CenterTimes

August 2021 | A Publication of The University of Texas Southwestern Medical Center | Campus Edition

UTSW ranked No. 1 Hospital in DFW for fifth consecutive year

UT Southwestern is ranked among the top 50 hospitals nationally in 9 specialties that range from brain to heart care.

From Staff Reports

For the fifth consecutive year, UT Southwestern's William P. Clements Jr. University Hospital is the No. 1 Best Hospital in Dallas-Fort Worth and the No. 2 Best Hospital in Texas in the annual *U.S. News & World Report* rankings. Also this year, nine UTSW clinical programs were ranked among the top 50 in the country – with eight of those in the top 25. The recognition follows the recent expansion of Clements University Hospital, which now includes around 900 beds.

Over the past year, UT Southwestern also has received national recognition for patient satisfaction, patient safety, and quality of care from several reviewing bodies, including the Centers for Medicare & Medicaid Services, Leapfrog, Healthgrades, and Press Ganey.

"While I know that our remarkably dedicated health care team – physicians, nurses, and staff working together – are principally motivated by their desire to best serve our patients and their families, I am delighted to see these rankings reflect their excellence in delivering on that commitment," said Dr. Daniel K. Podolsky, President of UT Southwestern.

UT Southwestern's nationally ranked specialties from nearly 5,000 hospitals across the country include:

#11 Cardiology and Heart Surgery
#17 Rehabilitation
#17 Urology
#19 Neurology and Neurosurgery
#22 Pulmonology and Lung Surgery
#23 Geriatrics
#24 Diabetes and Endocrinology
#24 Cancer
#35 Gastroenterology and GI Surgery

UTSW was rated nationally as high performing for orthopedics, placing that specialty among the top 10 percent of all rated hospitals, and was nationally rated for its expertise in 14 procedures and conditions – abdominal aortic aneurysm repair,

Please see RANKINGS on page 4

Conaway brings decades of bench science to role as Dean of Basic Research

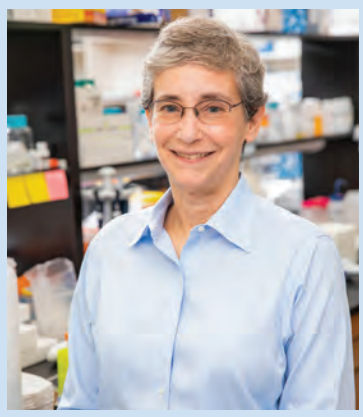
By Christen Brownlee

Dr. Joan Conaway has spent decades in laboratories investigating the mechanisms of transcription, the biological process by which the DNA of chromosomes is copied into RNA.

For more than 30 years, the Conaway Lab – which she led with her husband, Dr. Ron Conaway, at the Stowers Institute for Medical Research in Kansas City, Missouri – has made numerous discoveries that reveal the roles of proteins that work with RNA polymerase II, the multiprotein complex that transcribes DNA into RNA precursors. This area of basic research provides insights into processes that, when disrupted, can lead to cancer and other diseases.

As one of the first members of the Stowers Institute, Dr. Joan Conaway also worked to build up the careers of other scientists within the molecular biology field and beyond.

She sees this combination of experience – both as a scientist and a mentor – as key to her new role as Vice Provost and Dean of Basic Research at UT Southwestern, a position she assumed effective July 1.



Dr. Joan Conaway

Dr. Conaway succeeds Dr. David Russell, who has served as the institution's first Vice Provost and Dean of Research since 2010 and is retiring later this year after more than 40 years of service to UT Southwestern.

"Coming from a strong research background is central to this type of position. You can't lead a research faculty until you've had 'boots on the ground,'" said Dr. Conaway. "For a while, I've had a strong interest in trying to contribute not just to my own research program, but to

Please see CONAWAY on page 6

UTSW among top three companies in the nation for new graduates

From Staff Reports

UT Southwestern ranked No. 3 in the nation on *Forbes*' list of America's Best Employers For New Graduates, placing it in the top 1 percent, and highest among academic medical centers.

Forbes and market research company Statista identify the companies most liked by new workforce entrants for their annual ranking, compiled by surveying 20,000 Americans with less than 10 years of professional experience working for businesses with at least 1,000 employees. Participants were asked to rank their employer on criteria such as safety, opportunities for advancement, effectiveness of diversity programs, and company image.

"As new graduates transition from school to starting their careers, they seek not only job opportunities, but training, support, and benefits that can help establish a strong foothold for their future. As a nationally recognized academic medical center, UT Southwestern is able to offer those essential tools that can make a real difference in getting their careers off to a good start," said Janelle Browne, Vice President of Human Resources and Chief

Please see BEST EMPLOYERS on page 8

RNA-driven phase separation may protect against aging, neurodegenerative diseases

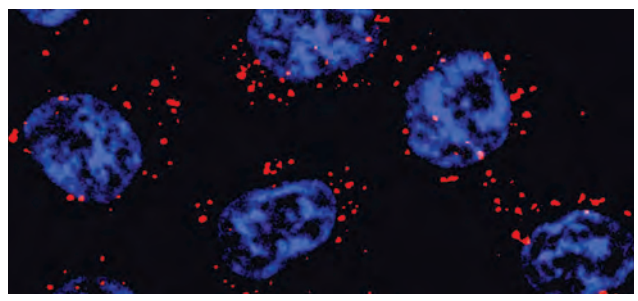


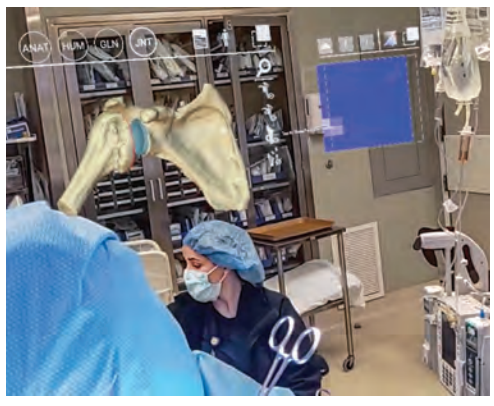
Image shows cells with oil droplet-like 'NORAD-Pumilio bodies' in red and nucleus in blue. Credit: Mahmoud Elguindy.

By Christen Brownlee

A phenomenon in which an RNA named *NORAD* drives a protein named Pumilio to form liquid droplets in cells, much like oil in water, appears to tightly regulate the activity of Pumilio. A new study led by UT Southwestern scientists suggests that such RNA-driven "phase separation," in turn, protects against genome instability, premature aging, and neurodegenerative diseases, and may represent a previously unrecognized way

Please see RNA on page 5

UT Southwestern completes first augmented reality shoulder replacement surgery in Texas



Dr. Michael Khazzam's view from his AR headset, which shows a patient's 3D surgical plan in real time.

By Jan Jarvis

By the time Monte Perkins arrived at UT Southwestern, the pain in his right shoulder was so intense that it was "driving him into the ground," he said. The 74-year-old Irving resident had fallen in his front yard in December, and over the next few months he and his wife, Lynda, visited several doctors in search of relief.

It wasn't until they were referred to Dr. Michael Khazzam, a shoulder specialist and Associate Professor of Orthopaedic Surgery, that they felt confident Mr. Perkins would get his life and business back on track.

"The minute we got to UT Southwestern, we felt like we were Dr. Khazzam's only patient," said Mrs. Perkins. "And he just told it like it was. He showed us on the MRI that Monte had torn two tendons in his shoulder."

Mr. Perkins, a third-generation jeweler, is one of the first patients in Texas to undergo augmented reality (AR) shoulder replacement surgery, right here at UTSW.

Dr. Khazzam is the first orthopedic surgeon in Texas – and one of only a handful in the world – to use augmented reality in the operating room for shoulder arthroplasty. Worldwide, UTSW is one of just 15 surgical centers using this next-generation arthroplasty technique, which was approved by the Food and Drug Administration in July 2020.

"We were just blown away by what they could do. It's almost like a 'Star Wars'-type thing," said Mr. Perkins of his May 3 surgery. Using the AR headset, "Dr. Khazzam was able to layer everything together and make sure it all fit perfectly – just like a puzzle."

A better reality

For years, augmented reality has been used before surgery to develop a 3D model of the procedure, making it possible to preserve more of the patient's natural anatomy. Now it's possible to take this innovation a step further by virtually overlaying the 3D surgical plan over the patient's anatomy in real time. This approach provides an intricately personalized procedure with the highest level of precision, said

Please see AR SURGERY on page 7

IN MEMORIAM

Dr. Jean Wilson: Renowned endocrinologist's discoveries led to popular prostate treatments

By Patrick Wascovich

Dr. Jean D. Wilson, an internationally known endocrinologist whose scientific discoveries led to profound insights into the mechanisms underlying sexual differentiation and widely used treatments for prostate disease, died June 13. He was 88.

Dr. Wilson, Professor Emeritus of Internal Medicine, was largely responsible for current understanding of the mechanisms by which steroid hormones induce male sexual differentiation. He also was instrumental in identifying the scientific underpinnings of a widely prescribed class of drugs known as *5-alpha-reductase* (*5AR*) inhibitors such as Proscar to treat enlarged prostate and balding in men.

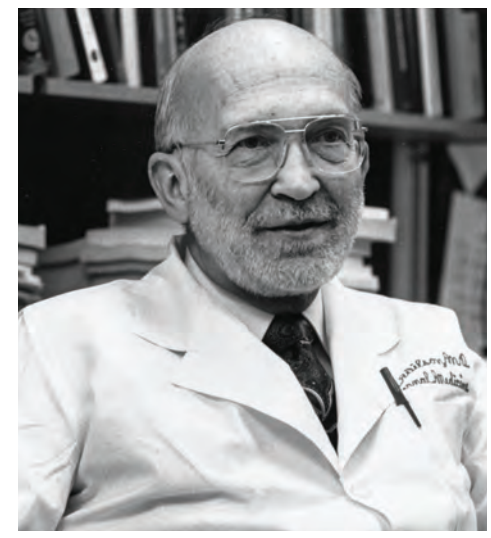
"Dr. Wilson's discovery of *5-alpha-reductase* and the identification of dihydrotestosterone as the primary hormone associated with the growth of the prostate transformed our understanding of prostate gland growth and paved the way for new effective treatment of prostate disease," said Dr. Daniel K. Podolsky, President of UT Southwestern. "His findings led to the first medical therapy for benign prostatic hyperplasia, and also provided the basis for understanding of the mechanism underlying the differentiation of male and female genital development. His legacy will be found in the legions of patients who have benefited from the therapy made possible by his discoveries."

"Jean Wilson was one of the most critical and helpful sources of information concerning the development of two important drugs we were developing at Merck – the statins, for control of LDL cholesterol, and Proscar, for treatment of benign prostate enlargement," said Dr. P. Roy Vagelos, former Chairman, President, and CEO of Merck & Co. and now Chair of the Board of Regeneron Pharmaceuticals.

Dr. Wilson's research included the study of cholesterol metabolism and steroid hormone action. The UT Southwestern Medical School graduate and former National Institutes of Health (NIH) researcher earned international prominence for his investigations of testosterone – including its formation from cholesterol as well as its metabolism and action. His efforts elucidated disorders resulting from genetic defects that lead to disruption in sex hormone biosynthesis with corresponding alteration in development.

Collaborations at UT Southwestern with Dr. David Russell, Professor of Molecular Genetics, led to the cloning of the *5AR* gene, development of animal models for *5AR* deficiency, and eventually the finding that a *5AR* inhibitor blocked prostate growth. The human androgen receptor later was cloned in 1989, allowing Dr. Wilson and colleagues to identify the receptor as a transcription factor that could regulate both the receptor and *5AR* expression in prostate cancer.

Among his numerous awards, Dr. Wilson received the Kober Medal from the Association of American Physicians (1999); the Fred Conrad Koch Award from The Endocrine Society (1993); Gregory Pincus Award from the Worcester Foundation for Experimental Biology (1992); Henry Dale Medal from the Society for Endocrinology (1991); Amory Prize from the American Academy of Arts and Sciences (1977); and the Eugene Fuller Award from the American Urological Association. He was elected as a member of the American Academy of Arts and Sciences (1982), the National Academy of Sciences (1983), and the National Academy of Medicine (1994), as well as the American Philosophical Society and served as President of the Endocrine Society, the American Society for Clinical Investigation, and the Association of American Physicians.



Dr. Wilson, photographed here in 1992, was a highly sought-after attending physician valued for his vast expertise in endocrinology and medicine.

Dr. Wilson, who had held the Charles Cameron Sprague Distinguished Chair of Biomedical Research, was known as a collaborative colleague and empathetic adviser to students and fellows.

At UT Southwestern, he served as the first Director of the Medical Scientist Training Program, and it was recently announced that the Physician Scientist Training Program in Internal Medicine would be known as the Jean Wilson Society. The Jean D. Wilson Center for Biomedical Research and The Jean D. Wilson, M.D. Award, which honor excellence in scientific research mentorship, are named in his honor.

The Center was established with support from Dr. Wilson and his sister, the late Dr. Margaret Sitton, to promote research in endocrinology, developmental biology, and genetics, along with the J.D. and Maggie E. Wilson Distinguished Chair in Biomedical Research. In addition, he served among editors of two foundational medical textbooks – *Williams Textbook of Endocrinology* and *Harrison's Principles of Internal Medicine*. He authored *The Memoir of a Fortunate Man*, which chronicles his life growing up in the Texas Panhandle through his rise to pioneering academic physician and researcher.

"Jean was a popular and highly sought-after attending physician on the wards of Parkland Memorial Hospital, valued for his vast expertise in endocrinology and medicine in general," said Nobel Laureates Drs. Joseph Goldstein, Chair of Molecular Genetics, and Michael Brown, Director of the Erik Jonsson Center for Research in Molecular Genetics and Human Disease.

He had a rich life outside of the Medical Center, as well. An avid opera buff, Wilson collected antique gramophones that could play every type of recording that had ever been produced.

"He took memorable trips to places like the North Pole, Antarctica, the Galapagos Islands, and the Easter Islands. He often incorporated science into his trips, visiting the Kangaroo Island in Australia to study sexual development in wallabies and to Kenya to biopsy the phallus of the spotted hyena. Fearless in the pursuit of knowledge, he performed a rectal examination on a lion to estimate the size of the prostate," Drs. Goldstein and Brown said.

Born in Wellington, Texas, in 1932, Dr. Wilson obtained an undergraduate degree in chemistry from UT Austin and graduated from UT Southwestern Medical School in 1955. After residency, he spent two years at the NIH, where he studied ethanolamine biosynthesis. He joined the UT Southwestern faculty in 1960 where he began his studies of testosterone and worked in 1970 at Cambridge University. In all, he spent 60 years at UT Southwestern and was named Professor Emeritus in UT Southwestern's storied Department of Internal Medicine in 2011.

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Dr. Brown, a Regental Professor, holds The W.A. (Monty) Moncrief Distinguished Chair in Cholesterol and Arteriosclerosis Research, and the Paul J. Thomas Chair in Medicine.

Dr. Goldstein, a Regental Professor, holds the Julie and Louis A. Beecherl, Jr. Distinguished Chair in Biomedical Research, and the Paul J. Thomas Chair in Medicine.

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

Dr. Russell holds the Eugene McDermott Distinguished Chair in Molecular Genetics.

More online: Read the full story in the newsroom at **utsouthwestern.edu/newsroom**.

Giving brown fat a boost to fight Type 2 diabetes

Study suggests increasing a protein concentrated in brown adipose tissue remodels white adipose tissue to lower diabetes risk

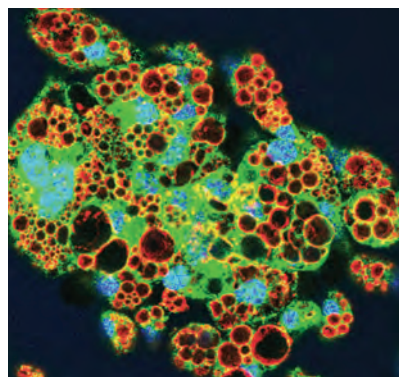
By Christen Brownlee

Increasing a protein concentrated in brown fat appears to lower blood sugar, promote insulin sensitivity, and protect against fatty liver disease by remodeling white fat to a healthier state, a new study led by UT Southwestern scientists suggests. The finding, published online in *Nature Communications*, could eventually lead to new solutions for patients with diabetes and related conditions.

"By taking advantage of this natural system, we may be able to help make fat depots more metabolically healthy and potentially prevent or treat obesity-associated diabetes," said study leader Dr. Perry Bickel, Chief of the Division of Endocrinology.

Type 2 diabetes is characterized by elevated blood sugar and resistance to insulin, the hormone that allows cells to use blood sugar for energy. This disease has been linked to obesity, with excess white adipose tissue (WAT) associated with elevated blood sugar and insulin resistance in susceptible people. A second type of fat called brown adipose tissue (BAT) can burn fat to increase body heat in cold temperatures. BAT has been investigated as a potential target for weight loss, said Dr. Bickel, but may also have a role in improving blood sugar independent of weight loss.

In the study, Dr. Bickel and his colleagues, including co-leader Dr. Violeta I. Gallardo-Montejano, Instructor of Internal Medicine, found that brown fat could play an important protective role against diabetes. The researchers made this discovery while studying perilipin 5 (PLIN5), a protein that coats lipid droplets inside cells, particularly in BAT.



Shown are lipid droplet-filled brown adipocytes with staining for perilipin 5 in green, perilipin 1 in red, and cell nuclei in blue.

When the team genetically engineered mice that made extra PLIN5 in BAT, the animals maintained significantly lower blood sugar concentrations and higher insulin sensitivity compared with mice that had normal PLIN5 levels. The PLIN5-surplus mice also were less likely to have fatty liver disease, a condition associated with Type 2 diabetes.

Searching for the mechanism behind these positive changes, the scientists found that the BAT's mitochondria in the genetically engineered mice had adapted to burn even more fat, similar to that seen in animals placed in cold temperatures. However, the adaptation was not enough to explain the blood sugar-lowering effect. Looking closer, the researchers found that the white adipocytes of animals that had extra PLIN5 in their brown adipocytes were smaller and had reductions in some markers of inflammation – changes that are associated with improved sensitivity to insulin and metabolism of sugar.

Dr. Bickel, also Associate Professor of Internal Medicine, noted that BAT appears to communicate with WAT in some unknown way, potentially sending a molecular factor through the bloodstream when PLIN5 levels increase inside brown adipocytes.

"The next question we want to address," he said, "is what that factor is and whether we can harness it for therapeutic benefit."

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Dr. Bickel holds the Daniel W. Foster, M.D. Distinguished Chair in Internal Medicine.

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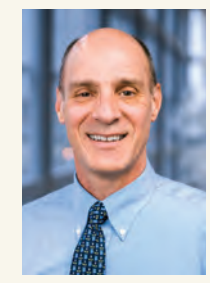
NEWS

MAKER

Crandall honored for postdoc mentoring



Dr. Craig Crandall

Understanding, compassion, encouragement, and drive are key to effective mentoring, according to Dr. Craig Crandall, Professor of Internal Medicine. The Postdoctoral Association (PDA) at UT Southwestern recently selected Dr. Crandall for its 2021 Excellence in Postdoctoral Mentoring Award.

"Dr. Crandall was nominated by his current postdoctoral fellows who attested to his unique style of mentorship," said Dr. Stephan Daetwyler, President of the PDA and a postdoctoral researcher in the lab of Dr. Reto Fiolka, Assistant Professor of Cell Biology and in the Lyda Hill Department of Bioinformatics. "They all emphasized his superb scientific acumen, very supportive personality, highly effective and timely communication, and his unique ability to cultivate strong personal, yet professional relationships with each of his trainees."

During his 25 years at UT Southwestern, Dr. Crandall has mentored 24 postdoctoral fellows (including his current three), five doctoral students, three visiting professors, and several undergraduate and master's-level students. In his lab, each fellow is expected to drive at least one project while supporting the other ongoing projects, with more experienced fellows providing guidance.

"I view those interactions as valuable training opportunities for the more experienced postdocs. I expect each fellow to assist in each other's projects – there are no silos in my lab," he said. "I focus my efforts in assisting the fellows to obtain the requisite experience, skills, publications, etc., necessary for them to get a tenure-track job and succeed as an independent investigator."

As part of National Postdoc Appreciation Week, which celebrates the contributions postdocs make to research and discovery, Dr. Crandall will speak at a PDA-hosted award ceremony and seminar planned for Sept. 22 on North Campus.

CenterTimes

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New sculptures make vibrant additions to Seldin Plaza

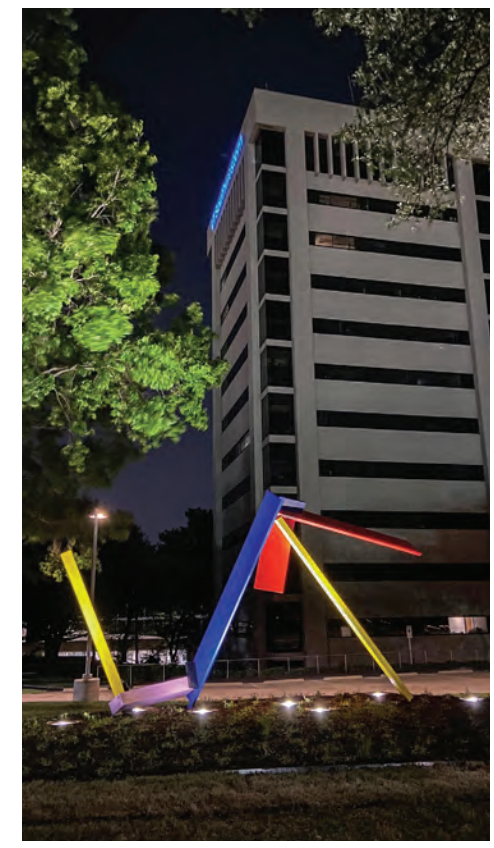
By Carol Marie Cropper

Two dramatic new sculptures have joined UT Southwestern's growing art collection on Dr. Donald Seldin Plaza, the outdoor space on South Campus that leads to the library, lecture halls, offices, and Tom and Lula Gooch Auditorium.

One is a colorful sculpture by renowned New York sculptor Joel Shapiro, while the second is a work of stainless steel and copper from acclaimed painter and sculptor Christopher Wool. Both are gifts from Nobel Laureate Dr. Joseph Goldstein, Professor and Chair of Molecular Genetics, who gifted two earlier pieces to UT Southwestern in 2019 – one by Mr. Shapiro and another, *Dumna*, by Ursula von Rydingsvard. All four pieces are on display on Seldin Plaza.

"UT Southwestern's collection has been made possible by the generosity of supporters and the desire to create an environment that provides for the total well-being of our faculty, staff, students, patients, and their families," said UT Southwestern President Dr. Daniel K. Podolsky. "The sculptures on Seldin Plaza, exemplified by these most recent additions, are at once a surprising and an uplifting welcome to those who enter this front door of our campus. We are deeply indebted to Dr. Goldstein for these wonderful gifts as one more way in which he has made an indelible impact on UT Southwestern."

Untitled, 2020 by Joe Shapiro, is the latest art installation on Seldin Plaza. © 2019-2020 Joel Shapiro/ Artists Rights Society (ARS), New York.



The colorful sculpture joins several other artwork gifts of Nobel Laureate Dr. Joseph Goldstein.

Colorful Shapiro piece installed in April

Dr. Podolsky, Dr. Goldstein, and Mr. Shapiro were present as the Shapiro work was installed April 21, just in time to welcome more employees returning to campus as UT Southwestern expanded on-campus operations following several months of improved COVID-19 conditions across the region. UT Southwestern Art Curator Courtney Crothers and Senior Construction Manager Jake Roysdon, who coordinated the installation, were also present.

The 10-foot-tall, 19-foot-long cast aluminum sculpture was driven from New York in sections on a flatbed truck before being assembled in a copse of oak trees near the Eugene McDermott Academic Administration Building. Shortly after noon, the protective plastic wrapping was removed to reveal the colorful artwork – first orange, then yellow, then bright blue, and light violet.

The sculpture is called simply *Untitled*, 2020.

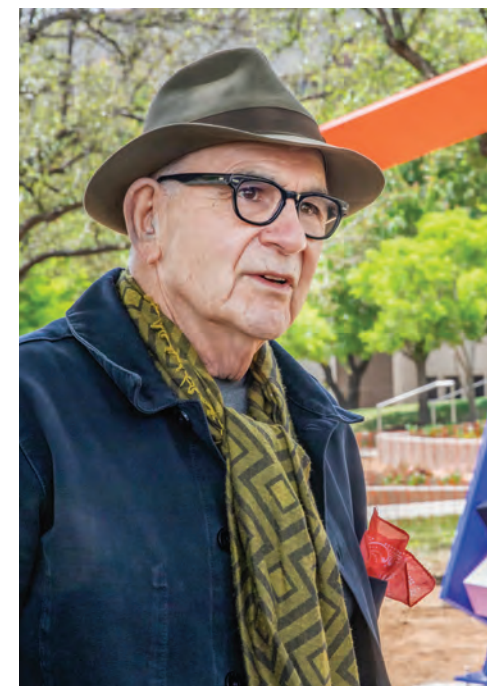
"I don't like to title them," Mr. Shapiro said, explaining that his work is abstract in nature and his talent runs more toward the visual than the verbal. "Regardless of how much art and how many works I've done, unveiling a piece is always accompanied by a sense of trepidation," he said as the piece was uncovered. When the wait was over, he deemed his creation a success. "I think it's really playful. The colors are great. I think the color's vibrant. It is very lively – has a lot of energy. It's a wild piece," Mr. Shapiro said.

"It surprises me. I think it's terrific," declared Dr. Goldstein. "This is Shapiro's first multicolored outdoor piece."

UTSW's earlier Shapiro installation is closer to the Plaza's footpath and is more monumental, standing about 21 feet tall and is made of bronze with a dark, natural patina, said Talley Dunn, eponymous owner of the Dallas gallery that worked with Dr. Goldstein to arrange the acquisitions. The new arrival is more lyrical, she added.

Artist Christopher Wool stands beside the 15-foot-tall sculpture near the Eugene McDermott Administration Building. Christopher Wool, *Untitled*, 2019, copper-plated steel. © 2019 Christopher Wool. All rights reserved. *Gift of Joseph L. Goldstein, M.D., 2021, and of Christopher Wool in memory of Glorye Wool, M.D., and Ira Wool, M.D., Ph.D.*

Dr. Goldstein said he came to know Mr. Shapiro's work over the past 25 years as he visited various sculpture gardens and museums. Sculptures by the artist are at the National Gallery of Art in the District of Columbia, The Museum of Contemporary Art in Los Angeles, and the Tate in London, among other locations. In Dallas, examples can be found at the Nasher Sculpture Center and NorthPark Center shopping mall.



Joel Shapiro, artist © 2019-2020 Joel Shapiro/ Artists Rights Society (ARS), New York.

"It's original," Dr. Goldstein said to explain why Mr. Shapiro's work appealed to him. "No other artist I know of does this kind of work."

Mr. Shapiro is known for constructing sculptures from simple rectangular shapes that convey an exuberant and often human quality. The idea, he said, is to find a form that visually and emotionally resonates.

"I think they're all playful – I hope so. They're very serious, but they're also playful. Play is a big part of making art."

Texas-inspired Wool work joins landscape

A work of art inspired by the ranches of Far West Texas now sits in the shade of two live oak trees near Seldin Plaza. The 15-foot-tall sculpture cast of solid stainless steel and clad in weathered copper was created by acclaimed painter and sculptor Christopher Wool.

Called *Untitled*, this newest artwork addition has a connection beyond that of the donor, Dr. Goldstein. As a young artist, Mr. Wool worked as a studio assistant to Mr. Shapiro, creator of two other sculptures nearby.

At the time, Mr. Wool focused on painting and would become known for his word paintings featuring stenciled letters on a white canvas background. A move to Marfa, Texas, in 2007 took his work in a new direction. In walks across ranchland, Mr. Wool would find small, swirling tangles of discarded steel wire left behind by ranchers mending their fences. He was intrigued by their spontaneous forms.

"I was trying to get that line myself in some of my paintings," Mr. Wool said of the three-dimensional loops and twirls he saw in the wire.

He began picking up the most interesting shapes and taking them back to his studio to manipulate into a finished form.

Today, the small maquettes Mr. Wool creates are 3D-scanned into a computer, where they are refined and reviewed by engineers to ensure the finished sculpture – blown up to massive scale – will be stable, said Mike Koller, a New York digital media technician who works with several sculptors to create digital 3D models. The design is then sent to a metal foundry north of Manhattan to be cast and welded.

Mr. Wool's first such creation was displayed in front of the Solomon R. Guggenheim Museum in 2013-2014. Later, in 2014, the same sculpture was moved to the Art Institute of Chicago, where Dr. Goldstein saw it and became intrigued.

"I'd never seen a sculpture like this before," he said.

Now he can see similarly impressive work simply by looking out his window onto Seldin Plaza.

"It's a unique piece of art," Dr. Goldstein said of the new sculpture, installed June 23. Ever the scientist, he compared the work's 184 welded steel sections to the fragments the human body assembles into genes.

Dr. Goldstein was joined by Dr. Podolsky and Ms. Crothers as the 6,000-pound sculpture was installed on an 18-inch-thick concrete foundation. Also present were Ms. Dunn, who arranged the purchase; Lawrence Luhring, of the Luhring Augustine gallery that represents Mr. Wool; and Mr. Roysdon, who oversaw site preparation prior to the sculpture's arrival.

"Dr. Goldstein's work and impact on this campus has long rested on the decades of discoveries made together with Dr. Mike Brown, which in addition to their scientific importance, have set a standard of excellence that is a cornerstone of UT Southwestern," said Dr. Podolsky. "With this sculpture, his generosity has created another legacy, which will enhance the experience of all who work [on] or visit the campus."

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Dr. Brown, a Regental Professor and Director of the Erik Jonsson Center for Research in Molecular Genetics and Human Disease, holds The W.A. (Monty) Moncrief Distinguished Chair in Cholesterol and Arteriosclerosis Research, and the Paul J. Thomas Chair in Medicine.

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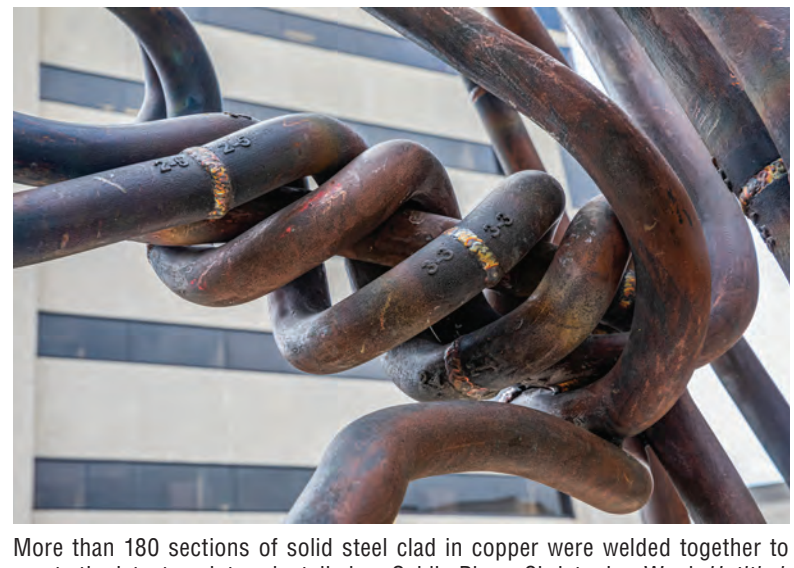
Untitled, by Christopher Wool, was inspired by the tangles of wire left behind by ranchers repairing their fences on ranchland near Marfa. Christopher Wool, *Untitled*, 2019, copper-plated steel. © 2019 Christopher Wool. All rights reserved. *Gift of Joseph L. Goldstein, M.D., 2021, and of Christopher Wool in memory of Glorye Wool, M.D., and Ira Wool, M.D., Ph.D.*



More than 180 sections of solid steel clad in copper were welded together to create the latest sculpture installed on Seldin Plaza. Christopher Wool, *Untitled*, 2019, copper-plated steel. © 2019 Christopher Wool. All rights reserved. *Gift of Joseph L. Goldstein, M.D., 2021, and of Christopher Wool in memory of Glorye Wool, M.D., and Ira Wool, M.D., Ph.D.*

Neurosurgery Chair envisions building on UTSW's clinical, research strengths to advance treatment

By Carol Marie Cropper

The opportunity to draw upon UT Southwestern's dual strengths in outstanding clinical care and translational research to develop new treatment options attracted Dr. Nader Pouratian, a neurosurgeon known for innovative surgical care for depression, blindness, and movement disorders, to the role of Chair of Neurological Surgery. UT Southwestern is ranked No. 19 in the nation by *U.S. News & World Report* in neurology and neurosurgery.

Additionally, the powerful potential of the Medical Center's Peter O'Donnell Jr. Brain Institute and the chance to help build the young brain research and treatment center caught his attention.

Dr. Pouratian, who joined UTSW April 1, holds an M.D. and a Ph.D. in neuroscience and was previously a Vice Chair at UCLA's David Geffen School of Medicine. He succeeds Dr. Hunt Batjer, who retired in December after serving as Chair of Neurological Surgery since 2012, and Dr. Carlos Bagley, Associate Professor of Neurological Surgery and Orthopaedic Surgery, who served as Interim Chair.

At UCLA, Dr. Pouratian was Professor and Vice Chair of Academic Affairs in the Department of Neurosurgery, with additional appointments and affiliations in Neuroscience, Bioengineering, and Radiation Oncology.

In his clinical practice, Dr. Pouratian focuses on surgical treatments for movement disorders, psychiatric disease, facial pain, and chronic pain syndromes, using modern techniques such as brain and spinal cord stimulation, radiosurgery, microsurgery, and targeted ablation. He is also a clinical researcher and prolific author of peer-reviewed scientific publications and a passionate educator and mentor.

Dr. Pouratian is currently involved in clinical trials testing surgically implanted stimulators in the brain to remedy blindness and treatment-resistant depression. He said he hopes to use advances in technology to develop new procedures to treat stroke, brain injuries, and neurological and psychiatric diseases.

Dr. Pouratian received his undergraduate degree in neuroscience from UCLA, then earned a combined medical degree and Ph.D. from the David Geffen School of Medicine, followed by a neurosurgical residency and functional neurosurgery fellowship at the University of Virginia.

"Dr. Pouratian's expertise will allow him to work closely with researchers and clinicians to improve treatment options for brain diseases and injuries and to discover ways to prevent such illnesses," said Dr. W. P. Andrew Lee, Executive Vice President for Academic Affairs, Provost, and Dean of UT Southwestern Medical School. "This strategic cooperation between the Department of Neurological Surgery and the O'Donnell Brain Institute will further elevate UT Southwestern as a national hub for excellence in neuroscience discovery and clinical care."

Indeed, the potential for such synergies is one of the reasons Dr. Pouratian listed for his decision to join UT Southwestern. In an interview during his first month here, he shared his vision for the Department.

Why did you decide to join UTSW?

Most of all it was the vision of UT Southwestern and its leadership to continue to transform and evolve as a leader in academic medicine.

The primary reason I decided to become an academic neurosurgeon was, first and foremost, the opportunity to take care of patients with diseases of the brain. But I was almost equally intrigued by the unique opportunity neurosurgery provides to study and learn about how the brain works. To do this kind of human neuroscientific discovery takes a collaborative environment with clinician-scientists like myself and translational neuroscientists who want to work together and maximize the opportunity.

At the O'Donnell Brain Institute, under Director Dr. William T. Dauer, human neuroscience is a high priority and a major area of investment. Building bridges between basic sciences and human neuroscience is a big part of the vision, which was attractive to me.

What are some areas of special interest?

Personally, my passion has been at the intersection of neurological care, engineering, and technology, with a focus on developing new therapies – including for patients whom we have not traditionally cared for with neurosurgical therapies, like patients with psychiatric disease or patients with blindness.

I am currently involved in a clinical trial treating a small number of patients with complete blindness using a specially designed device that is implanted in the patient's brain. Together with a California company that I also consult for, Second Sight Medical Products Inc., we received National Institutes of Health funding to develop and test the device. Our preliminary investigations have revealed positive results, allowing people with complete blindness to see patterns of flashing lights that they are learning to interpret and decode. This trial began when I was at UCLA, and I am hoping to continue this clinical research soon at UT Southwestern, as well.

Dr. Nader Pouratian

Another area of particular interest is the treatment of patients with treatment-resistant major depression. Just like other diseases that we treat with brain stimulation – like Parkinson's disease – depression affects the brain and results in abnormal brain activity. We have a fairly good but incomplete understanding of the parts of the brain and the networks in the brain that are involved in depression. Our approach is to put stimulators in these precise areas of the brain, using advanced neurosurgical techniques with cutting edge imaging. By stimulating those areas of the brain that are critically related to depression, we aim to make those brain networks function more normally and help people with depression. We are looking forward to launching two separate clinical trials here in this area in collaboration with our outstanding colleagues in Psychiatry.

What areas do you want to focus on as Chair?

UT Southwestern neurosurgery is known for its innovation. I hope to continue to promote and build on that spirit of innovation. One of the newest and most innovative technologies we have at UT Southwestern as part of the O'Donnell Brain Institute is focused ultrasound. This technology uses precisely targeted ultrasonic energy to treat or destroy tissue inside the body without the need to make an incision. The FDA has approved this technology for treating essential tremor and tremor-dominant Parkinson's disease.

Beyond treating movement disorders, we are excited to collaborate with our partners in Radiology to explore even more innovative applications. For example, we are looking forward to launching a novel study to open the blood-brain barrier to better deliver targeted therapies to the brain, treating epilepsy as well as potentially treating tumors and chronic pain. This is just one example of helping to invent the future of our field, in collaboration with our outstanding clinical and scientific partners at UTSW.

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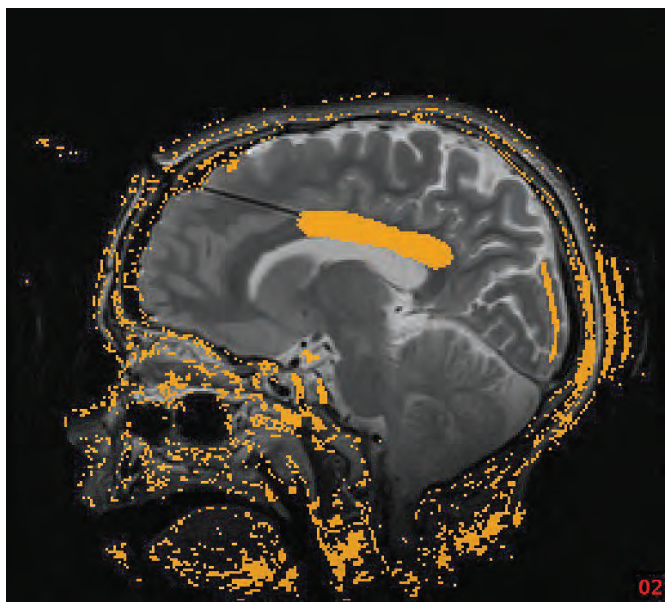
Dr. Dauer holds the Lois C.A. and Darwin E. Smith Distinguished Chair in Neurological Mobility Research.

Dr. Lee holds the Atticus James Gill, M.D. Chair in Medical Science.

Dr. Pouratian holds the Lois C.A. and Darwin E. Smith Distinguished Chair in Neurological Surgery.

Laser procedure offers advantages for rare pediatric epilepsy surgery



MRI with heat map overlay shows laser ablation of the main body of the corpus callosum. Credit: Dr. Angela V. Price.

By Christen Brownlee

Using a laser for a rare brain surgery to treat drop seizures, which cause a child with epilepsy to suddenly fall, holds some advantages over a traditional open craniotomy, including shorter hospital stays for patients, a study led by UT Southwestern researchers indicates. The findings, published in the *Journal of Neurosurgery,* provide the first quantitative data comparing the two types of surgery, called corpus callosotomies.

"Our data shows that laser corpus callosotomies are easier on the child to recover from and, consequently, easier on parents and families," said Dr. Angela V. Price, Assistant Professor of Neurological Surgery and Pediatrics, who also leads the surgical epilepsy service at Children's Health.

In recent years, Dr. Price and a few other pediatric neurosurgeons across the country have used a minimally invasive procedure in which a tiny laser is inserted through a small incision in the skull to burn away a portion of the corpus callosum, a band of tissue that connects the left and right hemispheres of the brain. The traditional operation – an open corpus callosotomy – involves a large incision to remove a portion of the skull for access.

The study by Dr. Price and colleagues reviewed 19 patients who underwent 24 procedures: 16 had gone through open corpus callosotomies and eight underwent laser procedures.

For both procedures, drop seizures were practically eliminated and post-surgical complications were minimal. But the laser technique required a patient to spend less than half the time in the pediatric ICU and decreased the overall length of stay in the hospital (4.6 days versus 5.7 days). In addition, children required no inpatient rehabilitation compared with about 20 percent of those receiving open repair, and lost 12 times less blood (7 milliliters versus 84 milliliters).

Dr. Price noted that the operating time for laser procedures was nearly double that of the open procedure group (492 minutes versus 249 minutes), partially due to MRI imaging before and during the operation. The laser patients also took corticosteroid drugs about three times longer than those who had open procedures.

"Children's Medical Center is the only hospital providing these procedures in Dallas, and one of relatively few in the U.S.," said Dr. Price, also a member of the Peter O'Donnell Jr. Brain Institute. "As surgeons better understand the advantages of these procedures, I predict they'll become a more popular option for patients whose seizures are best controlled by these minimally invasive procedures."

Rankings Continued from page 1

aortic valve surgery, back surgery (spinal fusion), COPD, colon cancer surgery, diabetes, heart attack, heart bypass surgery, heart failure, hip fracture, kidney failure, lung cancer surgery, pneumonia, and stroke.

UT Southwestern Pediatric Group faculty at Children's Medical Center Dallas earned recognition again this year. Children's Medical Center Dallas was rated among the nation's best pediatric hospitals by *U.S. News* for 2021-2022, and is the only pediatric hospital in North Texas to rate in all 10 specialties.

Clements University Hospital previously received national distinction for high patient satisfaction scores, quality and safety efforts, and innovative design. UTSW is listed among the top 5 percent of hospitals nationally for consistent delivery of clinical quality, and among top hospitals for patient experience and routine specialty care in areas including cardiovascular, gastroenterology, orthopedic, and neurosurgical care. Organizations also rate UTSW high for patient satisfaction efforts such as physician and nurse communications, medication and hospital discharge instructions, and hospital cleanliness and quietness.

"The recognition reflects a commitment to service excellence that resonates across our health system and is shared by our physicians, nurses, advanced practice providers, trainees, and vital supporting staff," said Dr. John Warner, Executive Vice President for Health System Affairs. "By working together, our multidisciplinary teams advance the quality of care and outcomes we are able to achieve for our patients and their families."

The 12-story, three-tower Clements University Hospital, along with recent expansions of its brain, cancer, and radiation oncology care and its outpatient clinical space, means the health system is ideally positioned to continue to meet Texas' burgeoning health care needs. The hospital expansion has prepared UT Southwestern for referrals from continued growth of the Southwestern Health Resources network, a partnership with Texas Health Resources to better integrate delivery of care across North Texas. The network encompasses four of the top six rated hospitals in DFW.

Besides Clements University Hospital, this network includes Texas Health Presbyterian Hospital Dallas, ranked No. 3 in DFW; Texas Health Harris Methodist Hospital Fort Worth, tied for No. 4; and Texas Health Harris Methodist Hospital Southwest Fort Worth, No. 6 in DFW.

In other institutional measures, UTSW rates No. 1 among global health care institutions in the 2021 Nature Index for its published research, UT Southwestern Medical School rates nationally among "Best Graduate Schools," and the Medical Center has nationally rated programs in the UT Southwestern Graduate School of Biomedical Sciences. UT Southwestern's Harold C. Simmons Comprehensive Cancer Center is the only National Cancer Institute-designated comprehensive cancer center in the region – one of 51 in the nation, placing it among the top 4 percent of the approximately 1,500 cancer centers in the U.S. UTSW is designated an Advanced Comprehensive Stroke Center by the Joint Commission and the American Heart Association/American Stroke Association, and has one of the nation's leading epilepsy clinics – a Level 4 center, the highest possible level by the National Association of Epilepsy Centers – part of the Peter O'Donnell Jr. Brain Institute.

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

Dr. Warner holds the Jim and Norma Smith Distinguished Chair for Interventional Cardiology, and Nancy and Jeremy Halbreich, Susan and Theodore Strauss Professorship in Cardiology.

Program offers help for those suffering long after a COVID-19 infection

By Carol Marie Cropper

Stephen Lummus knew he was putting himself at risk when he went to New York last year to help beleaguered hospital workers during the COVID-19 surge. "This could be the last time you see your family," he remembered thinking.

The 58-year-old physician assistant survived his April 2020 trip to the Northeast. He also survived when, after returning to the Dallas area, he caught the virus that causes COVID-19 in December while working long hours testing patients for COVID-19 at urgent care facilities in North Texas.

But in many ways, the worst began after he "recovered" from COVID-19. Mr. Lummus – like hundreds of others who have sought treatment at UT Southwestern's COVID Recover rehabilitation program – discovered that symptoms can linger for months after the virus abates. In January, two weeks after he thought he had beaten COVID-19 with just a quarantine at home, a flare-up came with mental fog, shortness of breath, and unbearable fatigue that finally put him in the hospital.

Perhaps 20 to 30 percent of COVID-19 patients experience such aftereffects – a problem referred to as "long-haul," "long," or post-acute COVID if symptoms linger for four weeks or more following the initial infection, said Dr. Surendra Barshikar, who directs UTSW's COVID Recover program and is Vice Chair and Assistant Professor of Physical Medicine and Rehabilitation. The UTSW program is thought to be the first and still one of just a few such programs in North Texas.

An April article in *Nature Medicine* examined studies from around the world and found varying prevalence rates for long-term symptoms. Of 488 patients surveyed after discharge from 38 Michigan hospitals, 32.6 percent complained of persistent symptoms. In a report from the United Kingdom, 74 percent of those studied who had survived hospitalization for COVID-19 had post-acute symptoms. Of 1,733 patients evaluated in Wuhan, China, six months after contracting the virus, 76 percent still had at least one symptom, according to yet another report. Fatigue, shortness of breath, joint pain, and loss of taste/smell were among the most common aftereffects.

At UT Southwestern's COVID Recover program, with locations in Dallas and Frisco, the No.1 symptom is fatigue, Dr. Barshikar said, followed by mental fog and shortness of breath. Then there are psychological problems such as anxiety, worsened depression, and even post-traumatic stress disorder, followed by dysfunction of the autonomic nervous system that regulates heart rate and digestion, which can cause dizziness and heart rate spikes.

Stephen Lummus participates in an exercise program as part of UT Southwestern's COVID Recover program, aimed at helping those suffering from longer-term effects of COVID-19.

Cause of long-term symptoms unknown

"The exact cause of these lingering symptoms is not known," said Dr. Barshikar. "We don't know how soon patients will recover, but we are seeing progress and do expect them to improve."

It is known that COVID-19 attacks the lungs and leads to a massive inflammatory response. The heart, kidneys, and liver also can suffer damage.

Residual inflammation of nerves and muscles may be at the root of some of the long-term symptoms, such as fatigue, Dr. Barshikar said. Scarring of the lungs can cause shortness of breath and difficulty breathing. Being isolated and fearful while hospitalized or quarantined could contribute to psychological problems, he added.

Rehabilitation physicians anticipated some residual problems for patients requiring ventilator support and hospitalized for a long period, said Dr. Juan Cabrera, Assistant Professor and Medical Director of the Physical Medicine & Rehabilitation Clinic at UT Southwestern's Frisco campus and head of the COVID Recover program there. More surprising and challenging has been the number of survivors with persistent symptoms following mild to moderate COVID-19 symptoms – a group that makes up the majority of those being treated for long COVID at UT Southwestern, he said.

Dr. Surendra Barshikar directs the COVID Recover program.

Dr. Kathleen Bell, Chair of Physical Medicine & Rehabilitation, was one of the early experts to sound the alarm. UT Southwestern opened its COVID Recover clinics in April 2020, soon after the state's March lockdown. Drs. Bell and Barshikar became speakers in panel discussions and media briefings arranged by the Centers for Disease Control and Prevention and the Infectious Diseases Society of America to discuss long-term COVID-19.

UTSW's COVID Recover clinics offer a combination of physical therapy to help patients regain strength and mobility, occupational therapy to improve activities of daily living, and speech therapy for cognitive rehabilitation. A four-week virtual group therapy program is offered to help patients address psychological, sleep, and other issues they may face. Neuropsychologists and licensed professional counselors are available at each site for those who need more individualized attention. If needed, consultants have been identified in pulmonology, cardiology, neurology, and psychiatry for additional care.

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Dr. Bell holds the Kimberly-Clark Distinguished Chair in Mobility Research.

Seeking a return to normal

James Doyle, a Lewisville pharmaceutical marketer who believes he contracted COVID-19 on a plane ride home from a conference in June 2020, joined the COVID Recover program in September. Mr. Doyle, 55, spent two weeks at William P. Clements Jr. University Hospital in July 2020 after returning from his conference. "I was 20 or 30 minutes away from being on a ventilator," he recalled.

He got out of the hospital late that month but said "August and September were miserable. Just getting out of bed and going to the restroom was like a marathon. I just couldn't breathe."

For a man used to snow skiing in Utah and hiking in Wyoming, the change was hard to accept. "We're a very athletic family, so it was very surprising to me to be out of breath as I walked down the street," Mr. Doyle said.

In November – two months after entering the COVID Recover program – he was about halfway back to normal, he said. By January, when he left the program, he was almost his old self. While he still can't exercise as long as he did before, he was able to go skiing with his family in February and hike in Wyoming in May.

James Doyle, another COVID Recover patient, receives plasma treatment during his initial treatment.

Meanwhile, Stephen Lummus, who entered the program this March, is still working toward recovery. By early June, he still hadn't been able to return to work. Brain fog sometimes makes it difficult to say the right word. He told of having to describe the family TV ("that thing in our room – the thing you watch") because he couldn't think of the word for it.

He has some difficulty breathing, but that and most of the other problems have improved. "Before, I couldn't speak without breathing hard. Now I can take 30-minute walks. It's so much better than it was and it is getting better," he said.

Mr. Lummus, with his medical training, said he likes the COVID Recover program's multidisciplinary approach, addressing neuropsychology, physical therapy, pulmonary, and cardiology concerns. But the best part is simply the reassurance that what he is going through isn't all in his head – and that he is not alone.

"Not only do I feel like I'm not going crazy, I feel like there's hope for the future. I can see that the light at the end of the tunnel isn't a train. Hey, I'm going to make it through to the other side," he said.

RNA Continued from page 1

for RNAs to regulate cellular processes.

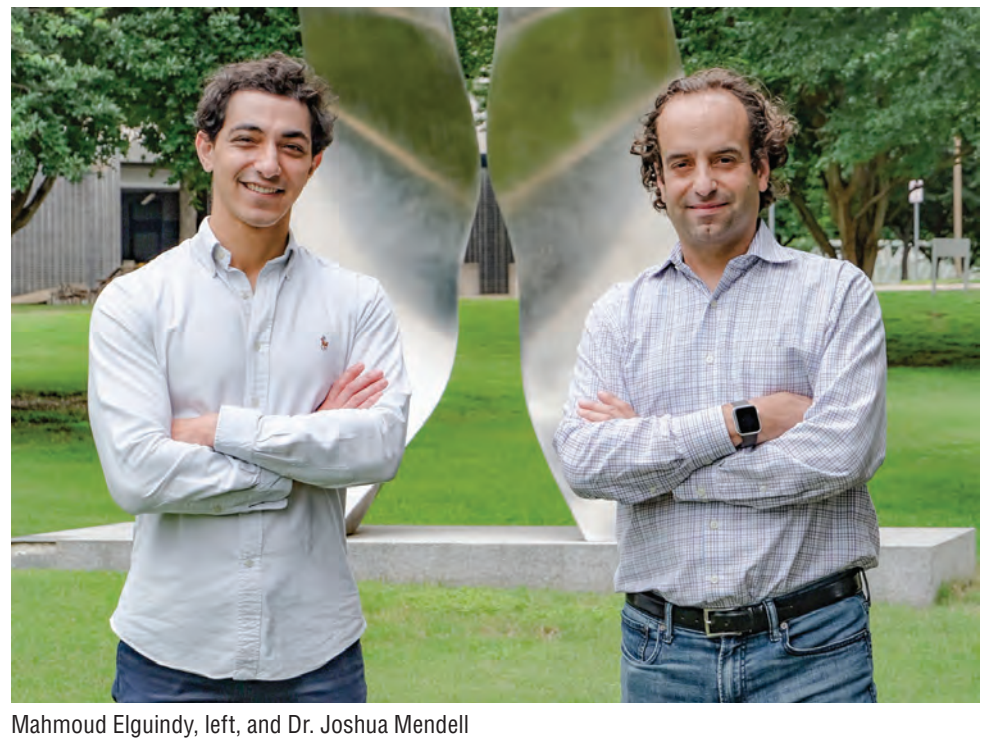
"It's becoming more and more clear that phase separation is an important organizing principle in cells," said Dr. Joshua Mendell, Professor of Molecular Biology and a Howard Hughes Medical Institute (HHMI) Investigator at UTSW who led the study published in *Nature*.

Other scientists at UTSW, including Dr. Michael Rosen, Chair of Biophysics, a member of the National Academy of Sciences (NAS), and an HHMI Investigator, and Dr. Steven McKnight, Professor of Biochemistry and a member of NAS and the National Academy of Medicine, have previously found that phase separation participates in many cellular pathways.

"Our work," said Dr. Mendell, "builds upon their findings, uncovering how phase separation enables some RNAs to regulate the activity of proteins that they interact with."

Dr. Mendell and Mahmoud Elguindy, a student in UTSW's Medical Scientist Training Program, uncovered this role for phase separation by studying an RNA known as "non-coding RNA activated by DNA damage," or *NORAD*. Although *NORAD* isn't directly responsible for generating proteins, it binds and inhibits Pumilio, a protein that represses the expression of hundreds of other messenger RNAs that encode proteins involved in cell division.

Previous work from the Mendell lab showed that human cells and lab animals genetically engineered to lack *NORAD* have too much active Pumilio, which prevents them from maintaining consistent numbers of chromosomes during cell division and causes them to prematurely age.



Mahmoud Elguindy, left, and Dr. Joshua Mendell

On the flip side, mutations that lead to too little Pumilio have been linked to neurodegenerative diseases in humans.

But a fundamental question remained as to how *NORAD* regulates Pumilio to prevent disease. Because *NORAD* is only one RNA of hundreds in the cell that is bound by Pumilio, it was unclear how *NORAD* is able to outcompete these other RNAs to control levels of active Pumilio.

To answer this question, Dr. Mendell and Mr. Elguindy used microscopy to locate *NORAD*-Pumilio complexes in cells. They found that these complexes dotted the cells' interiors, forming their own oil droplet-like structures separate from the cytoplasm, which they named "*NORAD*-Pumilio bodies."

Further investigation showed that about half the Pumilio in cells was sequestered in *NORAD*-Pumilio bodies, and that phase separation was critical for concentrating Pumilio in these structures. Not only did Pumilio bind to numerous sites on each *NORAD* molecule, but interactions between Pumilio molecules also played a central role in droplet formation. This combination of attraction between the RNA and protein molecules provides a strong driving force that separates Pumilio proteins from the surrounding cellular environment, Mr. Elguindy said, preventing them from interacting with other RNAs.

When the researchers used techniques to disrupt this phase separation, *NORAD* was no longer able to sequester enough Pumilio, leading to chromosomal abnormalities.

"While phase separation has been observed in many different settings in cells, the scientific community has debated which cellular activities require this process," said Mr. Elguindy. "Our study showed that in this instance, when you perturb phase separation, there are real consequences."

Dr. Mendell added that better understanding the *NORAD*-Pumilio system could lead to new ways to counter symptoms associated with aging and to treat neurodegenerative diseases. In addition, looking for more examples of phase separation by other RNA molecules could shed light on how cells regulate other key processes.

This work was funded by grants from the National Institutes of Health (R35CA197311, P30CA142543, P50CA196516) and The Welch Foundation (I-1961-20180324). Drs. Mendell, McKnight, and Rosen are all members of the Harold C. Simmons Comprehensive Cancer Center.

■

Dr. McKnight holds the Distinguished Chair in Basic Biomedical Research.

Dr. Rosen holds the Mar Nell and F. Andrew Bell Distinguished Chair in Biochemistry.

ADVANCES IN RADIATION ONCOLOGY

Anti-tumor mechanisms may improve radiation therapy

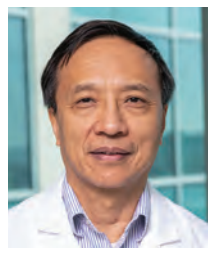
From Staff Reports

An international team of cancer researchers has identified important mechanisms that activate anti-tumor immune response during radiation therapy, findings that could help improve the efficacy of radiation treatments.

The team, which includes members from UT Southwestern's Harold C. Simmons Comprehensive Cancer Center, identified two key inflammasome sensors – complex proteins that sense damage or threats to cells from disease or tissue damage. These sensors play a key role in rallying the body's innate immune system in response to radiation.

Radiation therapy (RT) primarily relies on killing tumor cells but also depends on immune system stimulation. The inflammasome is a double-edged sword that promotes inflammation-associated diseases, including cancer, and contributes to radiation-induced tissue damage. It also plays a role in anti-tumor immunity through mechanisms that are poorly understood. In this study, the research team from Dallas, Chicago, and China demonstrated that the radiation-induced activation of AIM2 and NLRP3 inflammasomes coordinate to induce some of the anti-tumor effects of radiation.

Dr. Hasan Zaki



Dr. Yang-Xin Fu

"Our study demonstrated a potential mechanism of anti-tumor immune response of radiation and showed that the inflammasome plays a critical role in orchestrating radiation-induced anti-tumor immunity," said Dr. Hasan Zaki, Assistant Professor of Pathology and corresponding author of the study in *Science Immunology*.

Researchers first observed that radiation is less effective in suppressing tumor growth in caspase-1-deficient mice, suggesting that the enzyme caspase-1 plays an important role in inhibiting tumor growth following radiation therapy, explained senior author Dr. Yang-Xin Fu, Professor of Pathology, Immunology, and Radiation Oncology and a Cancer Prevention and Research Institute of Texas (CPRIT) Scholar in Cancer Research.

"As we dissected which inflammasome sensor is involved in RT-induced anti-tumor activity, we found that both AIM2 and NLRP3 inflammasomes are required for effective radiation responsiveness," Dr. Fu said.

As they investigated further, they identified how the pathways function: The IL-1 receptor signaling in dendritic cells promotes cross-priming of T cells following irradiation of the tumor.

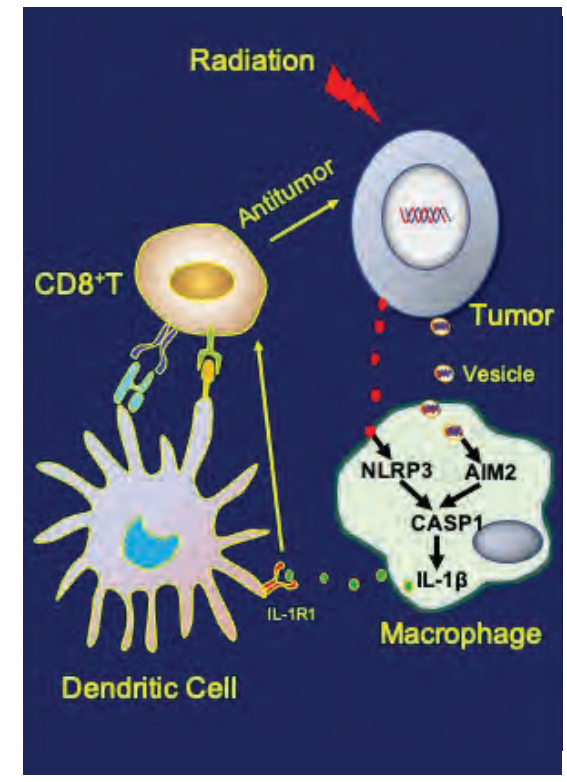
"These mechanisms offer a potential means of enhancing the efficiency of radiation therapy," said Dr. Fu, who investigates the mechanisms underlying IR-induced extrinsic resistance and tests newly developed personalized immunotherapies to overcome these resistance mechanisms for improved and long-lasting tumor control.

Dr. Zaki's lab is working to understand the physiological functions of pathogen recognition receptors and exploring the role of those receptors in the pathogenesis of intestinal inflammatory diseases and cancer.

■

Dr. Fu holds the Mary Nell and Ralph B. Rogers Professorship in Immunology.

More online: Read the full story in the newsroom at **utsouthwestern.edu/newsroom**.



Radiation activates AIM2 and NLRP3 inflammasomes to enhance IL-1 signaling in dendritic cells, leading to anti-tumor immunity.

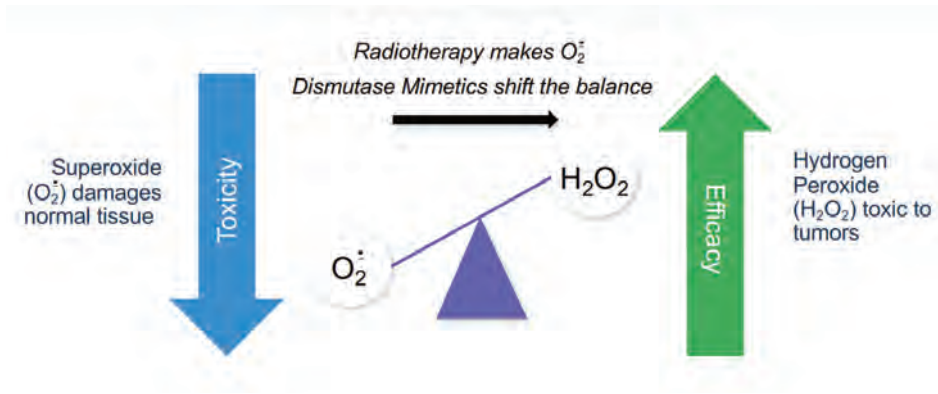
Experimental drug makes radiation therapy more effective

By Christen Brownlee

An experimental drug that has shown promise in protecting healthy tissue from damage caused by radiation therapy also appears to enhance radiation's capacity to kill tumors, a UT Southwestern-led study shows. The findings, published online in *Science Translational Medicine*, could provide a much-needed boost for radiation treatments to fight cancer.

The drug, avasopasem manganese (AVA), has already shown potential in clinical trials to prevent the side effect of acute mucositis. This condition commonly occurs in head and neck cancer patients when radiation therapy damages mucous membranes. However, for this drug to become part of clinical care, it should protect healthy cells from radiation but not cancer cells, explained study leader Dr. Michael Story, Professor of Radiation Oncology and a member of the Harold C. Simmons Comprehensive Cancer Center.

Dr. Michael Story



The experimental drug avasopasem manganese protects healthy tissue while enhancing radiation's capacity to kill cancerous tumor cells by converting superoxide to hydrogen peroxide. Credit: Dr. Michael Story.

To determine whether AVA was accomplishing this goal, Dr. Story and colleagues at UTSW and the University of Iowa treated cancerous cell lines with this compound before exposing them to radiation. The cells that received the drug were not protected from radiation and, surprisingly, appeared in some cases to respond more to radiation compared with those that did not receive AVA, particularly at high radiation doses.

This phenomenon also occurred in cancerous cells that had been implanted in mice and allowed to grow into tumors. The tumors shrank significantly more when animals were treated with AVA before receiving a single high dose of radiation, similar to a technique known as stereotactic ablative radiotherapy (SAbR) that is used for cancer therapy, compared with mice that did not receive the drug. When the treated mice received the drug both before and after radiation, in some cases, their tumors disappeared.

These positive results in animals were found in lung, pancreatic, and head and neck cancers. Further experiments showed that AVA appears to exert its enhanced tumor-killing effects by converting superoxide – damaging oxygen ions generated by high doses of radiation – to hydrogen peroxide at levels that overwhelm a tumor's ability to tolerate hydrogen peroxide. Furthermore, using an engineered cell line that overexpressed an enzyme that rids tumors of excess hydrogen peroxide, the anti-tumor effect was nearly eliminated.

Dr. Story, a member of the Simmons Cancer Center's Experimental Therapeutics Research Program, noted that AVA is currently being tested in phase one and phase two clinical trials to enhance therapy, including one clinical trial that combined SAbR with AVA that nearly doubled overall survival in pancreatic cancer patients.

"With this drug," he said, "the radiation doses we deliver could be profoundly more effective, while at the same time contribute to protecting adjacent normal tissues."

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Dr. Story holds the David A. Pistenmaa, M.D., Ph.D. Distinguished Chair in Radiation Oncology.

More online: Read the full story in the newsroom at **utsouthwestern.edu/newsroom**.

Conaway Continued from page 1

building an environment that can be conducive to providing the very best research opportunities to colleagues. As the Dean of Basic Research, my goal is to enable everyone to succeed."

Dr. W. P. Andrew Lee, Executive Vice President for Academic Affairs, Provost, and Dean of UT Southwestern Medical School, said Dr. Conaway will seek to advance the University's premier basic research programs.

"The vast experience and knowledge that Dr. Conaway brings positions her to guide the expansion and coordination of core resources and facilities needed to support state-of-the-art biomedical investigations and keep UT Southwestern at the forefront of innovation," Dr. Lee said.

UT Southwestern's legacy of research excellence attracted Dr. Conaway to her new role and she said her top goal as Dean will be to build upon that tradition.

In support of this goal, one area of emphasis will be bioinformatics, the subdiscipline of biology and computer science focused on acquiring, storing, analyzing, and disseminating biological data.

"Technologies such as advanced imaging and genomics, proteomics, and metabolomics all generate huge amounts of data," Dr. Conaway said. "A great many of the opportunities in science today come from the ability to leverage and interpret these large datasets."

To do that, she added, requires significant investment in computational hardware as well as people – additional faculty members with expertise in computational biology and data sciences, postdoctoral fellows, and students interested in the growing field. Ensuring that UT Southwestern has the right combination of tools and manpower will be an important part of her job, Dr. Conaway said.

Another critical factor will be continuing to expand diversity at all levels of basic science. As one of only a few women administrating basic research at an academic medical center in the U.S., Dr. Conaway said she's providing crucial representation for other women in the sciences. Continuing to increase the number of underrepresented minorities at all levels at UT Southwestern is another priority for advancing science here and beyond.

A Scientific Upbringing

Dr. Conaway's love of science took root as a child when she accompanied her scientist father to his lab on Saturday mornings, tinkering with lab supplies while he conducted experiments. Later, as a student at Bryn Mawr College, she was torn between majoring in political science or taking on a double major in chemistry and biology. Her decision was cemented after a summer research program at Squibb Corp., one of the precursor companies to Bristol Myers Squibb, where her father worked at the time as a clinical pharmacologist.

Dr. Joan Conaway tours UTSW basic science labs with Dr. David Russell, left, and Nobel Laureate Dr. Joseph Goldstein.

"Bench science brought together two things that I really enjoy: being able to think and solve problems, and working with my hands," she said.

Dr. Conaway earned her doctorate in cell biology from Stanford University School of Medicine, where she worked in the lab of Dr. Roger Kornberg, who later won the Nobel Prize in Chemistry in 2006. There, she began tackling the puzzle of transcription with Dr. Ron Conaway, whom she'd married two years prior – the beginning of a careerlong collaboration between the two scientists. As they migrated together to UT Austin, the Oklahoma Medical Research Foundation, and finally the Stowers Institute, their work remained a true partnership, with each taking turns as senior author on publications. Both were elected to the American Academy of Arts and Sciences in 2002. And last year, Dr. Joan Conaway was elected to the National Academy of Sciences.

Together, the two identified a collection of transcription factors including elongin and ELL and helped define their roles in transcription supporting RNA polymerase II and working with other cofactors. Subsequent research by their lab and others has shown that both elongin and ELL play key roles in cancer and other diseases in which transcription can go awry.

Crediting supportive colleagues and collaborators for encouraging these advances, Dr. Conaway – who will not have her own lab at UT Southwestern – noted that she hopes to build on UT Southwestern's tradition of research excellence and collegiality and continue to foster an environment conducive to discovery, where scientists celebrate each other's success.

"Being in a position where I can support faculty, staff, and students and see to the best of my ability that we have the resources, cutting-edge facilities, and colleagues needed so UT Southwestern is the best place in the world to do science will be tremendously satisfying," she said.

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Dr. Conaway holds the Cecil H. Green Distinguished Chair in Cellular and Molecular Biology.

Dr. Lee holds the Atticus James Gill, M.D. Chair in Medical Science.

Dr. Russell holds the Eugene McDermott Distinguished Chair in Molecular Genetics.

Congratulations UTSW graduates of 2021!

In May, the UT Southwestern Medical School and the Graduate School of Biomedical Sciences celebrated their graduations with in-person commencement ceremonies on South Campus. Dr. Helen Hobbs, UTSW Director of the Eugene McDermott Center for Human Growth and Development and a Howard Hughes Medical Institute Investigator, gave the May 8 commencement address for the Medical School. Dr. Lora Hooper, UTSW Chair of Immunology, delivered the May 20 keynote for the Graduate School ceremony.

More online: To see more photos from both commencement ceremonies, go to *Center Times Plus* at **utsouthwestern.edu/ctplus.**

Graduate students were happy to celebrate their achievements together after pandemic protocols separated the UTSW community for more than a year.

Dr. Reshma Narain receives her Medical School graduation hood from marshal Dr. Peter Michaely.

Dr. Mike Henne hoods doctorate recipient Dr. Sanchari Datta.

Medical School graduates recite the Physician's Oath.

Dr. Natasha Houshmand was announced as the 2021 Ho Din Award recipient during the Medical School ceremony.

Dr. Lora Hooper delivers the Graduate School commencement address.

Doctorate recipient Dr. Anna Lee is hooded by Dr. Luke Rice.

Dr. Beth Kennard congratulates doctorate recipient Dr. Lucas Zullo.

UTSW President Dr. Daniel K. Podolsky delivers opening remarks at the Medical School ceremony.

Dr. Helen Hobbs gives the Medical School commencement address.

AR Surgery Continued from page 1

Dr. Khazzam, who has completed about 30 augmented reality shoulder replacements since April.

"Essentially, we can perform the entire surgery and estimate post-surgical mobility and function in virtual reality before we even touch the patient in the OR," he said. "What's more, I can show patients what we'll do prior to surgery, which helps them feel more informed and engaged in their care."

The process begins when the patient's preoperative shoulder CT scan is entered into special software, which then generates a 3D model of the person's anatomy. Using this model, physicians can examine the patient's anatomy, plan incision points, mark the points for the anchor pins, and adjust the prosthetic device.

"We can conduct a virtual 'dry run' implanting the shoulder in the software environment so we can determine what works best for that patient's anatomy and pathology," Dr. Khazzam said. "Ultimately, this 'dry run' becomes our surgical plan."

A run-through of the surgery and estimate of post-surgical mobility and function can be done in virtual reality before the actual operation. Wearing the Microsoft HoloLens AR glasses during surgery makes it possible to see, navigate, and manipulate the entire surgical plan during the procedure. The surgeon can scroll through it and zoom in or out while comparing it in real time to the patient's anatomy. Being able to reference the surgical plan during the operation adds another layer of checks and balances to already highly precise shoulder replacement positioning and procedures.

"It's almost like what people see when playing Pokémon Go – you see the real world, with a cartoon-like overlay of the surgical plan," Dr. Khazzam said. "Rather than an immersive VR experience, it's a supplement to reality."

Because this technology is in its infancy, benefits regarding post-surgical pain and recovery times haven't been studied yet, although some research into the effects of AR in orthopedic surgery is underway.

Lynda and Monte Perkins

For now, this procedure is being performed for every shoulder replacement patient who has had CT imaging properly formatted to suit the software. It is anticipated that future improvements will enhance the accuracy of placing the implants, cutting the bone, and determining the trajectory of the screws in the hardware.

'The only way to go'

"We do know that better planning leads to better surgeries," Dr. Khazzam said. "Research shows that 3D modeling can result in a highly accurate restoration of the patient's anatomy and precise positioning of the implant. Augmented reality certainly seems like a game-changing advancement for shoulder repair and replacement surgery."

The results have exceeded the couple's expectations.

"When Monte went to his first physical therapy appointment, they could not believe the movement he had in his arm already," Mrs. Perkins said. "And every day, we notice he's able to do something he wasn't able to do before the surgery. This really is the only way to go."

Mrs. Perkins, whose husband has also battled lung and liver cancer since 2018, said she feels fortunate to have an academic medical center nearby because physicians are constantly learning new techniques and patients have access to the most up-to-date treatments.

"Monte's excited and proud to be one of the first people to have had an augmented reality shoulder replacement done," she said. "He's back at our family jewelry store in Irving, working, and I joke with him that I'm living with a celebrity."

UT Southwestern celebrates first Founders Day with tradition of giving

By Robert D. Waller

From the beginning, community generosity has fueled UT Southwestern's achievements. Numerous academic and civic leaders have shaped the University's vision, but Dr. Edward H. Cary planted the first seed in 1943 when he pitched Dallas philanthropist Karl Hoblitzelle and a coalition of business leaders the idea for a leading medical center in North Texas.

What started with their act of giving 78 years ago led to the UT Southwestern of today. Ranging from award-winning patient care and groundbreaking discoveries to accomplishments of renowned scholars and Nobel Laureates, the University's litany of accolades is surpassed only by its impact on the lives of students and patients through exemplary education, research, and patient care.

On May 5, alumni honored that heritage by commemorating the anniversary of the institution's creation by starting a new Founders Day tradition. Founders Day is an opportunity for all alumni to celebrate UT Southwestern's achievements with a day of giving back to the institution. In the weeks leading up to May 5, alumni were encouraged to make a gift – of any amount – to invest in the institution's future.

Hughes challenge amplifies scholarship giving

A gift from UTSW alumni Drs. Linda and Lannie Hughes magnified fundraising efforts. Inspired by the message of Founders Day and hoping to inspire generosity from others, the couple gave $25,000 to be used as a matching challenge to raise additional funds for UT Southwestern Medical School student scholarships.

The Hughes' gift provided an opportunity for alumni of the Medical School to double their scholarship giving for Founders Day. Gifts were matched dollar-for-dollar up to the $25,000 goal. Enthusiastic responses surpassed the challenge, doubling the impact of the Hughes' generosity.

For the married couple, it was a chance to give back and create opportunities for future generations of UT Southwestern physicians.

"When we graduated from medical school it was inexpensive. We ended up with no debt," said Dr. Linda Hughes. "That is simply not true today, as so many students face enormous debt."

Dr. Lannie Hughes graduated from UTSW in 1966 and went on to specialize in gastroenterology care and serve as a battalion surgeon in the Vietnam War. A founding member of the Dallas Diagnostic Association, he retired as founding physician and Medical Director of Baylor Scott & White – Plano. Dr. Linda Hughes was one of four women to graduate from UTSW in 1967 and later served as President of the UT Southwestern Alumni Association. A board-certified psychiatrist, she was the first female Medical Director of Charter Medical Center and held the same role at several other psychiatric hospitals and programs.

"Both of us feel fortunate to have attended UT Southwestern, and this gift is very much a reflection of our gratitude," said Dr. Lannie Hughes. "We've always felt the quality of education was just outstanding, and it gave us the vital preparation to go into our chosen practices."

Organizers are already planning Founders Day activities for May 5, 2022, to encourage alumni giving and community support.

Drs. Lannie and Linda Hughes

Family touched by lung transplant patient's gift pays it forward

By Carol Marie Cropper

Sometimes "paying it forward" creates a web of good works that leads right back to the giver. That's the story of Tim Ervin, who in 2014 received a lifesaving double-lung transplant at UT Southwestern.

Mr. Ervin was a talented trumpet player before pulmonary fibrosis damaged his lungs and forced him to rely on oxygen tanks while awaiting an organ transplant. He would recover, going on to fulfill a life goal of playing at a professional sports venue. His career had been helped along by Jack W. White, the father of a high school friend and fellow bandmate who was an Associate Professor of Music and Director of Bands at Northeast Louisiana University (now University of Louisiana at Monroe).

Tim Ervin plays taps at the August 2020 funeral of Jack W. White, his college music professor, mentor, and friend. Photo courtesy of Paul Stillings.

Jack W. White holds a microphone for Tim Ervin as he performs a solo during halftime at a 1979 Northeast Louisiana University football game. Photo courtesy of Alan Moore.

Mr. White recruited Mr. Ervin with a college scholarship in 1976, then trained him in the rigor required of a professional musician. The band director and former National Guardsman also became a friend whom Mr. Ervin would remain in touch with through the years. "There's just some people in your life whom you connect with, and I connected with him on a really good level," Mr. Ervin said.

During one visit, Mr. White, who played the trumpet at Mr. Ervin's wedding, asked a favor of the younger man. "He said, 'When I die, I want you to play taps for my memorial service,'" Mr. Ervin recalled. "I said, 'Sure, Mr. White. I hope that's a very long time from now.'"

The years that followed brought trials for both men – a disabling lung disease for Mr. Ervin and Alzheimer's disease for Mr. White. On Aug. 19, 2020, Mr. White died of complications from Alzheimer's.

Ashley White Kyle, one of Mr. White's four children, sent Mr. Ervin a message to let him know. "I knew Tim would have never, ever forgotten what my father had asked," she said.

At a graveside service three days later, Mr. Ervin, today a minister of music at First Baptist Church in Mount Pleasant, Texas, practiced his music in the pickup truck he had driven 200 miles to play a song that lasts about a minute. "It will go down for me as one of the great honors, other than playing taps for my own father," who served in the Navy during the Korean War, he said.

Jack W. White (left) with Tim Ervin in 2010. Photo courtesy of Allison White Greenup.

"It was really touching," Mrs. Kyle said. "What a blessing it was that Tim was able to fulfill that wish for my father."

Her brother, Jay White – Mr. Ervin's high school friend – suggested that he and his sisters repay the kindness. "We thought doing something in Tim's honor to help someone else would be appropriate. Let's give back to a place that kept Tim alive."

Along with Mr. Jay White and Mrs. Kyle, siblings Allison White Greenup and Beth White settled on a contribution in Mr. Ervin's honor to support UT Southwestern's lung disease/disorder research.

"We are always grateful for the donations that help make our work possible," said Dr. Lance Terada, Professor of Internal Medicine and Surgery and Chief of the Division of Pulmonary and Critical Care Medicine, who oversees such research. "In this case, it was especially gratifying since the funds came from a family appreciative of the work our lung transplant team did to restore Mr. Ervin's health, who was then able to play the trumpet at their father's funeral."

"Tim Ervin received the gift of a double-lung transplant in 2014, which allowed him to pursue his life's passion, playing the trumpet," added Dr. Michael Wait, Professor of Cardiovascular & Thoracic Surgery and the surgeon who performed Mr. Ervin's transplant. "I first heard him play at the American Airlines Center when he performed the national anthem prior to a Dallas Mavericks game.

"In a poignant encore, he has continued his intrepid journey with gifted lungs, honoring a former music professor by his rendition of taps. Mr. Ervin is an inspiration to all of his transplant team, and does great honor to the donor who gave him the ultimate gift ... of life's breath."

■

Dr. Terada holds the Dr. Carey G. King, Jr. and Dr. Henry M. Winans, Sr. Chair in Internal Medicine.

Best Employers

Continued from page 1

Human Resources Officer at UT Southwestern, which has approximately 18,800 nonfaculty employees and an operating budget of $4 billion.

"As an academic institution, our culture of learning is not confined to the classrooms. It is infused in every aspect of our mission, so we offer support systems to help ensure our employees succeed so they can perform at their best, and provide that top-level service to our patients and peers throughout the scientific and medical communities," she added.

UT Southwestern has established online and in-person training and mentoring programs that address diversity and inclusion; help groom those interested in future management and leadership roles; provide technical skills needed to adapt and conquer new software and technologies; and offer resources for employee wellness, managing stress and finances, and sharing common interests.

"We appreciate that our employees are people who are trying to balance commitments to work and home life. For those just starting out, learning how to successfully balance those demands is important for future success and advancement, so finding institutions like UT Southwestern that can offer those extra resources and training opportunities provides a valuable advantage," Ms. Browne said.

For example, UT Southwestern's Office of Institutional Equity & Access' Division of Diversity and Inclusion oversees various initiatives, including business resource groups, also known as employee resource groups or affinity groups. These voluntary, employee-led groups serve as a resource for members and the organization for events that promote networking, mentor opportunities, and career development. At UT Southwestern, these include the African-American Employee BRG (Business Resource Group), Asian-Pacific Islander BRG, Hispanic-Latino BRG, LGBT & Allies BRG, Veterans BRG, and Women & Allies BRG.

In addition to the *Forbes* listing, UT Southwestern has been recognized by *The Scientist* among best places to work for postdocs and holds Magnet designation in nursing, which recognizes health care organizations for quality patient care, nursing excellence, and innovations in professional nursing practices. UT Southwestern also has been recognized as a mother-friendly worksite by the Texas Department of State Health Services and has the Platinum Fit-Friendly Worksite Designation from the American Heart Association.

CLASS NOTES

IN MEMORIAM

Medical School
Staton P. Champion, M.D. ('70)
Richard R. Constant, M.D. ('63)
Robert M. Kuhne, M.D. ('60)
Harold L. Miller, M.D. ('78)

Housestaff
William F. Falls, M.D.
Gerald F. Geisler, M.D.
Samuel Jagoda Jr., M.D.
Jason L. Moshier, M.D.
Richard M. Nannally, M.D.
John R. Richmond, M.D.
Robert D. Russell, M.D.

School Of Health Professions
Lelon G. Thompson ('82)

MEDICAL SCHOOL

Class of 1964: Doug Puryear III, M.D., has published his seventh book and first novel, *Alma Means Soul*, the story of a woman overcoming the limitations of her childhood. The book is a psychological drama written in an unusual style. When he is not writing, Dr. Puryear enjoys spending time with his wife, Martha, fly fishing, playing guitar, and visiting family, including three great-grandchildren.

Class of 2001: Christy (Mitchell) Huff, M.D., has been appointed Director of the Benzodiazepine Information Coalition, a nonprofit that educates about the adverse effects of prescribed benzodiazepines. After suffering a protracted withdrawal syndrome from prescription Xanax, Dr. Huff now advocates for better physician education about benzodiazepine safety through writing and speaking about her experience.

For the latest updates on alumni events and news, visit engage.utsouthwestern.edu/alumni and follow @utswalumni on Facebook.

Please send your Class Notes contributions or address changes to the Office of Development and Alumni Relations, UT Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75390-9009, email alumni@utsouthwestern.edu, or call 214-648-4539.