comprehensive Epilepsy Program (TCEP) at UTHealth Neurosciences in Houston. Most other centers seemed to be focused on childhood epilepsy, but they had doctors who specialized in adult epilepsy. When you’re in your 60s, you have different needs than a 3-year-old.”

When Merrill called TCEP, they asked if she could come in the following week. “This was the beginning of November 2018, and I was stunned that I could get an appointment so quickly. I wasn’t used to that.”

Around Thanksgiving, the Merrills traveled to Houston, where they met with adult epileptologist Stephen Thompson, MD, director of the Stereotactic SEEG Program, an assistant professor in the Department of Neurology at McGovern Medical School at UTHealth, and an expert in presurgical and invasive evaluation of intractable focal epilepsies.

“Mrs. Merrill had a developmental abnormality on the left frontal lobe, a type of vascular dysplastic lesion that didn’t fall into a clear category,” says Thompson, who changed her medication to lacosamide, which she tolerated with minimal side effects.

In December 2018, she went off her medication and spent five days in the Epilepsy Monitoring Unit at Memorial Hermann-Texas Medical Center. Thompson presented the results of her tests at the

Epilepsy Patient Management Conference. “She was a good candidate for surgery because she had an epilepsy clearly related to the anomaly, an area readily accessible and surgically removable without the risk of significant deficit. Moving forward with surgery was a straightforward decision.”

Nitin Tandon, MD, professor and vice chair in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School and director of epilepsy surgery at Memorial Hermann-Texas Medical Center, operated on Merrill in January 2019. Tandon has performed more than 800 cranial procedures for the localization and treatment of epilepsy and recently performed his 175th robotic SEEG implantation with zero-percent morbidity from the placement of nearly 2,500 electrodes. His track record has made TCEP a world leader in epilepsy surgery.

“No one should have to live with focal epilepsy for decades,” Tandon says. “Because the lesion was in the dominant frontal lobe, neurosurgeons were concerned about operating on her. A vascular lesion around the eloquent cortex does not preclude neurosurgery. We performed an awake craniotomy for Mrs. Merrill to map the lesion and maximize resection without endangering vitally important areas of the brain. Now she can get on with her life.”

Three months later, she and her husband traveled to Australia and New Zealand on vacation. Her six-month follow-up EEG and MRI in Houston in July 2019 were normal.

“My husband said it best: ‘You don’t know high quality until you experience it,’” Merrill says. “I posted on their website that if you don’t have time for research, listen to me and go to Houston. Dr. Tandon will talk to you in terms you understand and make you feel like you’re his most important patient.

“It’s horrible to have epilepsy and not be able to tell anyone,” she says. “So this is my coming out. Houston will be my medical home whether I’m in Colorado or Georgia. It’s worth the trip. If even one person reads this and sees Dr. Thompson and Dr. Tandon, then my job is done.” #

“No one should have to live with focal epilepsy for decades. Because the lesion was in the dominant frontal lobe, neurosurgeons were concerned about operating on her. We performed an awake craniotomy for Mrs. Merrill to map the lesion and maximize resection without endangering vitally important areas of the brain. Now she can get on with her life.”

– Nitin Tandon, MD

Using Our Brains to End Epilepsy



Samden Lhatoo, MD, is the new director of the Texas Comprehensive Epilepsy Program and co-director of the Texas Institute for Restorative Neurotechnologies.

Over the past five years, physicians at the Texas Comprehensive Epilepsy Program (TCEP), a Level 4 National Association of Epilepsy Centers-certified center, have offered patients new, minimally invasive surgical treatments and seen rapid growth in volumes of both medically and surgically treated patients. This is good news for the 3 to 4 million Americans who live with epilepsy.

TCEP is a collaboration among UTHealth Neurosciences, McGovern Medical School at UTHealth, and Mischer Neuroscience Institute at Memorial Hermann-Texas Medical Center. At its heart is a state-of-the-art seven-bed adult Epilepsy Monitoring Unit (EMU) and a six-bed pediatric EMU. The program also houses one of the most experienced magnetoencephalography centers in the nation; together they comprise the largest and most comprehensive monitoring unit of its kind in the region. Now, TCEP is the centerpiece of the newly created UTHealth Texas Institute for Restorative Neurotechnologies, which integrates neuroinformatics and neural engineering into epilepsy care. (See the related article “UTHealth’s New Texas Institute for Restorative Neurotechnologies Seeks Cures for Brain Disorders.”)

“Our goal is to help epilepsy patients gain control of their seizures and regain their quality of life using the most advanced and effective treatment options,” says Samden Lhatoo, MD, FRCP (Lon), the new director of TCEP and co-director of the UTHealth Texas Institute for Restorative Neurotechnologies. “While available anti-seizure medications help the majority of people with epilepsy, about a third receive little or no relief from medical treatment. Many patients with medically

refractory epilepsy are candidates for surgery and can have dramatic relief from their seizures. Dr. Nitin Tandon’s track record has made TCEP a world leader in epilepsy surgery.”

TCEP has evaluated thousands of patients and carried out more than 800 cranial procedures for the localization and treatment of focal epilepsy. In addition to the more conventional procedures of focal cortical resection, lobectomy, hemispherectomy, and corpus callostomy, several new, innovative surgical procedures are available for patients who qualify. Among them is robotic stereoelectroencephalography (SEEG) for 3D investigation of epileptic foci in the brain with stereotactic placement of intracerebral electrodes.

TCEP was the second program in the country to adopt robotic SEEG, and more than 175 robotic SEEG implantations have been performed so far with a zero-percent morbidity from the placement of nearly 2,500 electrodes. (See the related article “Landmark UTHealth Study Shows That Intracranial Evaluation With SEEG Is Safer and Produces Better Outcomes Than SDE.”)

“We are also a pioneering site for MRI-guided laser interstitial therapy (MRIgLITT) using the Visualase® system,” says Tandon, professor and vice chair in the Vivian L.

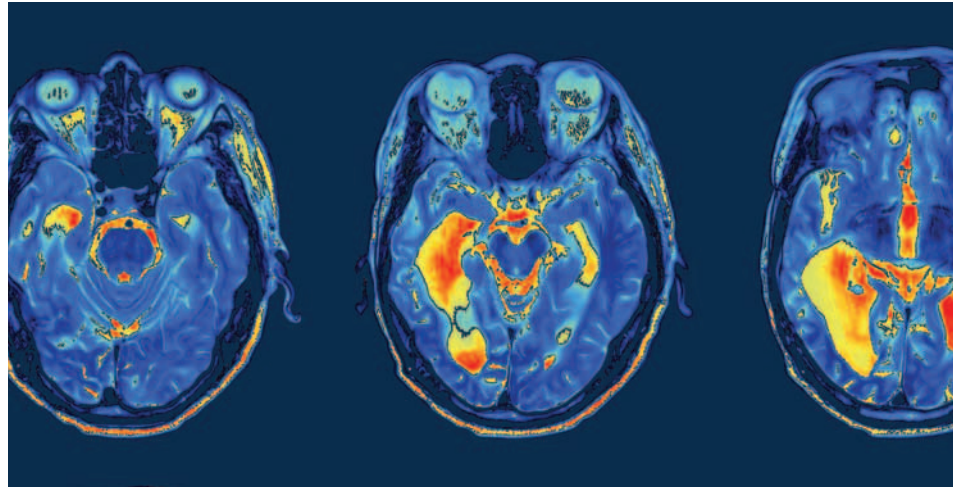
Smith Department of Neurosurgery at McGovern Medical School and director of the epilepsy surgery program at UTHealth Neurosciences. “We offer this minimally invasive procedure, known as laser ablation, to patients who have well-delineated focal epilepsy. We are also applying a combination of SEEG and laser ablation to a particularly challenging type of epilepsy – periventricular nodular heterotopia.”

Before the laser ablation procedure, the epileptogenic focus is precisely located using high-resolution MRI and robotically implanted SEEG electrodes. The TCEP neurophysiologists analyze and pinpoint seizure-causing brain tissue, which then becomes the target for ablation. During the procedure, a 3.2-millimeter hole is drilled in the skull using either a stereotactic frame or stereotactic robot to achieve the best trajectory for the laser beam. The laser applicator is inserted through the drill hole into the target region. After the applicator has been positioned, the patient is placed in an MRI scanner. The abnormal tissue in the epileptogenic zone is destroyed by elevating the laser beam to a very high temperature while minimizing the risk of potential damage to healthy tissue. Real-time MRI imaging allows the surgeon to confirm the results immediately. Most patients are hospitalized for 24 hours and go home the day after the procedure.

Neurosurgeons at the TCEP use the ROSA® robot to ensure precision during epilepsy surgery. ROSA acts as a kind of GPS for the skull, allowing physicians to create 3D maps of the brain and plan the best approach to implant depth electrodes during stereoencephalography, place probes for laser ablation, or perform brain biopsies. Surgery with ROSA is minimally invasive, allowing surgeons to use needle-thin instruments inserted through a tiny hole, which means a shorter surgery and faster recovery.

If testing in the EMU does not locate a single epileptogenic focus, or if patients have uncontrolled seizures and are not candidates for brain surgery, they may benefit from responsive neurostimulation therapy (RNS), deep brain

stimulation (DBS), or vagus nerve stimulation (VNS). Responsive neurostimulation therapy with the NeuroPace RNS® System is offered to certain patients who cannot be treated by conventional or laser surgery. A device is implanted in the skull and connected to two electrodes that target the hippocampus. The NeuroPace System detects abnormal brain activity and delivers stimulation that interrupts the signal and helps control seizures.



Some patients are candidates for deep brain stimulation, which alters brain activity just enough to prevent or limit the spread of a seizure. Neurosurgeons implant electrodes in the anterior nucleus of the thalamus to moderate seizures that are hard to localize because they originate in multiple regions of the brain. Medtronic’s system for DBS was approved by the U.S. Food and Drug Administration in 2018 for use in adults with medically refractory focal epilepsy. Research continues to improve neurostimulation therapies for epilepsy.

The TCEP team goes beyond medical and surgical treatment of epilepsy to offer general support via a network of community counselors who help people cope with the psychosocial and emotional aspects of their condition. An active patient support group, overseen by physicians, a specialist nurse, and coordinating administrative staff, meets every month at UTHealth Neurosciences in the Texas Medical Center. 🧩

The Texas Comprehensive Epilepsy Program has evaluated thousands of patients and carried out more than 800 cranial procedures for the localization and treatment of focal epilepsy.

For more information or to refer a patient, call 713-486-7760.

Landmark UTHealth Study Shows That Intracranial Evaluation With SEEG Is Safer and Produces Better Outcomes Than SDE

“If patients are refractory to three medications or, just as commonly, unable to tolerate the doses that will control their seizures without losing their vocational or family life, they should be referred to a specialized epilepsy surgery center. In that way all options are laid out early, and patients are in charge of deciding when and if they want to move on beyond medications.”

– Nitin Tandon, MD

The use of minimally invasive stereoelectroencephalography (SEEG) to determine whether patients with drug-resistant epilepsy are candidates for brain surgery is safer, more efficient, and leads to better outcomes than the traditional approach, according to investigators at McGovern Medical School at UTHealth.

Their landmark study, published online in March 2019 in *JAMA Neurology*,¹ showed that patients who underwent SEEG experienced fewer complications and made quicker, less painful recoveries than patients who underwent craniotomy with subdural electrode (SDE) implantation. The SEEG patients who went on to neurosurgery for epilepsy also were more likely to be seizure-free at one year, compared with those who underwent SDE implantations.

“We expected lower morbidity, less blood product use, less use of pain medications, and an overall better patient experience with SEEG based on our surgical experience, but we were not expecting to see a difference in outcome,” says Nitin Tandon, MD, professor and vice chair in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School, director of the epilepsy surgery program at UTHealth Neurosciences, and the lead author of the article. “These findings give new hope to epilepsy patients who previously may have ruled out surgery for various reasons.”

The retrospective study reviewed the cases of 239 patients with medically refractory epilepsy who underwent a total of 260 procedures between 2004 and 2017 to locate the source of their seizures and determine their suitability for surgery. Of those 260

procedures, 139 cases were traditional SDEs, which require a large craniotomy. A sheet of electrodes is placed on the surface of the brain to pinpoint the origin of the seizures, and the skull is closed for an observation period, usually a week to 10 days. If the seizure focus is identified, surgery to resect it is done immediately following the observation period to avoid a second craniotomy.

Another 121 cases were performed using robotic SEEG, in which electrodes are implanted via fine probes threaded through small drill holes in the skull, resulting in minimal blood loss and less pain. Patients undergo a similar observation period. Following electrode removal, patients are typically discharged from the hospital. If they are candidates for surgery, they will return in a few weeks for surgery for resection or laser ablation of the seizure focus.

Of the patients who underwent resection or laser ablation to remove the lesion causing their seizures, 76% of SEEG cases were either free of disabling seizures or had them rarely at the one-year mark, compared to 55% of SDE cases. The minimally invasive technique also produced more favorable outcomes among patients with nonlesional epilepsy, for which surgery tends to be less successful. Nearly 7 of 10 SEEG cases (69.2%) had good outcomes at the one-year mark compared to just over a third (34.6%) of SDE cases. A greater propor-

tion of SEEG cases were nonlesional epilepsy – 56.2% as opposed to 28.8% of SDE cases.

“This makes the case for SEEG even stronger,” Tandon says. “There are three reasons why it can achieve better results. First, the technique doesn’t constrain where the electrodes can be implanted, enabling us to study brain networks in a much more comprehensive fashion to pinpoint the seizure sources. Second, SEEG allows for precise targeting of deeper structures, which makes it better at localizing the epilepsy focus in many patients. Third, the absence of time pressure to evaluate the test results, and the fact that no craniotomy has been done, allows us to select patients likely to do well, fully consider various options, and implement the optimal surgical plan. We also have a much better opportunity to discuss the data with patients and engage them in discussion of scenarios that might emerge from either resection or laser ablation.”

In addition, results showed that SEEG patients required significantly less narcotic medication than SDE patients. Results also showed the minimally invasive procedure was more than twice as fast, with the average time in surgery at just over two hours for SEEG cases, compared to more than five hours for SDE cases.

This is good news for the vast numbers of undertreated patients with epilepsy who are candidates for surgery. “Patients with drug-resistant epilepsy constitute approximately one-third of the population with epilepsy, and this population has a high incidence of accidental injury, seizure activity for 30 minutes or more, and sudden unexpected death,” Tandon says. “Less than 10% of those eligible undergo surgery. Many have been discouraged by the invasiveness of subdural electrode implantation. SEEG is much less invasive and better tolerated by patients. In the study we showed a 6% risk of complications with SDE, and no complications with SEEG.”

The transition from SDE to SEEG at UTHealth Neurosciences was incremental and allowed for comparative analysis of outcomes using the two techniques. “Initially

we used SEEG mostly in patients with deep lesions or those who had previous surgery, and in bilateral cases, which are challenging for subdural electrode implantation,” he says. “With the availability of robotic technology, we switched from performing mainly SDE evaluations to SEEG in 2013. We were seeing a distinct difference in the patient experience. Today we’re using SDE to evaluate neocortical epilepsy located around eloquent cortex and in young children, whose skulls are too thin to hold the anchor bolts for SEEG.”

When should a general neurologist consider referring a patient to a tertiary or quaternary epilepsy center? “Stopping the seizures is always the goal. If that goal is not met, we should leave no stone unturned,” Tandon says. “If patients are refractory to three medications or, just as commonly, unable to tolerate the doses that will control their seizures without losing their vocational or family life, they should be referred to a specialized epilepsy surgery center,” he says. “In that way all options are laid out early, and patients are in charge of deciding when and if they want to move on beyond medications.”

SEEG has moved epilepsy surgery to a better place. As the second group in the U.S. to have a robot for SEEG, UTHealth Neurosciences has been at the forefront of the journey, using robotics for minimally invasive techniques that are much better tolerated by patients and more likely to be effective. The procedure can also be performed without robotic assistance.

“We hope these findings give more patients whose epilepsy cannot be controlled by medication the confidence to consider surgery, and also help other institutions transition more quickly to providing this minimally invasive procedure,” Tandon says.

UTHealth coauthors of the study were Brian Tong, a third-year medical student who played a crucial role in data compilation and analysis; Elliott Friedman, MD, neuroradiologist; Jessica Johnson, BSN, epilepsy nurse practitioner; and neurologists Giridhar Kalamangalam, MD, DPhil; Stephen Thompson, MD; Gretchen Von Allmen, MD; Melissa Thomas, MD; Omotola Hope, MD; and Jeremy Slater, MD. ■

¹Tandon N, Tong BA, Friedman ER, Johnson JA, Von Allmen G, Thomas MS, Hope OA, Kalamangalam GP, Slater JD, Thompson SA. Analysis of Morbidity and Outcomes Associated With Use of Subdural Grids vs Stereoelectroencephalography in Patients with Intractable Epilepsy. *JAMA Neurology*. 2019 Jun 1;76(6). doi: 10.1001/jamaneurol.2019.0098.

Research and Innovation at McGovern Medical School at UTHealth

Physicians affiliated with UTHealth Neurosciences and McGovern Medical School are engaged in a broad and intensive research program focused on the mechanisms, treatment, and cure of neurological disease and injury.

“We take a lot of pride in this trial because it represents more than 10 years of work. Testing MultiStem in our lab in an animal model helped us understand how some types of cell-based therapies work, and it also advanced our understanding of the mechanism of moderating the inflammatory response after stroke.”

– Sean Savitz, MD

They use diverse approaches – molecular, transgenic, and electrophysiological techniques – in biomedical studies, translational research, clinical trials, and technology development and assessment.

“Most of our faculty do some sort of research, whether it’s basic, translational in animal models, or transitioning into human research with clinical trials,” says Louise McCullough, MD, PhD, professor and chair of the Department of Neurology at McGovern Medical School and co-director of the Mischer Neuroscience Institute at Memorial Hermann-Texas Medical Center. “We’re pushing the envelope and discovering new knowledge about stroke, cognitive disorders, epilepsy, and other neurological disorders with high rates of support from the National Institutes of Health and foundations.”

Research funding for the Department of Neurology for the 2019-20 academic year exceeds \$28.5 million, including grants and contracts. Neurology research has been expanded with the creation of the Institute for Stroke and Cerebrovascular Disease at UTHealth, directed by Sean Savitz, MD, professor and Frank M. Yatsu, MD, Chair in Neurology.

Research funding for the Vivian L. Smith Department of Neurosurgery is more than \$17.4 million for the 2019-20 academic year, including grants and contracts. “We’re a young department with enormous growth over the past few years,” says Balveen Kaur,

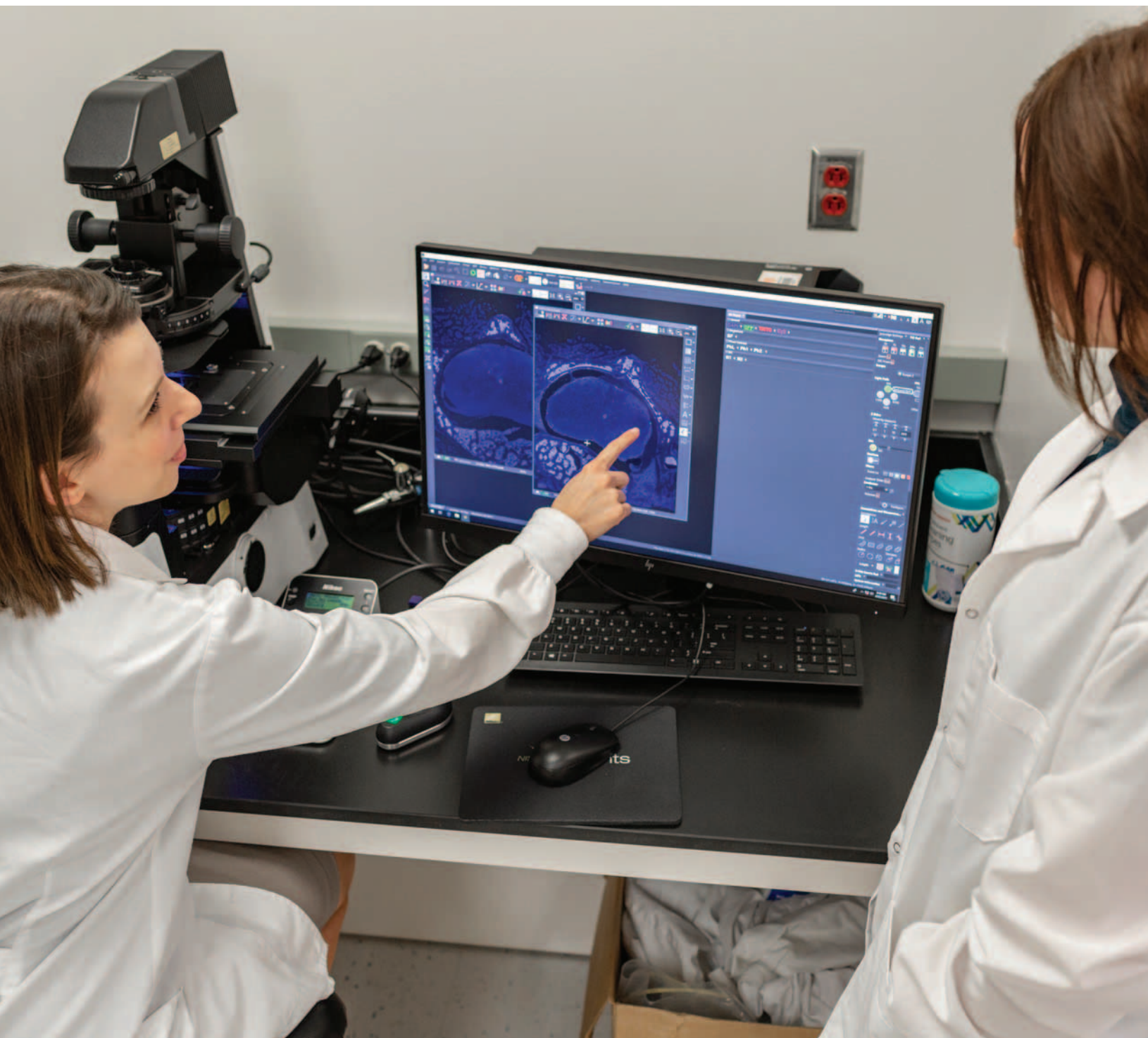
PhD, professor, vice chair for research, and John P. and Kathrine G. McGovern Distinguished Chair in the Vivian L. Smith Department of Neurosurgery. “Our goal is to increase our efforts to grow translational and basic research to reduce the burden of neurological disease.”

Department of Neurosurgery Ranks 8th in NIH Funding Among US Clinical Science Departments

Last year (2019), the Vivian L. Smith Department of Neurosurgery was ranked No. 8 nationally in research funding awarded by the National Institutes of Health to neurosurgery departments (Source: Blue Ridge Institute for Medical Research). All data are derived from the NIH Research Portfolio Online Reporting Tools. Individual researchers in both the Department of Neurology and the Vivian L. Smith Department of Neurosurgery are also highly ranked in the listing.

Claudio Soto, PhD, the Huffington Foundation Distinguished Chair in Neurology, is ranked No. 6 among principal investigators of NIH-funded clinical science research studies in neurology. Soto is professor of neurology and director of the George and Cynthia Mitchell Center for Alzheimer’s Disease and Related Brain Disorders at McGovern Medical School at UTHealth. His research laboratory is investigating the molecular basis of neurodegenerative diseases associated with the

*Rachael Sirianni, PhD,
in her lab.*





Researchers and physicians at McGovern Medical School at use diverse approaches in biomedical studies, translational research, clinical trials, and technology development and assessment to discover new treatments for neurological disorders.

misfolding and brain accumulation of proteins, particularly in Alzheimer's disease, Parkinson's disease, and prion-related disorders. The lab's work includes basic science projects as well as translational research aimed at the development of novel strategies for treatment and diagnosis of these diseases.

Georgene Hergenroeder, PhD, associate professor in the Vivian L. Smith Department of Neurosurgery and director of the Innovation and Quality (IQ) Program at UTHealth Neurosciences, was ranked No. 7 in NIH funding for all neurosurgery research funding. Hergenroeder's primary research interests center on improving patient outcomes after spinal cord and brain injury. Her focus is on biomarker discovery aimed at predicting which patients may benefit from future intervention, and discovery of potential new targeted treatments, including identifying factors associated with the development of neuropathic pain after spinal cord injury (SCI). SCI-induced disruption of the blood-

spinal cord barrier can cause the immune system to elicit an IgG response against central nervous system proteins. Her laboratory aims to identify autoantibodies contributing to neuropathic pain.

Pivotal Adult Stem Cell Trial for Stroke Underway at UTHealth

Researchers led by Sean Savitz, MD, are testing a human bone marrow stem cell product to determine if it improves recovery after stroke. The Phase III study, titled MultiStem Administration for Stroke Treatment and Enhanced Recovery Study-2 (MASTERS-2), is evaluating MultiStem® cell therapy treatment of patients who have suffered an ischemic stroke.

Over the past decade, Savitz has researched both autologous stem cells and allogeneic stem cell products. He conducted and published early preclinical studies of MultiStem and has enrolled the first UTHealth patients in MASTERS-2.

"We take a lot of pride in this trial because

it represents more than 10 years of work,” says Savitz, director of the Institute for Stroke and Cerebrovascular Disease and professor of neurology at McGovern Medical School at UTHealth. “Testing MultiStem in our lab in an animal model helped us understand how some types of cell-based therapies work, and it also advanced our understanding of the mechanism of moderating the inflammatory response after stroke. Phase II clinical trials have shown it to be safe and effective for neurologic improvement and protection of the brain after stroke. MASTERS-2 is a definitive efficacy study, and we hope to determine if the product truly benefits patients.”

The Phase III clinical trial, sponsored by Athersys, will enroll 300 patients in North America and Europe who have suffered moderate to moderate-severe ischemic stroke. Within 18 to 36 hours of stroke, study participants will receive either a single intravenous dose of MultiStem cell therapy or placebo, in addition to standard of care. Follow-up after infusion is 12 months. The primary endpoint will evaluate disability scores at three months.

“Stroke is a leading cause of death and serious disability worldwide,” Savitz says. “Currently therapies for ischemic stroke are limited to the clot-dissolving agent tPA and surgical intervention to remove the clot. Both must be administered within several hours of the stroke. With this limited time window, only a small percentage of stroke victims receive treatment with these therapies, and most end up receiving supportive care. The long-term costs of stroke include extended hospitalization, extended physical therapy, or rehabilitation, and many require long-term institutional or family care. We hope the results of this trial provide a new treatment option for many more patients.”

Scientists Engineer a Virus to Kill Brain Cancer

Investigator Balveen Kaur, PhD, and her team at McGovern Medical School at UTHealth have modified the herpes simplex virus type 1 to express a gene that activates cancer-killing T-cells. The virus proved effective in

fighting brain tumors in preclinical studies, reported the scientists in the journal *Nature Communications*.¹

“Brain malignancies are difficult to treat because they disarm the body’s natural defenses,” says Kaur, professor and John P. and Kathrine G. McGovern Distinguished Chair and vice chair for research in the Vivian L. Smith Department of Neurosurgery. “In the lab, we’ve developed a way to boost the body’s anti-cancer immunity using a modified version of the herpes simplex virus known to cause cold sores. The gene it expresses is frequently absent or mutated in tumors and its reconstruction enhances anti-cancer immunity.”

The researchers tested their modified virus in a mouse model of brain cancer and reported a cure rate of 40%. The virus also imparted protective immunity against a subsequent tumor challenge.

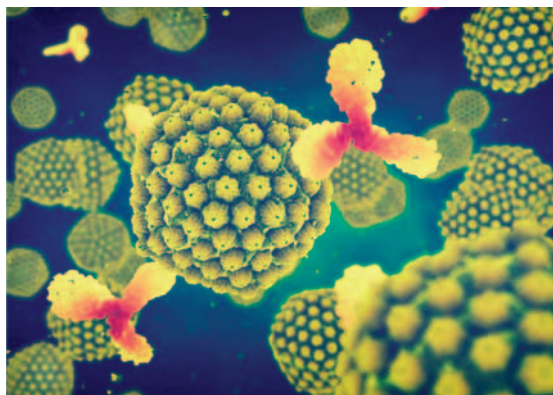
“Therapeutic viruses can destroy cancer without affecting normal tissue,” says Kaur, the study’s senior author. “A therapeutic virus has already been approved for use in patients with skin cancer. Arming these viruses with genes has the potential to enhance therapy.”

In this case, the investigators engineered herpes simplex type 1 to express a gene, PTEN, that triggers the body’s immune response. The authors reported, “Harnessing viruses as vehicles for gene transfer payloads to boost their anti-tumor efficacy is one way to improve the therapeutic index. Here we sought to boost both the anti-cancer and immune stimulating properties of an oncolytic (engineered herpes) virus through the addition of tumor suppressor gene PTEN.”

Kaur says that additional safety testing

“Brain malignancies are difficult to treat because they disarm the body’s natural defenses. In the lab, we’ve developed a way to boost the body’s anti-cancer immunity using a modified version of the herpes simplex virus known to cause cold sores. The gene it expresses is frequently absent or mutated in tumors and its reconstruction enhances anti-cancer immunity.”

– Balveen Kaur, PhD



Researchers at McGovern Medical School have boosted the body’s anti-cancer immunity using a modified version of the herpes simplex virus.

“Our latest research shows that the α Syn aggregates of PD and MSA have different properties, so by amplifying the abnormal aggregates we can detect with high efficiency which disease the patient has. This has huge implications for clinical care of the patient, and the development of new specific treatments for both diseases.”

– Claudio Soto, PhD

in animal models will be needed before the therapy can be made available to patients through clinical trials.

The study, titled “PTEN Expression by an Oncolytic Herpesvirus Directs T-Cell Mediated Tumor Clearance,” was supported by the National Cancer Institute and the National Institute of Neurological Disorders and Stroke, part of the National Institutes of Health. UTHHealth research team members who participated in the study include co-lead author Jessica Swanner, PhD; Yeshavanth Banasavadi-Siddegowda, PhD; Ji Young Yoo, PhD; and Bangxing Hong, PhD.

¹Russell L, Swanner J, Jaime-Ramirez AC, Wang Y, Sprague A, Banasavadi-Siddegowda Y, Yoo JY, Sizemore GM, Kladney R, Zhang J, Lehman NL, Ostrowski MC, Hong B, Caligiuri M, Yu J, Kaur B. PTEN expression by an oncolytic herpesvirus directs T-cell mediated tumor clearance. *Nat Commun.* 2018 Nov 27;9(1):5006. doi: 10.1038/s41467-018-07344-1.

Researcher’s Technology Differentiates Between Parkinson’s Disease and Multiple System Atrophy

Scientists have found a way to distinguish between two progressive neurodegenerative diseases, Parkinson’s disease (PD) and multiple system atrophy (MSA), using a technology developed at McGovern Medical School at UTHHealth. The discovery, which could allow doctors a look into the future to help select the right treatment, was published in February in *Nature*.²

“It is challenging to distinguish between the two diseases because the early signs are similar – disturbances in movement, tremors, uncontrollable movements during sleep, impaired speech, etc. – but the two diseases progress differently and require distinctive treatment plans,” says Claudio Soto, PhD, professor in the Department of Neurology at McGovern Medical School, director of the George and Cynthia W. Mitchell Center for Alzheimer’s Disease and Other Brain-Related Illnesses, and senior author of the article. “Physicians need an objective way to differentiate between PD and MSA to provide patients with the best care. Currently we differentiate them by watching how the disease progresses. By the time people show

progressed symptoms of MSA, which advances more rapidly than PD, a substantial amount of brain cells are already damaged or dead, and they can’t be brought back. It has been difficult to develop treatments for both diseases because of the high rates of misdiagnosis, so we had to find a way to distinguish between the two at the onset of early symptoms.”

Both diseases are characterized by deposits of a protein known as alpha-synuclein (α Syn) in the nervous system. The protein can change shape in a process called misfolding. Misfolded proteins clump together and poison surrounding healthy nerve cells responsible for brain functioning, particularly motor skills.

“These misfolded clumps can form for many years, even decades, before doing enough damage that a person shows signs of motor impairment,” Soto says.

Soto developed Protein Misfolding Cyclic Amplification (PMCA) technology, shown in previous studies to detect misfolded proteins associated with diseases such as Creutzfeldt-Jakob and Alzheimer’s disease, after targeting misfolded α Syn aggregates as a way of developing a sensitive biochemical diagnosis for PD. His latest research in *Nature* shows that the α Syn-PMCA can successfully discriminate between PD and MSA with an overall sensitivity of 95.4%, which gives doctors more information about the disease they need to address. The study also helps to understand the basis of these diseases at the molecular level.

“Our latest research shows that the α Syn aggregates of PD and MSA have different properties, so by amplifying the abnormal aggregates we can detect with high efficiency which disease the patient has,” Soto says. “This has huge implications for clinical care of the patient, and the development of new specific treatments for both diseases. Since cerebrospinal fluid is collected through spinal taps, the hope is that future research would enable optimization of the PMCA test to detect α Syn in blood or urine.

“I envision a world without these diseases, but the only way to achieve that is to couple early diagnosis with good and safe treatment,” he adds. “That means we have to detect the

abnormal proteins before they produce diseases and use safe preventive treatment. Many diseases like smallpox, diphtheria, and polio have been eliminated by scientific advances. I hope the same will happen with devastating brain diseases, like Alzheimer's and Parkinson's."

The research was funded in part by grants from the Michael J. Fox Foundation for Parkinson's Research and the National Institute on Aging. Soto is an inventor of patented PMCA technology and is the co-founder and chief scientific officer of Amprion, Inc., a biotech company focusing on the commercial utilization of PMCA for early diagnosis of Parkinson's, Alzheimer's and other neurodegenerative diseases. Soto and Mohammad Shah Nawaz, PhD, assistant professor in neurology, are the inventors of patented technology on the use of α Syn-PMCA for PD diagnosis.

The U.S. Food and Drug Administration has granted a Breakthrough Devices designation to Amprion's proprietary technology PMCA for its potential to diagnose Parkinson's disease at a much earlier stage than current diagnostic methods.

²Shah Nawaz M, Mukherjee A, Pritzkow S, Mendez N, Rabadia P, Liu X, Hu B, Schmeichel A, Singer W, Wu G, Tsai A-L, Shirani H, Nilsson KPR, Low PA, Soto C. *Discriminating α -synuclein strains in Parkinson's disease and multiple system atrophy.* *Nature.* 2020;578:pp. 273-277.

Nanotechnology for Drug Delivery: The Science of Moving Chemotherapeutic Drugs Directly to Brain Tumors

Only a very small amount of the chemotherapeutic drugs given systemically for the treatment of pediatric brain tumors actually reaches the brain, due to the blood-brain barrier's efficiency at excluding the entry of most agents that circulate in the blood. As a result, the current outlook for children with recurrent malignant brain tumors is extremely poor. Most clinical trials offer systemic chemotherapy or radiation therapy, both of which have side effects and often fail in children with recurrent tumors. Bioengineer and research scientist Rachael Sirianni, PhD, aims to change that by bringing novel nanomedicine approaches to the clinic to improve outcomes.

"There are many drugs available to treat

brain tumors, but most don't go directly to the site where they provide the most benefit," says Sirianni, an assistant professor in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth and faculty member of MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences. "My science is the science of drug delivery, and understanding ways to circumvent these barriers."

Sirianni and her team encapsulate drugs within biocompatible and biodegradable nanoparticles, which serve as carriers to prolong drug action and target specific tissue sites. "Early on, scientists discovered that nanoparticles have the capability to slide in between the spaces of the tumor's vasculature, such that they selectively accumulate within the tumor," she says. "This enhanced permeation retention enables nanoparticles to deliver encapsulated drugs preferentially to large tumors that are highly vascularized. However, there are some kinds of tumors and parts of tumors that do not receive a good blood supply. Delivery to these kinds of tumors remains a major challenge."

To address this challenge, Sirianni and her team are working on novel approaches. "Pediatric brain tumors have a tendency to metastasize along the surfaces of the brain and spinal cord. This is called leptomeningeal metastasis, and it remains very difficult to treat," she says. "Instead of delivering nanoparticles intravenously, we're working toward administering them directly to the cerebrospinal fluid that moves across these lesions to deliver more drug with less overall toxicity. Currently we're focused on engineering nanoparticles to possess the right properties to accumulate selectively within these metastatic lesions."

Because the polymers her laboratory uses are nontoxic and readily cleared by the body, degrading over weeks to months, there is potential to design new, safer chemotherapy for patients.

In May 2019 Sirianni was awarded a five-year, \$2.7 million R01 grant by the National Institute of Neurological Disorders and Stroke to tackle exactly this problem: designing nanoparticles that can target drug delivery to

"Early on, scientists discovered that nanoparticles have the capability to slide in between the spaces of the tumor's vasculature, such that they selectively accumulate within the tumor. This enhanced permeation retention enables nanoparticles to deliver encapsulated drugs preferentially to large tumors that are highly vascularized."

– Rachael Sirianni, PhD

leptomeningeal metastasis in pediatric medulloblastoma. Her laboratory will evaluate the safety and efficacy of these new approaches, as well as test whether delivery of drugs from nanoparticles can reduce the radiation dose needed to treat metastases.

In July, Sirianni received a second five-year, \$4.5 million R01 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development to study intrathecal delivery of radiation-sensitizing nanoparticles in pediatric neuro-oncology.

“High-dose craniospinal radiation damages a child’s developing nervous system, and few other treatment options are available once malignant cells have metastasized to the leptomeninges,” she says. “Our preliminary data demonstrate that intrathecally administered histone deacetylase inhibitor quisinostat distributes readily across brain and spinal cord surfaces and localizes to slow the growth of leptomeningeal metastasis in medulloblastoma. We expect these studies to advance new nanotechnology toward the clinic for better treatment of pediatric brain tumors.”

Researchers Study the Relationship of Haptoglobin to the Delayed Effects of Subarachnoid Hemorrhage

In the laboratory of Spiros Blackburn, MD, researchers are advancing their understanding of the role of haptoglobin – a hemoglobin-binding protein produced by the liver in larger quantities during injury, infection, or inflammation – in aneurysmal subarachnoid hemorrhage (SAH). Their goal is to predict which patients are likely to suffer late effects of SAH.

“FDA-approved medications are available to treat people who suffer delayed effects of subarachnoid hemorrhage,” says Blackburn, an associate professor in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth. “But for a drug to be effective, we have to prescribe it to the right patients.”

Of the 35,000 people who have ruptured brain aneurysms each year across the U.S., 30% to 40% will not survive. Those who live

face a spectrum of recovery. Some do well and return to work. Others suffer late effects of SAH including neurological deterioration, stroke, or other long-term neurological problems.

Once a brain aneurysm has ruptured, surgery is required to prevent subsequent episodes of bleeding. Even after the aneurysm is repaired, the initial bleeding into the space surrounding the brain can reduce normal blood flow and lead to tissue ischemia and tissue death. Haptoglobin (Hp) may have a role in facilitating the clearance of blood in the brain and reducing the risk of tissue death. Blackburn and his team are investigating the correlation between the haptoglobin genotype, hypercoagulability, and inflammatory biomarkers after SAH.

In a paper published last year in *Frontiers in Physiology*, he and other authors reported that much of the risk of significant morbidity and neurological deficit following SAH are related to blood in the subarachnoid space, which induces an “inflammatory cascade with numerous downstream consequences.”³

“Recent clinical trials have not been able to reduce the toxic effects of free hemoglobin or improve clinical outcomes because of our inability to identify patients at high risk for neurologic decline,” Blackburn says. “The haptoglobin 2-2 genotype has been identified as a factor in diabetes, sickle cell, and cardiovascular disease that contributes to increased complications. Clinical studies in patients with SAH have shown that Hp 2-2 patients may be at high risk for hemorrhage-related complications and poor outcomes.”

With nearly \$1 million in funding from the National Institutes of Health, the Blackburn laboratory is using human biological samples to validate haptoglobin as a predictor of clinical outcome after SAH, and correlating this with clot formation and cerebral inflammation. “Once we’ve discovered aspects of coagulation and inflammation that can be modified, we can test these pathways in animal models. Eventually we will be able to take a drug to clinical trials in the hope of saving lives and reducing disability,” he says.

“FDA-approved medications are available to treat people who suffer delayed effects of subarachnoid hemorrhage, but for a drug to be effective, we have to prescribe it to the right patients.”

–Spiros Blackburn, MD

³Blackburn SL, Kumar PT, McBride D, Zeineddine HA, Lelerc J, Choi HA, Dash PK, Grotta J, Aronowski J, Cardenas JC, Doré S. Unique Contribution of Haptoglobin and Haptoglobin Genotype in Aneurysmal Subarachnoid Hemorrhage. *Front Physiol.* 2018 May 32;9:592. doi:10.3389/fphys.2018.00592. eCollection 2018.

Ensuring That Patients at Community Hospitals Benefit from Lifesaving Stroke Treatments

The American Academy of Neurology has awarded Sunil Sheth, MD, assistant professor in the Department of Neurology at McGovern Medical School at UTHealth, the Clinician-Scientist Development Award in Interventional Neurology. The three-year award, funded by the American Brain Foundation and the Society of Vascular and Interventional Neurology, is designed to support a clinician-scientist's research related to interventional neurology, and consists of an annual salary of \$75,000 plus a \$5,000 per year stipend to support education and research-related costs. Sheth will be using the funds to research stroke treatments.

"While treatments that remove blood clots with minimally invasive techniques were initially reserved for stroke victims who could be treated within six hours of their symptoms, two research studies have shown that for select groups of patients, these treatments remain highly beneficial even 24 hours later," Sheth says. "The brain imaging techniques and analysis technologies used in these studies, however, are currently available only in large referral hospitals, meaning that the majority of patients won't have access to these treatments at their local hospitals."

Sheth's project will define how patient characteristics and brain imaging techniques that are widely available at hospitals across the country can perform just as well as the advanced techniques used in those two studies. "The goal of my work is to ensure that everyone who might benefit from these lifesaving stroke treatments gets a fair shot," he says. "Receiving this award was an absolute honor. The support that comes with it will allow me to work toward accomplishing what I have always wanted to do – identify ways to improve the lives of patients suffering from stroke."

Sedation Versus General Anesthesia for Endovascular Therapy in Acute Ischemic Stroke (SEGA)

Does modality of anesthesia influence outcomes in intra-arterial thrombectomy for the treatment of acute stroke? P. Roc Chen, MD, an associate professor in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth, is lead investigator in a multicenter study. The researchers aim to determine whether there is a difference in overall improvement in acute ischemic stroke patients randomized to general anesthesia compared with sedation during endovascular therapy. The study will also assess safety, rates of endovascular therapy procedural complications and reperfusion, as well as quality of life.

"Stroke treatment has improved dramatically, but the percentage of patients who have good outcomes remains smaller than we would like," Chen says. "While endovascular therapy with stent retrievers has been shown to improve outcomes in acute stroke patients, there is still controversy about the best type of anesthesia to be used during treatment: general anesthesia or conscious sedation. Both sedation and anesthesia are considered to be routine care although no randomized study has proven that one or the other produces better outcomes."

Chen says a retrospective data search suggests that conscious sedation is associated with a better outcome, shorter hospital and ICU stays, and fewer pulmonary complications in comparison with general anesthesia. "Many stroke centers in the United States, Europe, and Asia have

"While endovascular therapy with stent retrievers has been shown to improve outcomes in acute stroke patients, there is still controversy about the best type of anesthesia to be used during treatment: general anesthesia or conscious sedation. Both sedation and anesthesia are considered to be routine care although no randomized study has proven that one or the other produces better outcomes."

—P. Roc Chen, MD



Roc Chen, MD, is lead investigator in a multicenter study of outcomes in acute ischemic stroke patients randomized to general anesthesia versus sedation during endovascular therapy.

“This tradition of training residents who transform the care of neurological illnesses can be maintained only if we produce physician scientists for the next generation. The NINDS R25 grant will transform our training program, as well as propel faculty engagement in research. It’s an investment in training the future generation that will produce rewards over many decades.”

—Nitín Tandon, MD

shifted their practice to conscious sedation for intra-arterial thrombectomy,” he says. But undergoing intra-arterial thrombectomy with conscious sedation is stressful for most patients, especially with their impaired neurological function. General anesthesia would provide greater comfort. We expect the SEGA study to provide us with more information about which type of anesthesia is the better option, which may lead to a new treatment paradigm.”

The trial, called SEGA, is funded by the Weatherhead Foundation and supported in part by a Stryker Neurovascular research grant. It began in fall 2017 with an expected completion date of early 2021. Researchers plan to enroll 260 patients, with half randomized to general anesthesia and half to conscious sedation.

Ten comprehensive centers across the U.S. are participating in the UTHealth-led study. Co-principal investigators and steering committee members at McGovern Medical School are Andrew Barreto, MD, associate professor of neurology; Carlos Artime, MD, associate professor of anesthesiology; Sunil Sheth, MD, assistant professor of neurology; and Claudia Pedroza, PhD, associate professor of pediatrics.

UTHealth Receives NINDS Research Training Grant for Neurology and Neurosurgery Residents and Fellows


The Vivian L. Smith Department of Neurosurgery and the Department of Neurology at McGovern Medical School at UTHealth have joined the elite group of American neurosurgery and neurology programs offering residents and fellows protected research time during residency and fellowship, thanks to an R25 Research Education Program grant from the National Institute of Neurological Disorders and Stroke (NINDS).

“Neurosurgery has a long and storied tradition of basic and translational research leading to innovation,” says Nitín Tandon, MD, professor and vice chair in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School, director of epilepsy surgery at UTHealth Neurosciences, co-director of

UTHealth’s Texas Institute for Restorative Neurotechnologies (TIRN), and co-director of the R25 training program. “This tradition of training residents who transform the care of neurological illnesses can be maintained only if we produce physician scientists for the next generation. The NINDS R25 grant will transform our training program, as well as propel faculty engagement in research. It’s an investment in training the future generation that will produce rewards over many decades.”

Only 24 teaching institutions in the U.S. have active R25 training programs in the clinical neurosciences. “R25 grants attract the best and brightest, and create future physician scientists to conduct basic and translational research on the mechanisms, cure, and treatment of neurological disorders,” says Samden Lhatoo, MD, FRCP (Lon), John P. and Kathrine G. McGovern Distinguished Chair, director of the Texas Comprehensive Epilepsy Program at McGovern Medical School, co-director of the TIRN, and co-director of the R25 grant. “The grants support creative educational activities with a focus on research experiences that help develop physicians as research scientists. These experiences prepare clinicians to compete successfully for individual National Institutes of Health-mentored career development awards or independent research awards.”

Only one application per medical school or sponsoring institution is considered for funding each academic year. In addition to protected research time and resources, residents and fellows accepted to the program will have access to faculty across three departments at McGovern Medical School: the Department of Neurology, the Vivian L. Smith Department of Neurosurgery and the Department of Anatomy and Neurobiology.

“This is a great opportunity for young physicians who want to be clinician scientists and aspire to top-level National Institutes of Health and National Science Foundation funding,” says Tandon. “It pays for 80% of their clinical time to carry out research and prepare for career award grants that they will continue to pursue as future faculty members.” 

Epilepsy Expert Dr. Samden Lhatoo and Data Scientist Dr. GQ Zhang Join UTHealth Neurosciences



Samden Lhatoo, MD, FRCP (Lon)

Co-Director, Texas Institute for Restorative Neurotechnologies

Director, Texas Comprehensive Epilepsy Program

Professor and John P. and Kathrine G. McGovern Distinguished Chair, Department of Neurology

McGovern Medical School at UTHealth

Internationally renowned neurologist Samden Lhatoo, MD, FRCP (Lon), has joined McGovern Medical School at UTHealth as the John P. and Kathrine G. McGovern Distinguished Chair in the Department of Neurology. He is executive vice chair of neurology, director of the Texas Comprehensive Epilepsy Program, and co-director of the new Texas Institute for Restorative Neurotechnologies.

Samden Lhatoo received his initial medical training at the University of Delhi's Maulana Azad Medical College, followed by residency in internal medicine at the Postgraduate Institute of Medical Education and Research in Chandigarh. He obtained his Membership of the Royal College of Physicians in London in 1995. He trained in neurology at the Radcliffe Infirmary in Oxford, Frenchay Hospital in Bristol, and the National Hospital for Neurology and Neurosurgery (NHNN) in Queen Square in London, England. Board-certified in neurology in the United Kingdom in 2002, Lhatoo trained in epilepsy with a two-year fellowship at NHNN before completing an epilepsy research fellowship in EEG at the Cleveland Clinic Foundation. Before coming to Houston, he earned an MBA from the Cleveland Clinic Weatherhead Executive MBA Program and was a member of the faculty at Case Western Reserve University. He was recruited to McGovern Medical School and UTHealth Neurosciences in 2018.

Zhang is vice president and chief data scientist for UTHealth. He is a professor of neurology and co-director of the UTHealth Texas Institute for Restorative Neurotechnologies. Before joining UTHealth, Zhang was professor of

internal medicine and computer science at the University of Kentucky, where he served as the university's inaugural director of the Institute for Biomedical Informatics.

He received his PhD from the University of Cambridge. In the last decade, his research has revolved around human-data interaction, achieved through the development of innovative software and web-based applications spanning the biomedical data lifecycle. He led the development of data infrastructures and manages data resources, following the vision of the National Institutes of Health Data Commons, for the National Sleep Research Resource and the Center for Sudden Unexpected Death in Epilepsy Research, the largest and most comprehensive, well-annotated clinical data sets in the two disease areas.

See the related articles in this section "UTHealth's New Texas Institute for Restorative Neurotechnologies Seeks Cures for Brain Disorders" and "Using Our Brains to End Epilepsy." 🧠



GQ Zhang, MS, PhD

Vice President and Chief Data Scientist, UTHealth

Co-Director, Texas Institute for Restorative Neurotechnology

Professor Of Medicine, Biomedical Informatics, and Public Health

Department of Neurology

McGovern Medical School at UTHealth



Arthur L. Day, MD

Neurosurgeon and Director
of Clinical Education and
Cerebrovascular Programs

Professor, Co-Chair, and
Program Director
Vivian L. Smith Department of
Neurosurgery

McGovern Medical School at
UTHealth

Society of Neurological Surgeons Recognizes Dr. Arthur Day with Distinguished Service Award

Arthur L. Day, MD, professor and co-chair of neurosurgery at McGovern Medical School at UTHealth and program director and director of clinical education in neurosurgery at Mischer Neuroscience Institute at Memorial Hermann-Texas Medical Center, has received the prestigious Distinguished Service Award, the highest honor given by the Society of Neurological Surgeons (SNS). Day received the award in recognition of his lifelong commitment and outstanding leadership, dedication, and contributions to the field of neurosurgery.

Known as the Senior Society, the SNS is the American society of leaders in neurosurgical residency education, and is the oldest and most exclusive neurosurgical society in the world. Academic department chairs, residency program directors, and other key academicians comprise the active membership of the society, which is limited to 200 active members.

The Senior Society cited Day for his lifelong teaching and his stewardship of the organization's Committee on Advanced Subspecialty Training (CAST), which is responsible for accreditation of subspecialty training fellowships and for the development and updating of subspecialty training requirements. Under Day's leadership, CAST revamped the way fellowships are reviewed and standardized, and set standards for new fellowships in neuroendovascular surgery, critical care, tumor, and others.

"I am incredibly honored to receive the Senior Society's Distinguished Service Award," Day says. "It is deeply humbling to be added to the group of prior award winners – a real honor roll in neurosurgery."

Day is a board-certified, fellowship-trained neurosurgeon with specific expertise in cerebrovascular and skull base neurosurgery. He also specializes in microsurgical treatment of brain tumors and minimally invasive spinal surgery.

Day was awarded his medical degree from

Louisiana State University in New Orleans. He completed his internship training in Birmingham, Alabama, and subsequently completed his neurological surgery residency and fellowship in brain tumor immunology at the University of Florida College of Medicine in Gainesville.

Before joining UTHealth Neurosciences, he practiced at the University of Florida for 25 years, ultimately rising to the positions of professor, co-chair, and program director of the Department of Neurosurgery. In 2002, he moved to Boston as professor of surgery at Harvard Medical School and was also program director and chair of the Department of Neurological Surgery at the Brigham and Women's Hospital.

Day has held leadership positions in many medical professional societies, and received numerous awards and honors, including the Medal of Honor from the Neurosurgical Society of America; the Founders' Laurel Award from the Congress of Neurological Surgeons for his "exceptional service, lifelong dedication, and meritorious accomplishments in the field of medical education"; and the Harvey Cushing Medal from the American Association of Neurological Surgeons for his many years of outstanding leadership, dedication, and contributions to the field of neurosurgery.

He served as president of the Society of Neurological Surgeons from 2011 to 2012, has also been a member of the neurosurgical RRC, and chaired the American Board of Neurological Surgery. He has also been named multiple times to Best Doctors in America®. Day has published 200 journal articles and book chapters, and co-edited two books about neurological sports injuries.

NINDS Names Dr. Louise McCullough Outstanding Mentor

The National Institute of Neurological Disorders and Stroke (NINDS) has named Louise McCullough, MD, PhD, Roy M. and Phyllis Gough Huffington Distinguished Chair and professor in the Department of Neurology

at McGovern Medical School at UTHealth, the recipient of the 2019 Landis Award for Outstanding Mentorship.

“I’m incredibly grateful to receive the Landis Award,” McCullough says. “It recognizes mentorship, and advancing the careers of trainees is one of the things I’m most passionate about. It really is a lifetime award for mentorship and scholarship.”

The award emphasizes the high value NINDS places on mentorship and encouraging faculty to make mentorship a strong component of their careers, as well as encouraging institutional leaders to promote and reward excellent mentorship and include it as a criterion for evaluating academic success.

The Landis Award provides \$100,000 in direct costs toward an existing NINDS grant to support continuing efforts to foster the career advancement of trainees. McCullough will use the award in conjunction with her current mentorship program to support two applicants, an MD/PhD student and a nursing student, in an effort to bring more nursing researchers into science.

“We are thrilled to announce this year’s winners of the Landis Award. Good mentors play a key role in inspiring and encouraging current and future scientists, but they don’t always receive the recognition they deserve,” says Walter Koroshetz, MD, director of NINDS. “This award lets the community know how important mentorship is for sustaining scientific research enterprise.”

McCullough’s program, Camp McCullough, employs around 10 undergraduates per summer, selected from a growing list of applicants. Students spend the summer months in the lab developing projects and contributing to papers in an effort to be competitive for graduate or medical school. The McCullough laboratory focuses on stroke research, including sex differences in the brain’s response to damage and how aging and inflammation affect stroke recovery.

McCullough, a faculty member with the Programs in Immunology and Neuroscience at in the Department of Neurology at MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences, received her medical degree at the University of Connecticut School of Medicine and continued her training at Johns Hopkins with a neurology residency, followed by a fellowship in cerebrovascular disease. She later joined the faculty at Johns Hopkins Hospital and began her translational research career before relocating to Connecticut to serve as a professor at the University of Connecticut Health Center and John Dempsey Hospital, as well as director of stroke research and education at Hartford Hospital. McCullough has been with McGovern Medical School and served as co-director of the Mischer Neuroscience Institute at Memorial Hermann-Texas Medical Center since 2015.

Story Landis, PhD, was the director of NINDS from from 2003 to 2014 and established programs to help promote the development of neuroscientists. Landis was known for her dedication to mentorship, providing guidance to researchers at all stages of their careers.

Dr. David Sandberg Receives the American Association of Neurological Surgeons Humanitarian Award

David I. Sandberg, MD, FAANS, FACS, FAAP, has received the American Association of Neurological Surgeons 2019 Humanitarian Award, one of the highest honors bestowed by the organization. The award recognizes his extraordinary work with children suffering from neurosurgical disorders throughout the world.

Sandberg is professor and director of pediatric neurosurgery at McGovern Medical School at UTHealth, where he holds the Dr. Marnie Rose Professorship in Pediatric Neurosurgery. He is also director of pediatric neurosurgery at Children’s Memorial Hermann Hospital and Mischer



The award recognizes Sandberg's extraordinary work with children suffering from neurosurgical disorders throughout the world.

Neuroscience Institute at Memorial Hermann-Texas Medical Center, as well as co-director of the Pediatric Brain Tumor Program at MD Anderson Cancer Center. Fellowship-trained in pediatric neurosurgery with a special clinical and research interest in pediatric brain tumors, Sandberg specializes in minimally invasive endoscopic approaches to brain tumors, hydrocephalus, and arachnoid cysts, as well as surgical management of arteriovenous malformations of the brain, congenital spinal anomalies, Chiari malformations, and craniofacial anomalies. The recipient of numerous research grants, he is currently principal investigator of two single-center trials at Children's Memorial Hermann Hospital and McGovern Medical School investigating direct administration of chemotherapy into the fourth ventricle for

treatment of malignant brain tumors that originate from that ventricle.

Sandberg is a magna cum laude graduate of Harvard University. He received his medical degree at the Johns Hopkins University School of Medicine and completed neurosurgery training at Weill Medical College of Cornell University/New York-Presbyterian Hospital. During residency, he was awarded the Resident Traveling Fellowship in Pediatric Neurosurgery by the American Association of Neurological Surgeons and the Congress of Neurological Surgeons, which he completed at the Hospital for Sick Children in Toronto, Canada. He completed pediatric neurosurgery fellowship training at the Children's Hospital in Los Angeles. Before joining McGovern Medical School, Sandberg was an associate professor of clinical neurolog-

ical surgery and pediatrics at the University of Miami Miller School of Medicine.

He began his medical mission work in high school and college, accompanying his father, Miami ophthalmologist Joel Sandberg, MD, on trips to Jamaica, Antigua, and the Dominican Republic. His father was his inspiration to practice medicine and also to contribute to the health of the world through international mission work.

As a junior neurosurgery resident, Sandberg made two trips to Guatemala with Neil Feldstein, MD, director of the Division of Pediatric Neurosurgery at Columbia University Medical Center/New York-Presbyterian Hospital, performing surgery on children with spina bifida. As a resident in neurosurgery, he used his vacation time to spend a month in Tegucigalpa, Honduras. There, with the help of Mark Souweidane, MD, director of pediatric neurosurgery at Weill Cornell Brain and Spine Center, he brought an 8-year-old girl with a brain tumor to the U.S. for treatment. She was the first of several patients he brought to the U.S.

Sandberg has been on the Board of Directors of the Foundation for International Education in Neurological Surgery (FIENS) since 2004 and served as secretary of FIENS from 2013 to 2018. Through FIENS, he made multiple neurosurgical humanitarian trips to Honduras, Peru, and Guatemala. In 2006, he traveled to Uganda with CURE International.

Since 2007 he has worked with Project Medishare, a Miami-based nonprofit organization with a 20-plus-year history of empowering Haitians to provide quality health care through community-based, Haitian-led programs. Through medical volunteers, the organization treats more than 180,000 people annually. Sandberg leads a team of pediatric neurosurgeons, pediatric anesthesiologists, nurses, and surgical scrub technologists from Children's Memorial Hermann Hospital and McGovern Medical School; they make the trip annually.

"Education is a major focus for all of our mission trips to Haiti," he says. "We work with a local neurosurgeon, Dr. Yudy Lafortune, to teach him modern neurosurgical care for pediatric patients. This is the 'teach-a-man-to-fish' concept. We're training Dr. Lafortune to be the pediatric neurosurgeon for the children of Haiti."

Sandberg grew up in a family with a strong commitment to public service. "I think how lucky I am to have been born into my family in the United States, and to be able to contribute in a small way to helping children in other countries," he says. "This award is a huge honor for me, and I'm humbled to receive it."

Dr. Rachael Sirianni Named UTHealth Women Faculty Forum Rising Star

Rachael Sirianni, PhD, has been recognized with the 2019 Rising Star Award given by the Women Faculty Forum at McGovern Medical School at UTHealth. The excellence awards reception was held Oct. 7, 2019.

Trained as a biomedical engineer in the field of polymeric drug delivery, Sirianni earned her PhD from Yale University in 2008, and completed a postdoctoral fellowship in diagnostic radiology at the Yale School of Medicine.

Sirianni's research program, which has received funding from the Department of Defense and the National Institutes of Health, has designed creative approaches for treating central nervous system disease via encapsulation and tissue-specific delivery of drugs from polymeric nanoparticles. She also has developed biomaterial approaches for studying and manipulating the behavior of cells in engineered microenvironments mimicking the brain. These approaches have demonstrated preclinical success in applications ranging from neuro-oncology to neurodegeneration and neural engineering.

Sirianni's research methods are poised to make a significant impact in the field of pediatric neuro-oncology. Her goal at UTHealth is to develop nanoparticle systems that can effectively treat central nervous system



Rachael Sirianni, PhD

Assistant Professor,
Vivian L. Smith Department of
Neurosurgery

McGovern Medical School at
UTHealth



Aaron Gusdon, MD

Critical Care Physician

Assistant Professor,
Vivian L. Smith Department of
Neurosurgery

McGovern Medical School at
UTHealth

infiltration and metastasis in children affected by recurrent malignant brain tumors.

Her professional accomplishments include invitations to speak at major research conferences, service on an NIH study section, book editorship and extensive publications in the fields of biomaterials, drug delivery, and imaging.

The Women Faculty Forum at McGovern Medical School advocates on behalf of women faculty, provides opportunities for professional development, and offers an opportunity for networking among women faculty, as well as with leaders in academic science and medicine within and outside the institution.

McGovern Medical School at UTHealth Welcomes New Recruits

The Department of Neurology and the Vivian L. Smith Department of Neurosurgery welcome four faculty members to McGovern Medical School at UTHealth. They are Aaron Gusdon, MD; Wesley Jones, MD; Swathi Kondapalli, MD; and Jessica Stark, MD.

Aaron Gusdon, MD, joins the Vivian L. Smith Department of Neurosurgery as an assistant professor after completing fellowship training in neurocritical care at Johns Hopkins University. He earned his medical degree at the University of Pittsburgh School of Medicine, where he trained in neuropathology through the school's Physician Scientist Training Program. He completed neurology residency training at Weill Cornell Medical College/ New York-Presbyterian Hospital in New York City. Dr. Gusdon is the author of peer-reviewed publications and has presented his research nationally.

Wesley Jones, MD, is a dual fellowship-trained neurosurgeon who focuses on complex and minimally invasive spine surgery, endovascular surgery, cerebrovascular surgery, surgical neuro-oncology, and skull base surgery. He received his medical degree at Texas Tech University School of Medicine in Lubbock, where he was inducted into Alpha Omega Alpha Honor Medical Society and the Gold Humanism

Honor Society. He completed neurosurgical residency training at the Vivian L. Smith Department of Neurosurgery at McGovern Medical School. Fellowship-trained in two subspecialties, he completed a cerebrovascular and endovascular fellowship at UTHealth, and subsequently, a complex spine fellowship at Washington University School of Medicine in St. Louis in the Departments of Neurosurgery and Orthopedics.

Swathi Kondapalli, MD, joins the faculty of the Vivian L. Smith Department of Neurosurgery as an assistant professor after completing fellowship training in neurocritical care at McGovern Medical School. She received her medical degree at St. George's University School of Medicine in Grenada, West Indies, where she was inducted into the Gold Humanism Honor Society. She completed her preliminary year of residency training in internal medicine at Brookdale University Hospital and Medical Center in Brooklyn and her neurology residency at JFK Medical Center-JFK Neuroscience Institute in Edison, New Jersey. She is fluent in Telugu and Hindi.

Jessica Stark, MD, is fellowship-trained in spine surgery with a focus on trauma, degenerative conditions, tumors and minimally invasive spine surgery. She received her medical degree at Louisiana State University Health Sciences Center School of Medicine in New Orleans, where she was inducted into Alpha Omega Alpha Honor Medical Society. She completed residency training in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School, where she was chief resident. During residency, she completed a master's degree in public health at UTHealth School of Public Health and a Council of State Neurosurgical Societies Socioeconomic Fellowship for neurosurgical residents interested in socioeconomic education. She went on to complete a fellowship in spinal neurosurgery at the same institution. Stark is the coauthor of peer-reviewed publications and is actively involved in community service. ■



Wesley Jones, MD

Neurosurgeon

Assistant Professor,
Vivian L. Smith Department of
Neurosurgery

McGovern Medical School at
UTHealth



Swathi Kondapalli, MD

Critical Care Physician

Assistant Professor,
Vivian L. Smith Department of
Neurosurgery

McGovern Medical School at
UTHealth



Jessica Stark, MD

Neurosurgeon

Assistant Professor,
Vivian L. Smith Department of
Neurosurgery

McGovern Medical School at
UTHealth

Events at UTHealth Neurosciences

7th Annual Neuro ICU Symposium Draws More Than 250 Health Care Providers

With the goal of empowering success in the Neuro ICU, neurocritical care physicians at UTHealth hosted their seventh annual Neuro ICU Symposium April 3-5, 2019, at the Westin Oaks Galleria in Houston. The two-and-a-half-day course was designed to educate physicians and other health care professionals on how to provide neurocritical care at hospitals of all types and sizes.

The symposium's course director and committee chair was Tiffany R. Chang, MD, director of neurocritical care, director of the fellowship program, and an associate professor in the Department of Neurology and the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth.



Back this year was the Neuroscience Nursing Symposium, which featured a comprehensive program for critical care nurses and other health care professionals, as well as a Neurocritical Care Board Review. New talks this year included results from the MISTIE III Trial and the Future of Surgical ICH Treatment. The symposium also featured Hot

Topics: Neurological Illness from the Patient Perspective; Cross-Fire Debates in which the audience selected the winners; and Simulation Labs – hands-on workshops in small groups with experts.

The next Neuro ICU Symposium will be Nov. 4-6, 2020, at the InterContinental Hotel-Texas Medical Center.

For more information, visit UTneuroicusymposium.org.



Children With Neurological and Neurosurgical Conditions: An Update for Pediatricians

The annual Neuroscience Update for Pediatricians, held on May 4, 2019 at Children's Memorial Hermann Hospital, included a full day of informative lectures on diagnosing and treating neurological problems in pediatric patients, sponsored by McGovern Medical School at UTHealth and Children's Memorial Hermann. One hundred neurologists, pediatricians, family practitioners, neonatologists, mid-level practitioners, nurses, physical therapists, occupational therapists, and other health care practitioners attended.

Course directors were David I. Sandberg, MD, FAANS, FACS, FAAP, professor and director of pediatric neurosurgery in the Department of Pediatric Surgery and the Vivian L. Smith Department of Neurosurgery and the Dr. Marnie Rose Professor in Pediatric Neurosurgery, and Ian J. Butler, MD, professor and director of the Division of Child and Adolescent Neurology in the Department of



Tiffany R. Chang, MD

Director, Neurocritical Care Fellowship Program

Associate Professor, Department of Neurology and Vivian L. Smith Department of Neurosurgery

McGovern Medical School at UTHealth



David I. Sandberg, MD, FAANS, FACS, FAAP

Professor, Departments of Pediatric Surgery and Neurosurgery

Dr. Marnie Rose Professor in Pediatric Neurosurgery

McGovern Medical School at UTHealth

Director of Pediatric Neurosurgery

Children's Memorial Hermann Hospital and Mischer Neuroscience Institute



Ian J. Butler, MD

Professor, Department of Pediatrics

Jacobo Geissler Distinguished Chair in West Syndrome Research

Director, Division of Child and Adolescent Neurology

McGovern Medical School at UTHealth

Pediatrics and Jacobo Geissler Distinguished Chair in West Syndrome Research.

Speakers from McGovern Medical School were Stephen Fletcher, DO, associate professor of pediatric neurosurgery; Mary Kay Koenig, MD, associate professor of pediatrics; Pedro Mancias, MD, professor of pediatric neurology; Shadé Moody, MD, professor of pediatric neurology; Manish N. Shah, MD, director of the Texas Comprehensive Epilepsy Program and an assistant professor of pediatric neurosurgery; Nivedita Thakur, MD, assistant professor of pediatric neurology; Gretchen Von Allmen, MD, director of the Pediatric Epilepsy Program and professor and chief of pediatric epilepsy; and Michael Watkins, MD, assistant professor of pediatrics.

The conference offers CME, CNE, and PT/OT credits.

Epilepsy Symposium Set for Fall 2020

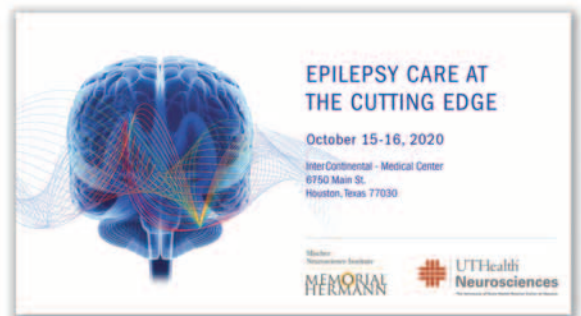
“Epilepsy Care at the Cutting Edge” is an educational symposium for health care professionals from all areas of epilepsy care—neurologists, neurosurgeons, advanced practitioners, nurses, pharmacists, scientists, first responders, and others who are involved in the treatment of patients with epilepsy.

This year’s course will expand attendees’ knowledge and understanding of epilepsy and will demonstrate how to offer top quality epilepsy care to patients. The event will be held in the Texas Medical Center, and will include a day of focus on neurology and a day of focus on neurosurgery. Course directors are Samden Lhatoo, MD, professor and John P. and Kathrine G. McGovern Distinguished Chair in the Department of Neurology at McGovern Medical School at UTHealth; and Nitin Tandon, MD, professor and vice chair of the Vivian L. Smith Department of Neurosurgery at McGovern Medical School. Both are co-directors of the UTHealth Texas Institute for Restorative Neurotechnologies.

Some of the many exciting highlights include:

- An exploration of new technologies in the management of intractable epilepsy
- A lecture and discussion around SUDEP
- A patient experience session, where attendees will hear a patient’s perspective on their journey through epilepsy diagnosis and treatment
- An interactive lab that presents cases to simulate different issues and surgical solutions

This event will be held on Oct. 15-16, 2020, at the InterContinental Hotel-Texas Medical Center.



For more information or to register for events at UTHealth Neurosciences, visit UTneuroevents.com.

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