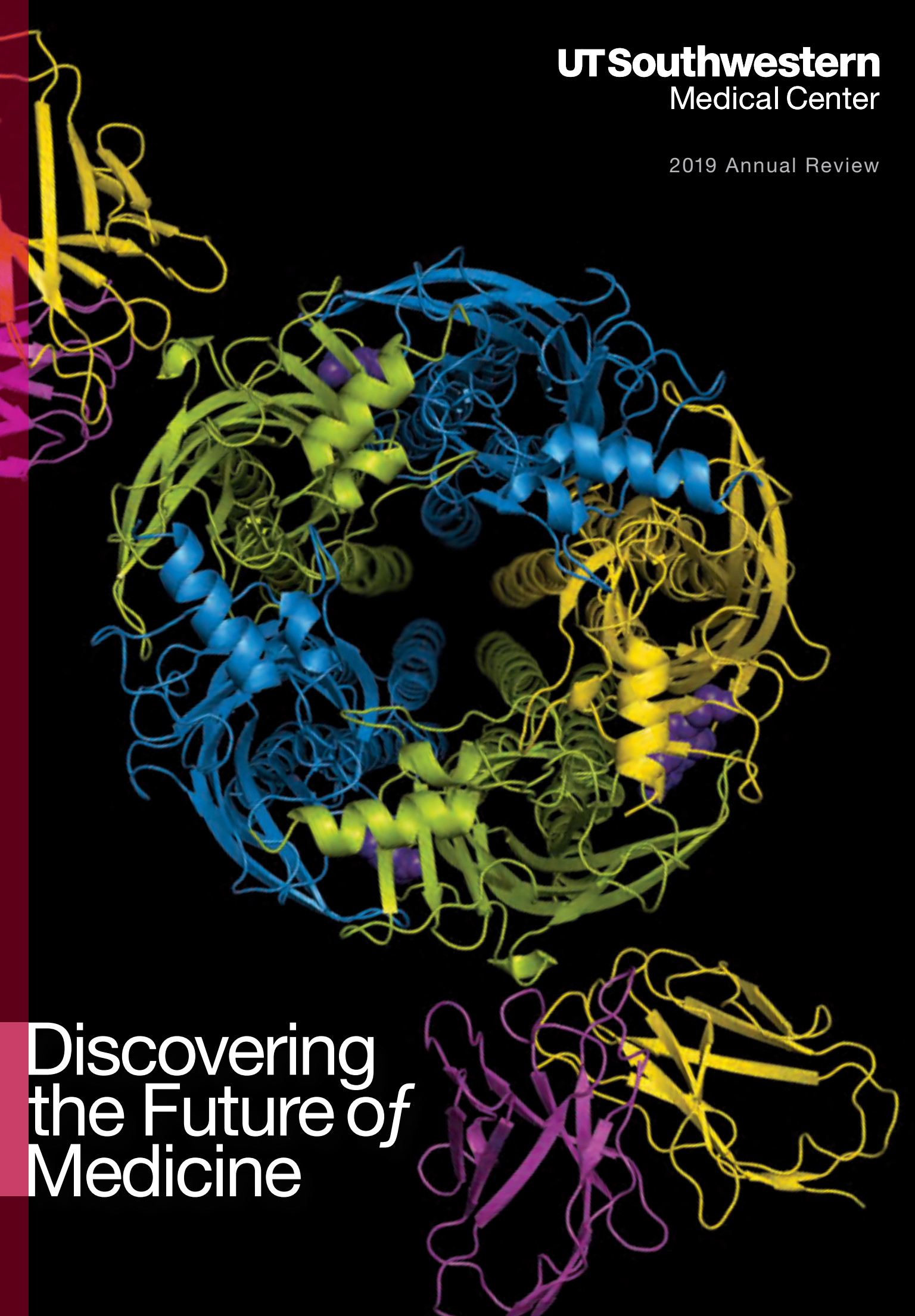
UTSouthwestern
Medical Center

2019 Annual Review



Discovering the Future *of* Medicine

Cover: *This illustration shows the molecular structure of the type A GABA receptor, a molecule that when bound to the neurotransmitter GABA suppresses neural activity related to anxiety. This receptor, the quintessential inhibitory receptor within the brain, is central to how some drugs work across a variety of disorders. Using cryo-electron microscopy, Dr. Ryan Hibbs and his team at UT Southwestern's Peter O'Donnell Jr. Brain Institute elucidated the receptor's structure to reveal critical information about how it works, creating the opportunity for new insights into disease and more effective therapeutics. Illustrated by Dr. Jeong Joo Kim.*

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Dear Friends,

In presenting this Annual Review for 2019, I am pleased to report once again that UT Southwestern is flourishing. Guided by our mission of promoting health and a healthy society that enables individuals to achieve their full potential, our faculty is making scientific discoveries, advancing patient care, and educating the next generation of physicians and scientists in ways that mean we are truly delivering the future of medicine, today.

We are deeply grateful for the support our stakeholders – our patients, our community friends, the federal government, and the state of Texas – have provided. It has been vital to our success, and we would not be the institution we are today without it. It has enabled us to build on the past, focus on the present, and shape the future as we pursue our goals for scientific leadership and clinical excellence.

Within the pages of this UT Southwestern Annual Review for 2019, you will find what we hope are engaging and informative stories and graphics about our most significant achievements and major milestones of the past academic year.

One of these stories highlights UT Southwestern's long-standing leadership in heart disease research. In 1985, Drs. Michael Brown and Joseph Goldstein were awarded the Nobel Prize in Physiology or Medicine for their identification of basic mechanisms controlling cholesterol metabolism, a discovery that led to the statin drugs used today to lower cholesterol. More recently, Dr. Helen Hobbs and her colleague, Dr. Jonathan Cohen, discovered the effect of the protein PCSK9 on cholesterol, leading to the development of PCSK9 inhibitors as another important weapon in the effort to control cholesterol. Generations of women in one family are now benefiting from the translational research that began with a Nobel Prize-winning discovery.

In our promise to deliver the future of medicine, our clinicians and researchers continue to adopt and test new technologies. Examples include installation of the GammaPod, a device that offers more precise, shorter duration breast cancer radiation treatments, and performing the first single-incision robotic surgery in Texas, a revolutionary technology that should mean less pain and a faster recovery for patients.

Perhaps the most challenging frontier in medicine is unlocking mysteries of the brain and diminishing the devastating toll of brain disease. We concluded a major national search for the inaugural Director of the Peter O'Donnell Jr. Brain Institute in 2019 with the appointment of Dr. William Dauer, a nationally acclaimed expert on Parkinson's disease. Our goal is for Dr. Dauer to expand the O'Donnell Brain Institute's programs, building on UT Southwestern's distinctive strengths in neuroscience research and clinical care, and to make the O'Donnell Brain Institute a national leader in advancing the understanding and treatment of brain disease, one of society's most compelling medical and social problems.

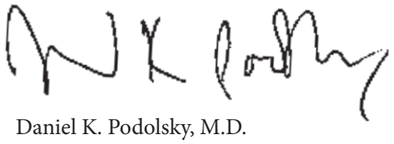
In the educational arena, our new Medical School curriculum, which was launched in 2015, is now firmly established; the Class of 2019 was the first Medical School class to graduate having completed all four years under the new curriculum. In addition, our students are taking full advantage of new learning opportunities to practice medicine on lifelike manikins in the new state-of-the-art Simulation Center, which opened in the fall of 2018 and is one of the largest in the country.

To support all of this important work, we are expanding our research and patient care facilities. A third tower is being added to the William P. Clements Jr. University Hospital, and it is scheduled to open in September 2020. We are also expanding our capacity to provide radiation therapy and are building a second radiation oncology building that will be ready for use in September 2021. In addition, we have broken ground on a new two-tower building on North Campus; one tower will house outpatient cancer care of the Harold C. Simmons Comprehensive Cancer Center, and the other tower will be research space for the O'Donnell Brain Institute. And already completed, we opened in December 2019 UT Southwestern Medical Center at Frisco, along with a joint UTSW/Texas Health Resources hospital, expanding our geographic reach in a rapidly growing area of North Texas.

As part of our newest initiatives, we will be establishing an outpatient facility in the Red Bird Mall in South Dallas and, in collaboration with UT Dallas, we will be building a biomedical engineering building at UTSW.

Your steadfast support has been essential to our aspirations and achievements. On behalf of the entire campus community, I thank you for your generosity and continued commitment to UT Southwestern's mission and goals.

Sincerely,



Daniel K. Podolsky, M.D.
President, UT Southwestern Medical Center

Revolutionizing Patient Care

Relentlessly pursuing the cure for a rare, fatal disease or finding more effective treatments for a condition that affects millions – UT Southwestern physicians shine at both. Innovative treatments or breakthroughs this past year ranged from a promising stem cell therapy for a paralysis-causing neurologic disorder to pioneering use of robotic surgical tools to improve patient recovery.

DNA sequence results used for finding mutations that can lead to cancer. UTSW has one of the premier clinical cancer genetics programs in the U.S.

Two lifesaving discoveries help four generations of women

Her great-grandmother volunteered in groundbreaking cholesterol research at UT Southwestern in the 1980s. Today, 10-year-old Zoe Allen is benefiting from that decision, receiving the best treatment available for her condition from UTSW's top heart care specialists.

Four generations of Texas women with a hereditary condition that affects how the body processes cholesterol – familial hypercholesterolemia – form a story interwoven around the discovery of new treatments founded on UTSW research that has helped millions.

It all started in the early 1980s with Zoe's great-grandmother, Estelle, who took part in UT Southwestern research on cholesterol. Then, just like her mother before her, Kathryn Geddie also had high cholesterol at a young age caused by familial hypercholesterolemia. So the Sunnyvale, Texas, mother of two began taking statin drugs to lower cholesterol levels measured in the upper 300s. (Normal range is less than 200 milligrams per deciliter (mg/dL).)

She also had her then 11-year-old daughter, Shanon, tested. Despite the child's young age, her cholesterol was soaring at 400 mg/dL.

Little did they know then that their shared medical struggle would lead them on a journey to help reverse the disease – a journey begun by a family member years before.

Drs. Michael Brown (left) and Joseph Goldstein once treated Kathryn Geddie's mother, Estelle, as part of their Nobel Prize-winning research on familial hypercholesterolemia and cholesterol metabolism.

Statin discovery

In the 1980s, UTSW Professors of Molecular Genetics Drs. Michael Brown and Joseph Goldstein wanted to know why people develop high cholesterol. Their question motivated the study of patients with familial hypercholesterolemia, including Mrs. Geddie's mother, Estelle. The two scientists identified the basic mechanism of cholesterol metabolism, a significant finding that resulted in their 1985 Nobel Prize in Physiology or Medicine.

Their discovery laid the scientific foundation for the development of statin drugs, which lower cholesterol and help prevent heart disease.

Today, Dr. Goldstein is Chair of Molecular Genetics and Dr. Brown is Director of the Erik Jonsson Center for Research in Molecular Genetics and Human Disease. Both are Regental Professors and hold the Paul J. Thomas Chair in Medicine; additionally Dr. Goldstein holds the Julie and Louis A. Beecherl, Jr. Distinguished Chair in Biomedical Research, and Dr. Brown holds The W.A. (Monty) Moncrief Distinguished Chair in Cholesterol and Arteriosclerosis Research.

Changing course

Knowing her mother's history with medical research, Mrs. Geddie enrolled her daughter in clinical trials with a UT Southwestern pediatric cardiologist. At age 16, Shanon began taking statins, just like her mom. Today, thanks to the drugs, Shanon Allen is a healthy 42-year-old mother of two.

However, Mrs. Geddie's health story became more complicated. "Three decades after I started taking them, the highest dose statin would no longer work," Mrs. Geddie said.

Her doctor added a new drug to her regimen called a PCSK9 inhibitor – one of

Cardiologist Dr. Parag Joshi confirmed Kathryn Geddie's diagnosis of familial hypercholesterolemia with genetic testing in late 2018.

Blood donations can help identify a life-threatening genetic condition

In the future, donating blood may provide an alert as to whether you carry the gene for a dangerous inherited cholesterol disorder.

Familial hypercholesterolemia (FH) is a genetic condition that causes extremely high levels of cholesterol at an early age. When one person is diagnosed, other family members can be identified. However, only an estimated 10 percent of the possible 1.2 million Americans with FH know they have it.

"For someone with FH, the risk of heart disease is higher because their clock started early. They've been bathed in high cholesterol since birth," said Professor of Internal Medicine Dr. Amit Khera, who completed his cardiology fellowship at UT Southwestern and holds the Dallas Heart Ball Chair in Hypertension and Heart Disease. "Sometimes by identifying one patient with FH, we find as many as eight or 10 more family members who are at risk."

A study last year by Dr. Khera in *JAMA Cardiology* describes how blood donation programs represent a unique opportunity to screen for diseases such as FH. According to the AABB, approximately 6.8 million people in the U.S. donate blood every year, and roughly a third are first-time donors.

Dr. Khera's team worked closely with Carter BloodCare in Dallas to review almost 1.2 million individual blood donation records specifically for markers of FH. They found more than 3,000 people who met criteria for FH based on their cholesterol levels, similar to the estimated prevalence in the general population. (The retrospective chart review had de-identified data, therefore no patient consent was required for this study, which received Institutional Review Board approval.)

The standard treatment for FH is diet and exercise, followed by the addition of statin medications in later childhood or early adulthood.

The UTSW cardiology team is working on a follow-up study to connect those identified as potentially having the disorder with the appropriate medical care – including family screening – and to continue evaluating the effectiveness of these interventions.

a class of powerful cholesterol busters also developed from game-changing research at UT Southwestern.

Renowned UTSW geneticist Dr. Helen Hobbs and her colleague, Dr. Jonathan Cohen, made the unexpected discovery of the effect of PCSK9 mutations while examining data from the Dallas Heart Study. This work provided insights into the genetic basis of cholesterol metabolism, eventually leading to the development of this new class of agents to treat hypercholesterolemia. PCSK9 inhibitors were approved by the FDA in 2015.

Dr. Cohen is a Professor of Internal Medicine who holds additional appointments in the Center for Human Nutrition and the Eugene McDermott Center for Human Growth and Development. Dr. Hobbs is Director of the McDermott Center, Professor of Internal Medicine and Molecular Genetics, and a Howard Hughes Medical Institute Investigator. Dr. Cohen holds the C. Vincent Prothro Distinguished Chair in Human Nutrition Research while Dr. Hobbs holds the Eugene McDermott Distinguished Chair for the Study of Human Growth and Development, the Philip O'Bryan Montgomery, Jr., M.D. Distinguished Chair in Developmental Biology, and the 1995 Dallas Heart Ball Chair in Cardiology Research.

All in the family

Mrs. Geddie was referred to UTSW cardiologist Dr. Parag Joshi, Assistant Professor of Internal Medicine, who confirmed Mrs. Geddie's diagnosis with genetic testing.

"Neither the statin nor the PCSK9 inhibitor alone were doing the trick. It was a combination of a dose of statin that she could tolerate, plus the PCSK9 inhibitor, that created an additive effect and got her cholesterol down to levels she had never seen before," Dr. Joshi said.

"I need to know I'm doing everything I can to manage my health as I age," said Mrs. Geddie, now 65. "We're proud to have a personal connection to UT Southwestern research that impacts so many."

The family is hoping for the best possible future, and they're thankful to Estelle. "If my grandmother had not taken part in the study, we might not have known we had the problem," Mrs. Allen said.

At a glance: Familial hypercholesterolemia

- This genetic disorder, also known as FH, leaves the body unable to remove low density lipoprotein (LDL) – or bad – cholesterol from the blood, resulting in high levels.
- FH increases the likelihood of narrowing of the arteries and heart attacks at an early age. Some signs of FH include fatty skin deposits over parts of the body, including the heels, elbows, and around the eyes.
- The disease is caused by a mutation in a gene that plays an important role in cholesterol metabolism.
- The condition affects about 1 in 250 people in Europe and the United States.

Sources: The National Institutes of Health, U.S. National Library of Medicine's MedlinePlus, and The FH Foundation

From left: Kathryn Geddie, Shanon Allen, and Zoe Allen all have a hereditary condition that causes unusually high cholesterol levels.

Reversing paralysis: Stem cell therapy aims to repair spinal cords afflicted by rare disorder

Don Winspear often dreams about slow dancing with his wife just as gracefully as when he met her in high school. When he wakes up, his legs are numb and immobile and a wheelchair is at his bedside.

Mr. Winspear, 60, is paralyzed from the chest down, afflicted with the severest form of transverse myelitis, a rare neurological illness that struck suddenly in late 2012.

His dreams of walking and dancing again are tied to an innovative treatment being tested at UT Southwestern's Peter O'Donnell Jr. Brain Institute. By injecting patients with stem cells engineered to repair the central nervous system – called progenitor cells – Dr. Benjamin Greenberg and fellow scientists are working to establish the first treatment to repair spinal cords inflamed by transverse myelitis.

> "It's exquisitely meaningful to show patients with these rare diseases that science is paying attention."
> *– Dr. Benjamin Greenberg*

If successful, the clinical trial could lead to similar therapies for other conditions, such as multiple sclerosis.

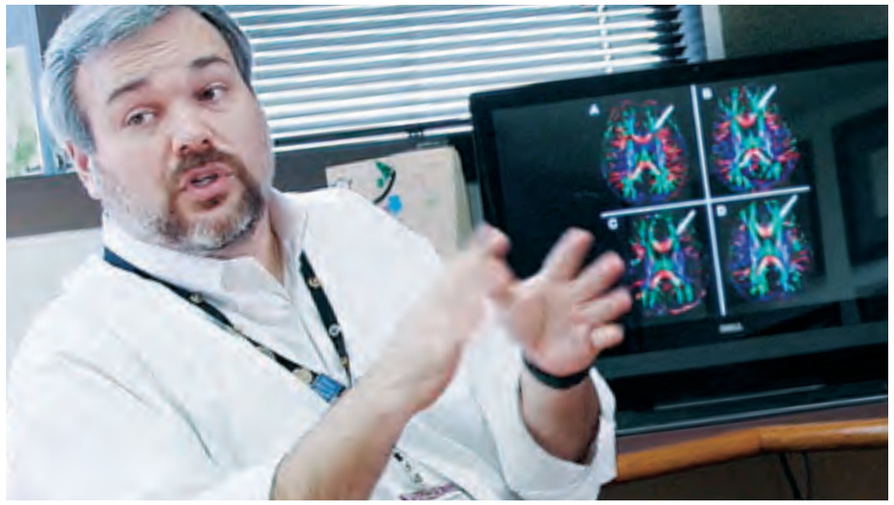
"The trial has been more than 15 years in the making, with a huge number of hurdles," said Dr. Greenberg, Professor of Neurology & Neurotherapeutics and Pediatrics, explaining the challenges of developing cells that could both find the damaged area and fix the problem. "It offers real hope to people like Don."

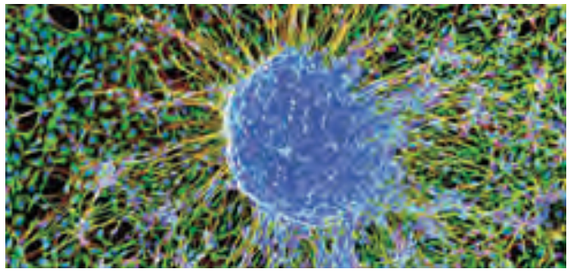
Transverse myelitis, or TM, is caused by inflammation in the spinal cord that damages myelin, a protective coating around neurons. The damage inhibits communication between nerve fibers in the spinal cord and the rest of the body, resulting in partial or total paralysis. Most patients see at least some improvement in the months after the attack, while a slim minority face permanent paralysis.

UT Southwestern's clinical trial will study the safety and effectiveness of implanting progenitor cells into the spinal cord, with the hope of reversing paralysis in patients like Mr. Winspear.

The trial is starting with nine participants with the most severe form of transverse myelitis. Each will receive a one-time injection of progenitor cells designed to produce myelin along the damaged area and reestablish critical nerve signaling. The cells have successfully repaired the central nervous system in animals.

The chance of enduring a transverse myelitis attack in any given year is as little as 1 in a million – less likely than getting struck by lightning. It struck Mr. Winspear during one of the happiest times of his life.





Clockwise, from top: Dr. Benjamin Greenberg aims to develop a treatment that would repair spinal cords inflamed by transverse myelitis (TM); the proposed therapy involves injecting patients with stem cells (like this one) engineered to repair the central nervous system; TM patient Don Winspear is hopeful that this clinical research may lead to a cure for the paralyzing disease.

Stem cell image – National Institutes of Health

Mr. Winspear and his wife, Ellen, were in North Carolina for their older son's wedding when he started feeling lower back pain and intense tingling in his feet.

"I took some painkillers, but it only got worse," said Mr. Winspear, a longtime Dallas resident.

The night after the wedding, he went to a hospital, where imaging showed a lesion on his spinal cord. Within the hour, Mr. Winspear could no longer uncross his legs as numbness crept up his body.

"I was scared to death," Mr. Winspear said. "I was thinking, 'What if it doesn't stop?'"

After learning the diagnosis, Mr. Winspear's son did a quick internet search and learned that UT Southwestern is one of only two places in the country focused on this disease.

Mr. Winspear was admitted to UT Southwestern, where he soon met Dr. Greenberg, one of the nation's leading experts on the disorder, who now manages his care.

Dr. Greenberg called Mr. Winspear's a "whopper of a case" of spinal cord inflammation. It soon forced him to replace favorite hobbies – hiking and canoeing, skydiving and scuba diving – for life as a paraplegic.

Despite the challenges, Mr. Winspear still works as a marketing research consultant and stays physically active, using an elliptical-type glider for cardio exercise and a neuromuscular electrical stimulator.

Dr. Greenberg, a Cain Denius Scholar in Mobility Disorders, is hopeful the new treatment can provide some benefit for TM patients such as Mr. Winspear.

"There's nothing worse than having a sense of hopelessness," Dr. Greenberg said. "It's exquisitely meaningful to show patients with these rare diseases that science is paying attention."

Unusual brain cell behavior helps predict epileptic seizures minutes in advance

Elizabeth Delacruz can't crawl or toddle around like most youngsters her age. A rare metabolic disorder that decimated her mobility has also led to blindness from brain damage and epileptic seizures.

Her mother, Carmen Mejia, is hoping doctors can find a way to detect and prevent Elizabeth's seizures that stem from the terminal disease known as pyruvate dehydrogenase deficiency (PDHD). In this disease, mitochondria don't provide enough energy for the body's cells.

A UT Southwestern study gives Ms. Mejia hope: By monitoring the activity of a specific brain cell type responsible for seizures, scientists now can predict convulsions at least four minutes in advance. The research, published in *Science Translational Medicine,* further shows that an edible acid called acetate may effectively prevent seizures if taken before they occur.

"We've found a new approach that should help us and other scientists tackle the root of seizures for many kinds of epilepsy," said Dr. Juan Pascual, a neurologist with UT Southwestern's Peter O'Donnell Jr. Brain Institute who led the study.

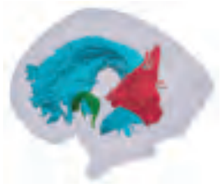
The study, supported by the National Institutes of Health, The Once Upon a Time Foundation, and other philanthropic donations, shows how astute patient observations can guide transformative research.

Dr. Pascual, a Professor of Neurology & Neurotherapeutics, Pediatrics, and Physiology who has an additional appointment in the Eugene McDermott Center for Human Growth and Development, holds the Ed and Sue Rose Distinguished Professorship in Neurology and The Once Upon a Time Foundation Professorship in Pediatric Neurologic Diseases.

(Upper left) Dr. Juan Pascual (center) analyzes study data with lab colleagues Dr. Vikram Jakkamsetti (left) and Dr. Qian Ma. The research team developed a mouse model of a rare metabolic disorder to learn more about the disease in their quest for a cure.

(Bottom left) A child undergoes an EEG, similar to the one Elizabeth had when doctors used this technology in research to help predict a seizure.

Elizabeth Delacruz



This diffusion tensor image shows development of white matter tracts – which connect neural centers – in the brain. This is the most vulnerable structure in pyruvate dehydrogenase deficiency.

GammaPod advances breast cancer patient care

UT Southwestern's GammaPod device – the second of its kind in the world – offers patients more precise, shorter duration breast cancer radiation treatments.

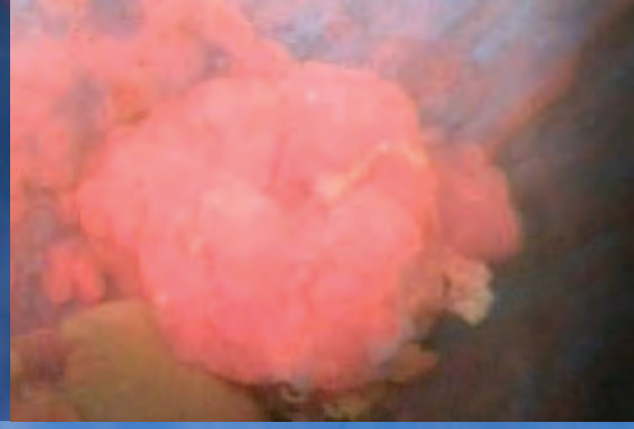
Dr. Asal Rahimi talks to a breast cancer patient about to undergo radiation treatment with the GammaPod, a device that uses one of the most advanced forms of technology available worldwide.

The GammaPod, added by the Medical Center last year, delivers higher doses of radiation to a narrowly targeted area, meaning breast cancer patients need fewer treatments over shorter periods of time. The device is just one of multiple leading-edge cancer care technologies that the Harold C. Simmons Comprehensive Cancer Center offers patients, in addition to access to clinical trials.

"It's a great service to the community and offers a lot to women who are facing breast cancer with the busy lives they have today," said Dr. Asal Rahimi, Associate Professor and Director of Clinical Research in Radiation Oncology at the Simmons Cancer Center. "Our mission is to try to provide very effective treatment in as little time as possible."

The GammaPod breaks new ground, targeting the tumor within 3 millimeters with high-level radiation without damaging healthy tissue. The device uses vacuum suction that temporarily immobilizes the breast, holding it perfectly still so radiation can hit its target. Suction pulls the breast up against the wall of a fitted plastic cup. Before stereotactic radiation is delivered, a CT scan pinpoints the tumor's exact location. The patient presses against the GammaPod's table, where there is an opening for the breast cup to slide through. The patient lies face down for treatment, so the breast is downward, eliminating radiation near the heart and lungs.

The GammaPod's unique configurations allow oncologists to narrow radiation down to a range of just 3 millimeters – less than the width of three stacked pennies. Standard breast cancer radiation treatment typically lasts four to six weeks. But with the stereotactic radiation delivered by the GammaPod, treatment can be shortened to one to five days, potentially lowering toxicity.



Tumor illuminated by blue-light cystoscope

Shining a blue light to improve bladder cancer treatment

When Mansfield physician Dr. Robert McMichael was diagnosed with bladder cancer in May 2018, he wanted the best treatment possible. His quest took him to UT Southwestern for exams using a new device, the blue-light flexible cystoscope.

UT Southwestern researchers were among those who tested this technology, so when the Food and Drug Administration cleared it for use in 2018, the Dallas-based institution became one of just four in the country to initially offer it for outpatient use. Dr. McMichael became patient No. 1. Since then, use of the technology has expanded to about a dozen institutions in the U.S.

"Blue light works better than white light (such as light from sunlight) because we instill a photosensitizing agent into the bladder that's taken up by cancer cells. When you shine a blue light on it, the cancer cells look pink and normal cells don't," said Dr. Yair Lotan, a Professor of Urology who completed an internship and two residencies at UT Southwestern. "We know we can miss 10 to 20 percent of cancers when we just look with white light."

Standard treatment for early stage bladder cancer consists of surgically removing cancer lesions, followed by immunotherapy. Patients then return for regular examinations of the inside of the bladder using a tube-like cystoscope to determine if new lesions have developed.

Blue-light cystoscopy using a rigid cystoscope had been available in some institutions' operating rooms, including UT Southwestern's. But outpatient exams can only be performed with a flexible scope because a rigid one would be too uncomfortable for patients who are awake, explained Dr. Lotan, who holds the Jane and John Justin Distinguished Chair in Urology, in Honor of Claus G. Roehrborn, M.D., and the Helen J. and Robert S. Strauss Professorship in Urology.

In the first year of the flexible scope's use, more than 110 blue-light flexible cystoscopy procedures were performed at UT Southwestern, Dr. Lotan said.

"Once you have bladder cancer, you have to be monitored indefinitely," said Dr. McMichael, who remains cancer-free but knows the risk of recurrence can be high for some. "If there's any cancer to be seen, the blue-light cystoscopy significantly improves the chances of seeing it."

One of UT Southwestern's first GammaPod patients, Patricia Salcido, 61, of Grand Prairie, said she was a bit nervous before her first treatment, but completely at ease afterward. She was a typical GammaPod patient, requiring five roughly 20-minute treatments.

"The new technology is wonderful. I totally believe in it," Ms. Salcido said at the time of one of her treatments. She finished the therapy last year and has remained cancer-free.

Since installation of the device in March 2019, more than 50 patients have undergone GammaPod treatment at UT Southwestern. Dr. Rahimi co-chairs the GammaPod Consortium with a doctor from the University of Maryland, where the GammaPod was developed. Clinical trials are ongoing and more are planned, she said. Doctors will likely combine the GammaPod with other resources in the Department of Radiation Oncology to personalize treatment to the size of patients' breasts and tumors.

The GammaPod, added by the Medical Center last year, delivers higher doses of radiation to a narrowly targeted area, meaning breast cancer patients need fewer treatments over shorter periods of time.

Making history

UTSW is first hospital in Texas to perform single-incision robotic surgery

In late 2018, UT Southwestern became the first hospital in Texas to perform single-incision robotic surgery – a revolutionary technology that can mean less pain and a faster recovery for patients.

With the technology, all necessary surgical tools are inserted through one small incision. Dr. Jeffrey Cadeddu, Professor of Urology and Radiology, first used the new technique at UTSW in November 2018 to perform surgery on a ureter, the duct that passes urine from the kidney to the bladder, in order to correct a blockage.

Single-incision robotic surgery is a type of laparoscopic surgery, or surgery performed through small incisions and made possible by a tiny video camera that can be inserted into the area of surgery, giving the surgeon a view inside the patient's body without cutting a large opening.

With this type of surgery, several incisions are usually needed to accommodate both the camera and surgical tools. Standard laparoscopic surgery to repair a ureter, for example, involves four small incisions.

Over the last decade, surgeons have looked for a way to reduce the number of openings. "Every incision means increased pain, increased risk of hitting a blood vessel," said Dr. Cadeddu, who won the 2018 Patricia and William L. Watson Jr., M.D. Award for Excellence in Clinical Medicine.

Physician assistant Brad Hornberger works at the patient's side during the pioneering, single-incision surgery. In the background at the console, surgeon Dr. Jeffrey Cadeddu guides the robotic device.

UT Southwestern performs single-incision laparoscopic surgery with a robotic device called the Single Port SP Robot. It has four arms that can insert through a single incision. Intuitive Surgical Inc., the company that makes the SP Robot, initially rolled it out to just a handful of medical centers, including UT Southwestern, considered one of the leaders in robotic surgery.

Besides Dr. Cadeddu, others trained to use the device include Dr. Jeffrey Gahan, Assistant Professor of Urology; Dr. Baran Sumer, Professor of Otolaryngology – Head and Neck Surgery, who holds the T.D. Lupton Family Professorship in Patient Care, in Honor of Dr. John Dowling McConnell and Dr. David Andrew Pistenmaa; and Dr. John Truelson, Associate Professor of Otolaryngology – Head and Neck Surgery, who holds the American Airlines Professorship in Cancer Research. UTSW faculty members have completed more than 100 single-incision robotic surgeries to date.

Dr. Cadeddu, who holds the Ralph C. Smith, M.D. Distinguished Chair in Minimally Invasive Urologic Surgery, has also combined single-incision techniques with the innovative use of magnets to control surgical tools inside the body to reduce scarring.

"We expect this to be the start of a cascade of improved surgical procedures with fewer incisions, meaning less pain and fewer complications for patients," Dr. Cadeddu said.

A liver transplant surgery is performed by Drs. Parsia Vagefi (left) and Steven Hanish. The surgeons are part of a team launching a new living-donor liver transplant program.

New living-donor liver transplant program to address severe shortage

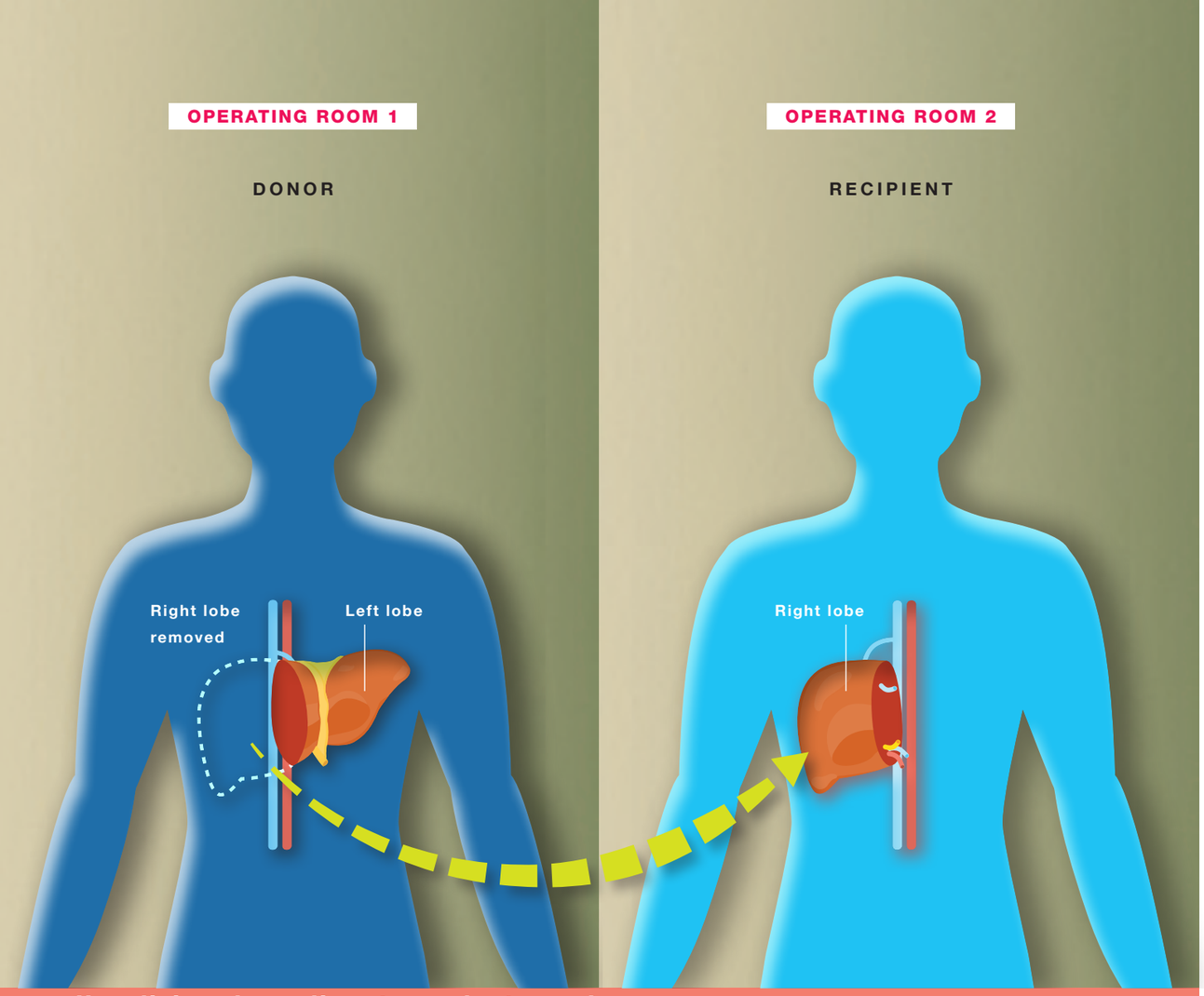
More than 1,700 patients in the U.S. die each year waiting for a liver transplant.

UT Southwestern's new living-donor liver transplant program hopes to lower that heartbreaking statistic by offering patients a route to expedited transplantation and improved survival.

"Living-donor transplantation helps address the critical need for more livers to transplant and is just what it sounds like – a living person can give part of his or her liver to another," said Dr. Steven Hanish, Surgical Director of UTSW's Living-Donor Liver Transplantation Program.

"The liver regenerates," Dr. Hanish explained. "Surgeons can remove a portion of a liver from a healthy donor – up to 70 percent – and transplant it into another person, and it will grow. The portion left behind in the donor will also regrow. That process happens in the first few weeks after surgery."

Living-donor liver transplantation has better outcomes than deceased-liver transplantation, partly because recipients are not on the waitlist for prolonged periods while their health declines, hoping for an available liver, said Dr. Hanish, also Associate Professor of Surgery.



How living-donor liver transplants work

1

PREPARATION

On transplant day, donor and recipient are in adjacent operating rooms, with a surgical team assigned for each.

2

SEPARATION

The donor's surgery occurs first, with up to 70 percent of the liver, usually the right lobe, removed.

3

ATTACHMENT

The recipient's damaged liver is removed. The donated liver lobe is immediately attached, joining blood vessels and bile ducts.

4

REGENERATION

The liver is the only internal organ that can completely regenerate. Within about two months, the portions of liver within both donor and recipient have grown to a normal size.

Not every liver transplant program has a living-donor component, Dr. Hanish noted. Living-donor liver transplant surgery is complex and requires advanced expertise – the kind found at UT Southwestern, he said. The procedure takes between six and eight hours and involves carefully separating the liver so that both pieces can remain functioning in the recipient and the donor.

Only 524 living-donor liver transplants were performed nationally in 2019, according to the United Network for Organ Sharing (UNOS), the nonprofit organization that manages the U.S. organ transplant system under contract with the federal government. UT Southwestern launched its living-donor liver transplant program in 2018.

Donors do not have to be related to the recipient. Historically, though, recipients' children, parents, and siblings – in that order – have been the most common donors, according to UNOS.

Once a transplant patient identifies a potential donor, the donor contacts UT Southwestern to arrange for a full medical and psychological evaluation, a process that takes place independent of the patient (recipient) evaluation.

If all evaluations are favorable, surgery is then scheduled with the living-donor transplant team.

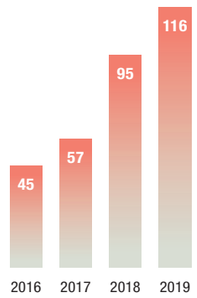
"Any patient who is on the liver transplant waiting list is potentially eligible to receive a liver from a live donor," noted Dr. Arjmand Mufti, Medical Director of Living-Donor Liver Transplantation and Assistant Professor of Internal Medicine.

Donors with a compatible blood type for the recipient must also be in good physical and mental health, have a BMI under 35, and range in age from 18 to 60.

The availability of living-donor liver transplantation is the latest mark of distinction for UT Southwestern's Liver Transplant Program, which saw a 103 percent increase in transplants between 2017 and 2019. Additionally, the program cut the length of stay after transplant from eight days to only five – one of the lowest in the country, said Dr. Parsia Vagefi, Associate Professor of Surgery, Chief of the Division of Surgical Transplantation, and holder of the Ernest Poulos, M.D. Distinguished Chair in Surgery.

"A leading-edge program in living-donor liver transplantation surgery is entirely consistent with our distinguished record in liver care and our status as one of the nation's leading academic medical centers," Dr. Vagefi said. "We're certainly proud of our past, but even more excited for our future."

Transplants



UT Southwestern's Liver Transplant Program saw a 103 percent increase in transplants between 2017 and 2019.

Use of new technology improves odds of liver transplant success

Since the first liver transplant in 1963, donated livers have been immersed in icy fluid inside a cold storage system for transport. Only after the organ is transplanted does the surgeon learn if it functions correctly.

UT Southwestern transplant surgeon Dr. Malcolm MacConmara is leading an international trial to test a better way. The study at 20 U.S. sites is examining the effectiveness of a new device, the portable Organ Care System (OCS) from TransMedics, which keeps donated livers warm and circulates blood during organ transport.

"It's like a virtual transplant," said Dr. MacConmara, Assistant Professor of Surgery. "By putting the liver on the machine, we can truly approximate the conditions of the body."

> "It's like a virtual transplant. By putting the liver on the machine, we can truly approximate the conditions of the body." – *Dr. Malcolm MacConmara*

The OCS is about the size of a small shopping cart. Inside, major blood vessels of the donated liver connect to tubes that infuse it with blood. The liver inside the device makes bile and processes medications.

Dr. Parsia Vagefi, Associate Professor of Surgery, Chief of the Division of Surgical Transplantation, and holder of the Ernest Poulos, M.D. Distinguished Chair in Surgery, explained why this might work better than the current system: "The longer a liver sits on ice, the more likely it is to have problems after transplant. It will become unusable if stored too long. With patients waiting for organs, this new way may expand the number of donated livers for transplant."

One recent beneficiary was Greg Nielsen, a Dallas construction worker. At 59, his liver was failing due to cirrhosis and cancer. When he reached UT Southwestern in June 2018, his options were running out.

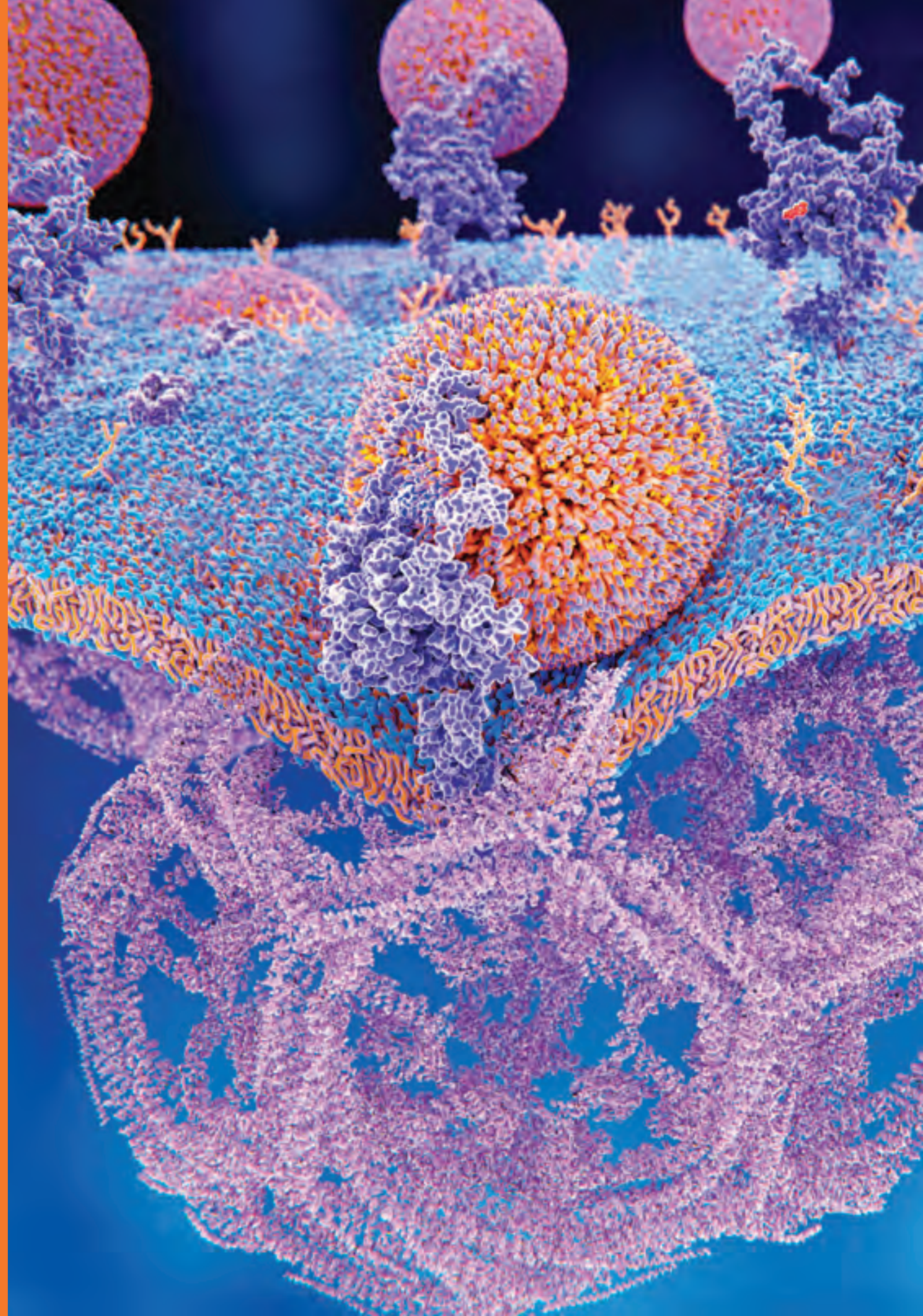
After a liver became available, Dr. MacConmara and his team traveled to the donor hospital, carefully placed the liver in the OCS, and returned to UT Southwestern. They monitored it as it produced bile and saw it was functioning well. Dr. Vagefi led the surgical team that transplanted it.

Mr. Nielsen went home three days later. "Before the surgery, I couldn't walk much at all," he said. "Now I walk 45 minutes every morning. It's like a miracle."

Dr. Malcolm MacConmara (right) shows patient Greg Nielsen the device that was used to transport a donated liver for his transplant. The machine keeps livers warm and circulates blood during transport, ensuring the viability of organs. Dr. Parsia Vagefi, left, led the surgical team that transplanted Mr. Nielsen's new liver.

Advancing Scientific Discovery

A breakthrough takes patience, attention to detail, and painstaking trial and error. But the payoffs can be huge. Significant research advances by UTSW scientists this past year ranged from efforts to unleash the body's cellular recycling process to fight infections to reprogramming neurons in a novel way and in turn uncovering clues about a vulnerability in Parkinson's disease.



This image shows LDL receptors binding to a cell membrane. UTSW research has revealed how circulating LDL cholesterol enters artery walls, causing plaque.

Leading a national effort to develop new weapons against pathogens

Amid growing concern about pathogens becoming more drug-resistant worldwide – and emerging new pathogens that have no current treatment – UT Southwestern is leading a five-year investigation into a promising new approach for controlling infections, funded by a grant of up to $37 million.

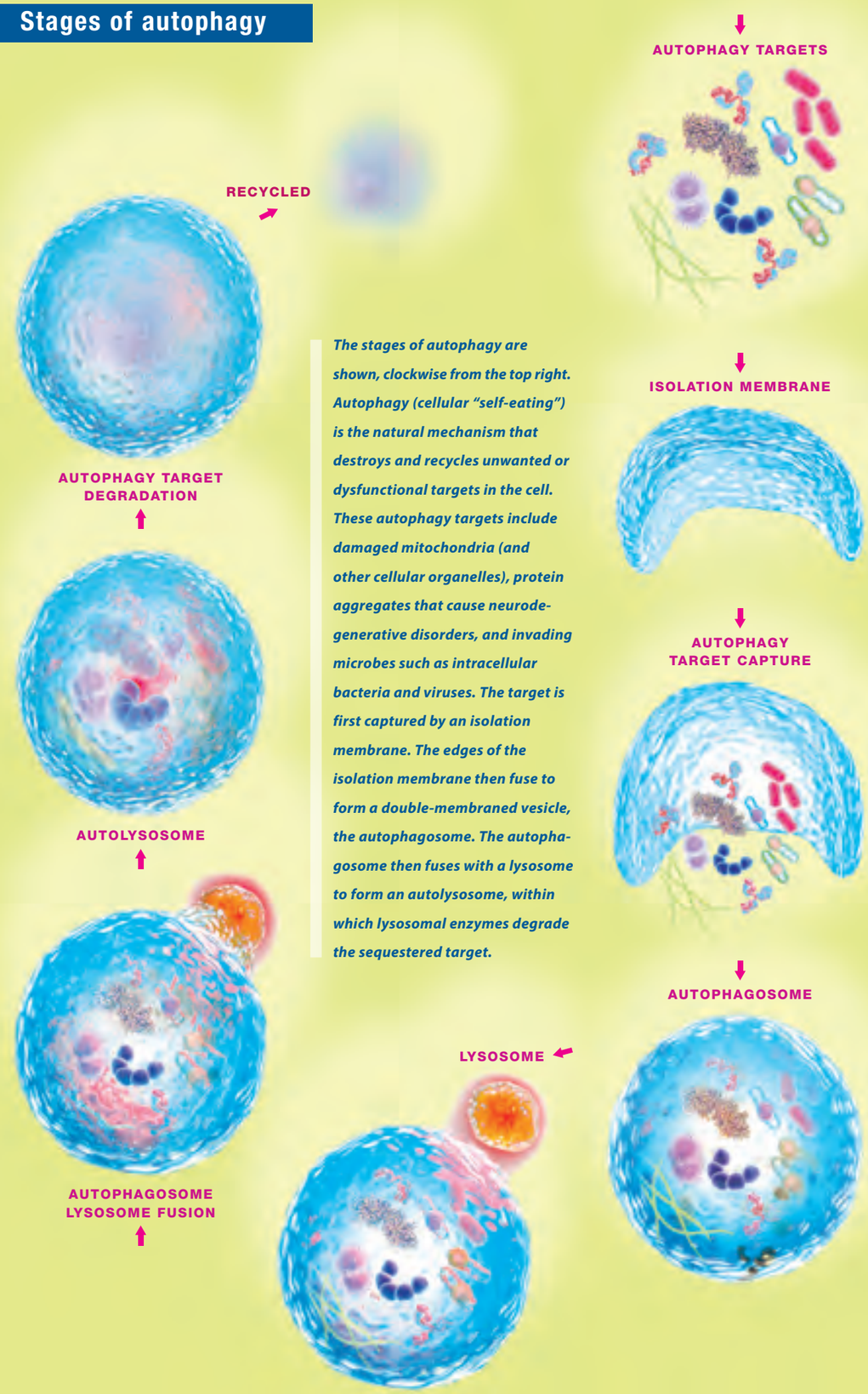
The National Institutes of Health (NIH)-funded program is headed by Dr. Beth Levine, Director of UT Southwestern's Center for Autophagy Research and a Professor of Internal Medicine and Microbiology. Dr. Levine serves as Program Director over five separate research projects at UT Southwestern and across the country – all focused on the potential to exploit a cellular process known as autophagy, a natural mechanism that destroys invading bacteria and viruses.

"The process of autophagy takes place inside all human cells and is used to break down damaged parts of the cell," explained Dr. Levine, an internationally recognized expert in the field and a Howard Hughes Medical Institute Investigator. "Since the late 1990s, there has been a growing body of research showing that cells can also use autophagy to destroy pathogenic invaders and to regulate host immune responses to infectious diseases."

"During autophagy, the target to be destroyed is encased in a double-membrane compartment inside the cell called an autophagosome, which then merges with other compartments containing enzymes and acids

As part of a large NIH grant, Drs. Beth Levine and Michael Shiloh are investigating how to use a cellular recycling process called autophagy to improve defenses against bacteria and viruses.

Stages of autophagy



The stages of autophagy are shown, clockwise from the top right. Autophagy (cellular "self-eating") is the natural mechanism that destroys and recycles unwanted or dysfunctional targets in the cell. These autophagy targets include damaged mitochondria (and other cellular organelles), protein aggregates that cause neurodegenerative disorders, and invading microbes such as intracellular bacteria and viruses. The target is first captured by an isolation membrane. The edges of the isolation membrane then fuse to form a double-membraned vesicle, the autophagosome. The autophagosome then fuses with a lysosome to form an autolysosome, within which lysosomal enzymes degrade the sequestered target.

to degrade the target," said Dr. Michael Shiloh, Associate Professor of Internal Medicine and Microbiology, who serves as the program's Associate Director. Dr. Shiloh holds the Professorship in Infectious Diseases, in honor of James P. Luby, M.D.

"Maximizing this natural defense could result in treatments effective against a broad range of pathogens – even before the cause of an illness is identified," Dr. Shiloh said. "That would make it a vital tool for combating a new outbreak or an act of bioterrorism requiring rapid response. Also, enhancing autophagy could kill infectious organisms that are resistant to traditional antibiotics."

Under the grant, awarded last year, UT Southwestern is working with five other research sites as a Center of Excellence for Translational Research supported by the National Institute of Allergy and Infectious Diseases: the Broad Institute in Cambridge, Massachusetts; Massachusetts General Hospital and Harvard Medical School in Boston; Vir Biotechnology Inc. in San Francisco; Washington University School of Medicine in St. Louis; and The Scripps Research Institute in La Jolla, California.

"The Center has been charged with investigating possible treatments for emerging and reemerging infectious diseases, in particular so-called 'priority pathogens' that are drug-resistant, have no treatment, or could be used by bioterrorists," Dr. Shiloh said.

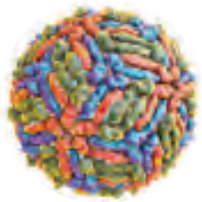
As co-leader of one of the projects, Dr. Shiloh is investigating use of autophagy to treat tuberculosis. This disease killed 1.6 million people worldwide in 2017 and has developed significant multidrug resistance, according to the World Health Organization, or WHO.

Dr. Levine leads a different project focused on how to ramp up autophagy within the body in order to augment host defenses against West Nile and other mosquito-borne viruses. In 2018, Dr. Levine's group published a report in *Nature* showing that genetically engineered mice with increased autophagy live longer and healthier lives. These findings raise the possibility that pharmacological strategies to increase autophagy, including in the setting of infectious diseases, may be well tolerated.

The new NIH grant follows a similar five-year award funded in 2013 in which UT Southwestern took part. Research conducted with the earlier funding generated several patents, licensing agreements, and promising compounds that can potentially be used to develop autophagy-inducing anti-infective agents, said Dr. Levine, who holds the Charles Cameron Sprague Distinguished Chair in Biomedical Science. With the new support, Drs. Levine and Shiloh are optimistic that even more breakthroughs to improve human health are possible.

In other work, UTSW research supported through a gift from Linda and Mitch Hart has indicated that autophagy enhancers may promote a healthy lifespan and longevity.

"If we can find ways to enhance autophagy in our cells, this could result in new treatments that would harness the body's own defenses to help fight infections," Dr. Levine said. "Moreover, such treatments could also be helpful to combat other diseases that may benefit from increased autophagy, such as certain neurodegenerative disorders and cancers."



Ramping up autophagy can augment host defenses against many types of bacterial or viral infections, such as the disease caused by the West Nile virus particle, pictured above.

Immunology advance provides clues to vitamin A infection link

Researchers have solved the longtime mystery about why people with diets deficient in vitamin A are more prone to skin infections. Last year, UT Southwestern investigators identified a previously unknown bacteria-killing protein on the epidermis that needs the vitamin to work, a finding that builds on the University's foundational research and growing expertise in immunology.

The research team discovered that one protein in the resistin-like molecule (RELM) family – RELMα – acts as an antibiotic to rapidly kill bacteria in mice. Both RELMα and the corresponding human RELM family protein, called resistin, are stimulated by dietary vitamin A.

"RELMα is the first example of an antimicrobial protein that requires dietary vitamin A for its bacterial killing activity. This finding gives us an important clue about how the skin defends itself against infection, and how skin defense is regulated by the diet," said Dr. Lora Hooper, Chair of Immunology and corresponding author of the study published in *Cell Host & Microbe* last year.

Dermatologists use synthetic vitamin A, called retinoid, to treat acne, psoriasis, and other skin conditions, although how those drugs work has long been a mystery.

Drs. Lora Hooper (left) and Tamia Harris-Tryon found that a bacteria-killing protein on the skin needs vitamin A to work, revealing why synthetic versions of the nutrient are effective against skin disease.

"The skin is the largest organ of the human body and is tasked with defending us against infection," said Dr. Tamia Harris-Tryon, Assistant Professor of Dermatology and Immunology. "If the skin immune system breaks down, infection results."

The team's experiments in human tissue and mice illuminate a previously unappreciated link between diet and innate immunity of the skin, suggesting why vitamin A derivatives are effective treatments for skin disease, said Dr. Hooper, a Howard Hughes Medical Institute Investigator and UTSW Professor of Immunology and Microbiology. Dr. Hooper has an additional appointment in the Center for the Genetics of Host Defense, holds the Jonathan W. Uhr, M.D. Distinguished Chair in Immunology, and is a Nancy Cain and Jeffrey A. Marcus Scholar in Medical Research, in Honor of Dr. Bill S. Vowell.

Using Dr. Hooper's colony of germ-free mice – raised from birth without exposure to germs – the researchers identified genes that are turned on when such mice are exposed to bacteria.

"Considering how often retinoids are used in dermatology, the implications of our findings are potentially vast," Dr. Harris-Tryon said. "This study gives us a better understanding of how diet impacts the ability of the skin to defend itself against bacterial infection – but more research will be needed to determine how these findings will impact patients with inflammatory skin diseases such as acne and psoriasis."

Dr. Philip Shaul (right) examines study data with postdoctoral researcher Dr. Linzhang Huang. Dr. Shaul's research team discovered how "bad" cholesterol enters artery walls to develop into heart-harmful plaque.

Investigation exposes how 'bad' cholesterol enters arteries

It could be called the great reveal: A study by UT Southwestern researchers has uncovered how cholesterol enters artery walls to cause the plaque that leads to heart attacks and strokes.

The study shows for the first time how a protein called SR-B1 (short for scavenger receptor class B, type 1) ferries particles of LDL – the so-called "bad" cholesterol – into and then across the endothelial cells that line arteries. The study also found that a second protein called dedicator of cytokinesis 4, or DOCK4, partners with SR-B1 and is necessary for the process.

Low density lipoprotein, or LDL, cholesterol entry into the artery wall drives the development of atherosclerosis, more commonly known as hardening of the arteries – and atherosclerosis leads to heart attacks and strokes. Future treatments preventing the process of LDL entry may help decrease the occurrence of these life-threatening conditions, said Dr. Philip Shaul, senior author of the study published last year by *Nature*.

Cardiovascular disease is the leading cause of death worldwide, and coronary artery disease (which underlies heart attacks) and strokes account for more than 60 percent of those cardiovascular deaths in the U.S., according to recent statistics from the American Heart Association.

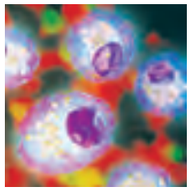
In the early stages of atherosclerosis, LDL that has entered the artery wall attracts and is engulfed by important immune system cells called macrophages that ingest, or "eat," LDL particles. LDL-laden macrophages become foam cells that promote inflammation and further the development of atherosclerotic plaques.

The plaques narrow the artery and can become unstable. Plaques that rupture can activate blood clotting and block blood flow to the brain or heart, resulting in a stroke or heart attack.

However, in studies of mice with elevated cholesterol, the investigators determined that deleting the SR-B1 protein from the endothelial cells lining blood vessels resulted in far less LDL entering the artery wall. As a result, fewer foam cells formed, and atherosclerotic plaques were considerably smaller.

"At the start of this work it was surprisingly unknown how LDL enters the artery wall to cause cardiovascular disease," said Dr. Shaul, Director of the Center for Pulmonary and Vascular Biology at UT Southwestern, who holds the Associates First Capital Corporation Distinguished Chair in Pediatrics. "The paper's findings solve that mystery and counter many scientists' prior assumption that LDL simply enters through sites of damage or disruption in the single layer of endothelial cells that serves as the artery wall's protective barrier."

In their studies, the researchers compared the abundance of SR-B1 and DOCK4 in areas of the mouse aorta that are prone to plaque formation with regions less likely to become atherosclerotic. They found higher levels of SR-B1 and DOCK4 in the disease-prone regions long before atherosclerotic



Foam cells are types of scavenger cells in atherosclerotic plaques that engulf LDL and accumulate lipid droplets.

plaques formed. This finding suggests that atherosclerotic lesions may be more common in particular artery sites because of the presence of more SR-B1 and DOCK4 at those locations, said Dr. Shaul, also Professor and Vice Chair for Research in the Department of Pediatrics.

To determine if these findings might apply to people, the researchers reviewed data on atherosclerotic and normal arteries from humans in three independent databases maintained by the National Institutes of Health. In all three databases, SR-B1 and DOCK4 were more abundant in atherosclerotic arteries compared with normal arteries.

The researchers are now exploring the possibility of using gene therapy to turn off or reduce the function of SR-B1 or DOCK4 in the cells that line arteries in order to prevent atherosclerosis, Dr. Shaul said.

"At the start of this work it was surprisingly unknown how LDL enters the artery wall to cause cardiovascular disease." – *Dr. Philip Shaul*

"If you could develop a drug that inhibits SR-B1 or DOCK4, or a gene therapy that silences them in those cells, you could potentially decrease atherosclerosis and, hence, reduce the incidence of coronary artery disease, heart attack, and stroke," he said. "Such strategies would complement current treatments that lower circulating LDL and be particularly valuable in situations in which LDL lowering is challenging."

The dangers of hidden fat: Exercise is your best defense to fight it

Excess fat of any type can be bad for your health, but it's the deeper, hidden fat within the body that's most dangerous. To combat this type of fat, called visceral fat, exercise is a better defense than medication to fight it. UT Southwestern scientists made this discovery last year in research published in *Mayo Clinic Proceedings*.

"Visceral fat can affect local organs or the entire body system. Systemically, it can affect your heart and liver, as well as abdominal organs," said cardiologist Dr. Ian J. Neeland, Assistant Professor of Internal Medicine and corresponding author of the study.

Obesity affects nearly 40 percent of adult Americans, according to the Centers for Disease Control and Prevention, and can lead to heart disease, stroke, Type 2 diabetes, and certain types of cancer.

The UTSW research team wanted to find out whether exercise or medication was the best weapon to fight visceral fat. Changes in visceral fat were evaluated in 3,602 participants during a six-month period measured by a CT or MRI exam. Both exercise and medicines reduced visceral fat, but the effects of exercise were more significant per pound of body weight lost.

The majority of exercise trials were performed in the U.S. and Canada, while the pharmacologic trials included the U.S., Canada, Sweden, Japan, and four multinational cohorts.

"The location of fat in the body and the type of fat is important. If you just measure weight or body mass index (BMI), you can underestimate the benefit to your health of losing weight," said Dr. Neeland, a Dedman Family Scholar in Clinical Care. "Exercise can actually melt visceral fat."

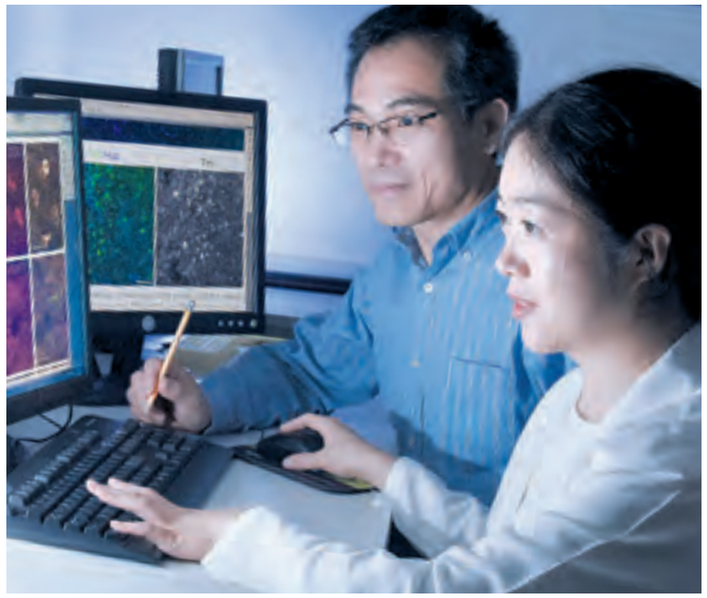
Dr. Neeland said researchers previously thought of fat as inert storage, but over the years this view evolved and fat is now seen as an active organ.

(Left) Dr. Ian J. Neeland's investigation found that exercise works better than medication to combat hidden, visceral fat.

"Some people who are obese get heart disease, diabetes, or metabolic syndrome – and others don't," Dr. Neeland said. "Our study suggests that a combination of approaches can help lower visceral fat and potentially prevent these diseases."

Basic research sheds new light on Parkinson's disease

While attempting to transform supporting brain cells into neurons, UT Southwestern researchers instead reprogrammed mature inhibitory neurons into a different type – nerve cells that generate the neurotransmitter lost in Parkinson's disease. The surprise discovery reveals new insights about this movement disorder.



Drs. Chun-Li Zhang (left) and Lei-Lei Wang unexpectedly reprogrammed mature inhibitory neurons into a different neuron type that is linked to Parkinson's disease. The research holds promise as a translational medicine discovery that could lead to new treatments for the incurable disease.

This basic research holds promise as a translational medicine discovery that may lead to new treatments for Parkinson's, an incurable neurodegenerative disease in which the brain cells progressively die.

The study, published in *Stem Cell Reports,* suggests mature neurons may be changed from one kind to another without relying on stem cells, contrary to the prevailing view.

"To find that we could manipulate neurons to change their identity in adulthood was truly unexpected," said Dr. Chun-Li Zhang, Professor of Molecular Biology and corresponding author of the study, adding that insights into neuronal plasticity and cell identity maintenance may someday lead to therapeutic strategies for treating neurological diseases through the reprogramming of local neurons.

The mouse study indicates that the brain's neurons are more changeable in adulthood than previously thought, said Dr. Zhang, also a W.W. Caruth, Jr. Scholar in Biomedical Research. The long-held belief was that a neuron's identity was sealed well before adulthood and that one kind of neuron could not morph into another variety, he added.

"Initially, I was a little disappointed that we altered the properties of medium spiny neurons and not the supporting glial cells we were targeting," he said. "But when we realized the novelty of our results, we were amazed. To our knowledge, changing the identity of resident and mature neurons had never been accomplished."

Boxing gives Parkinson's patients a fighting chance

Judy Danielson, who has Parkinson's disease, is fighting for her life. She is using a unique therapeutic strategy – boxing – and has already seen improvement. The rehabilitation program grew out of UT Southwestern research evaluating the benefits of exercise in Parkinson's patients.

"The first thing I thought of after being diagnosed was: This is not the plan I had for my life. This is not what my retirement was going to be," Ms. Danielson said.

While Ms. Danielson was visiting the UT Southwestern Gait Clinic, her therapist, Heather Mowry, suggested she check into the boxing program and research study designed to assist rehabilitation.

Ms. Danielson praised the program, saying she has seen a vast difference in her balance, her walking ability, her strength, and her emotional health. "It's about so much more than just boxing," she said.

Dr. Michael Braitsch, a 2016 UT Southwestern School of Health Professions alumnus, developed the noncontact boxing program that he hosts at Preston Hollow United Methodist Church in Dallas. The classes incorporate big dynamic functional movements, balance training, and aerobic exercise to improve cerebral blood flow and circulation throughout the body. After spending years in the financial services industry, Dr. Braitsch discovered his calling in helping patients like Ms. Danielson.

"In some ways, we're trying to fight back against impairments associated with Parkinson's. In other ways, we're trying to slow the progression of symptoms," Dr. Braitsch said.

UTSW Assistant Professor of Physical Therapy Dr. Staci Shearin joined the effort as Principal Investigator for the study. Both she and Dr. Braitsch have witnessed emotional and physical improvements in study participants.

"In our data, we've seen improvements in patients in several ways, including with functional strength and walking ability. We've seen some really cool results in functional mobility, especially in dual tasks – which is a really important skill for balance and safety for individuals with Parkinson's and their ability to do two things at once," Dr. Shearin said. "Exercise is probably one of the most important activities that can affect the progression of Parkinson's. We also find that the higher the intensity of exercise, the better the benefits."

UTSW School of Health Professions alumnus Dr. Michael Braitsch demonstrates boxing techniques to a class participant in a research study designed for patients with Parkinson's disease.

Because the neurotransmitter dopamine is lost in movement disorders like Parkinson's disease, many neuroscientists are interested in the possibility of someday creating new dopamine-producing neurons. Dopaminergic cells are important for controlling voluntary movement and emotions such as motivation and reward that drive behavior, Dr. Zhang explained.

For proper function, levels of the neurotransmitters GABA, dopamine, and others need to exist in a delicate balance in the brain, he said. Because dopamine is involved in reward behavior, including addictive behaviors, any potential treatment to increase dopamine levels would also need a way to keep the levels of other neurotransmitters in balance, he added.

The mature medium spiny neurons that changed their identities in this study usually produce GABA, an inhibitory neurotransmitter that targets other neurons throughout the adult brain, Dr. Zhang explained.

This work was supported by The Welch Foundation, The Michael J. Fox Foundation, The Decherd Foundation, and the Judith and Jean Pape Adams Charitable Foundation.

"When we realized the novelty of our results, we were amazed. To our knowledge, changing the identity of resident and mature neurons had never been accomplished." – *Dr. Chun-Li Zhang*

Unlocking the cellular connections to neurodegenerative diseases

UT Southwestern research that delves into the way certain proteins respond under metabolic stress could have far-ranging applications to understanding the development of neurodegenerative disorders such as amyotrophic lateral sclerosis, or Lou Gehrig's disease.

"There's pretty good evidence that variants of the human ataxin-2 protein are associated with neurodegeneration, and now we might have some clues as to why," said Dr. Benjamin Tu, a Professor of Biochemistry and UT Southwestern Presidential Scholar.

Two studies from Dr. Tu's lab published last year in *Cell* revealed several key functions of the yeast version of this poorly understood protein.

Using various approaches, the researchers tied yeast ataxin-2 to autophagy – the so-called housekeeping process that recycles nutrients to the cell during times of stress. They also found important implication for maintaining the health of the cell's energy source, the mitochondria. Finally, the research revealed an important role in the cellular defense against reactive oxygen species, also known as free radicals. Under normal conditions, ataxin-2 molecules form assemblies that regulate a pathway to help cells deal with that oxidative stress.

"Assembly formation is critical for ataxin-2 to do its job, and when its function is compromised, cells and neurons are more likely to die," said Dr. Tu, a W.W. Caruth, Jr. Scholar in Biomedical Research who holds the Martha Steiner Professorship in Medical Research.

He emphasized that finding ways to sustain or increase these protective functions of ataxin-2 could someday lead to neuron-saving treatments. His lab is interested in identifying small, drug-like molecules for this purpose.

Dr. Benjamin Tu has been studying a protein linked to neurodegenerative disorders. His research suggests that increasing the protective functions of this protein could lead to neuron-saving treatments.

Perot Foundation's $25 million gift advances brain science

A generous donation given by Margot and Ross Perot Sr. last spring (just prior to Mr. Perot's death in July) will accelerate UT Southwestern's efforts to discover new treatments and potential cures for brain and other neurodegenerative diseases.

The Perot Foundation's gift of $25 million last year supports neuroscience translational research at the Peter O'Donnell Jr. Brain Institute. With this latest gift, cumulative support from the Foundation has grown to more than $90 million since the 1980s.

"Our family supports UT Southwestern because we strongly believe in its mission to give every person a chance to live a healthy, productive life," Mrs. Perot said. "Our investment in the people who expand and deliver knowledge to advance science, technology, and medicine has reaped tremendous dividends. We are hopeful that this gift will lead to new treatments for brain diseases and, ultimately, cures."

The gift will expand activities in UT Southwestern's Perot Foundation Neuroscience Translational Research Center, renamed so in the family's honor. The Center's goal is to facilitate and enhance quality clinical research within the O'Donnell Brain Institute by providing resources for scientists, clinicians, and patients in the facilitation of research protocols and clinical trials and helping researchers obtain funding from the National Institutes of Health and other sources.

The gift also will help transform the Center's current biorepository into a state-of-the-art biobank, which will house large volumes of biological samples, neuroimaging, and electrophysiological data. The biobank will bring better understanding of how to maximize treatment outcomes through personalized medicine.

"Ross and Margot have always been true visionaries, driven and inspired by the potential of what the world could become," said Dr. Daniel K. Podolsky, President of UT Southwestern, who 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. "Over many decades, they have generated excitement around our institution's mission and vision through their collaborations and philanthropic gifts. This extraordinary gift will usher in new eras of innovation and development and accelerate the translation of discoveries into new treatments and cures for brain diseases and disorders."

Members of the Perot family, from left: Katherine Reeves, Suzanne McGee, the late Ross Perot Sr., Margot Perot, Ross Perot Jr., Nancy Perot, and Carolyn Rathjen

Remembering UTSW benefactor and legend Ross Perot Sr.

One of UT Southwestern's most steadfast benefactors for more than three decades, legendary Texan Ross Perot Sr., passed away July 9 at the age of 89, leaving an enduring legacy.

An enormously successful businessman, political leader, and philanthropist, Mr. Perot was known for his loyalty and commitment to his country, community, and family – typifying the great American citizen. He was a man possessed of tremendous drive, enviable business acumen, and keen intellect, with a clear sense of when and how he might improve the human condition.

UT Southwestern benefited immensely from his generosity and leadership. Mr. Perot and his wife, Margot, and the Perot Foundation have contributed more than $90 million to UT Southwestern, including more than $50 million to the *Innovations in Medicine* campaign.

"Mr. Perot's extraordinary support for UT Southwestern enabled us to establish and provide exceptional educational opportunities for generations of future physician-scientists and deliver impactful research and care that has left a lasting impact on Texas and the nation," said Dr. Daniel K. Podolsky, President of UT Southwestern.

Mr. Perot founded and later sold two high-tech companies, Electronic Data Systems and Perot Systems. He also was one of the most successful independent candidates for the U.S. presidency, winning nearly 19 percent of the popular vote in 1992. He ran for President again in 1996 as a Reform Party candidate. Mr. Perot also authored several books, including *Ross Perot: My Life & the Principles for Success* and *United We Stand: How We Can Take Back Our Country*.

In philanthropy, Mr. Perot set his sights on supporting internationally renowned institutions and became impressed with UT Southwestern's advancement from its humble beginnings in the 1940s.

The Perots and their Foundation provided generous support for UT Southwestern's Medical Scientist Training Program (MSTP) as well as Gulf War syndrome research efforts. Most recently, the Perot Foundation established the Perot Foundation Neuroscience Translational Research Center at UT Southwestern. This latest expression of the Perot family's generosity is supporting translational research at the Peter O'Donnell Jr. Brain Institute to move science more quickly from the laboratory to the patient's bedside and transform research discoveries into improved and innovative drugs, devices, and treatments.

"Mr. Perot was a true friend to the Medical Center and a remarkable man whose inspirational leadership touched all who knew him," said Dr. Podolsky. "He will be deeply missed."

Acclaimed neurologist leads O'Donnell Brain Institute

The deep commitment of UT Southwestern's leadership and community supporters to create a premier center for the study and treatment of brain disease, along with the Medical Center's renowned scientific culture, made Dr. William T. Dauer consider the offer to become inaugural Director of the Peter O'Donnell Jr. Brain Institute a compelling and exciting opportunity.

"The commitment of both the University and the surrounding community, with Mr. Peter O'Donnell at the forefront, is really unparalleled in any environment I know of," said Dr. Dauer, an acclaimed physician-investigator in dystonia and Parkinson's disease who was recruited after a national search.

"The dedication to make this an important priority to change the lives of people with brain disease will be the key ingredient for success."

In July, Dr. Dauer joined UT Southwestern as Director of the O'Donnell Brain Institute and Professor of Neurology & Neurotherapeutics and Neuroscience. His responsibilities include integrating the work of scientists and clinicians in fields that include neurology, neuroscience, neurosurgery, physical medicine and rehabilitation, neuroradiology, and psychiatry.

"Dr. Dauer's broad experience as a neurologist and a scientist positions him to provide strong leadership as the Peter O'Donnell Jr. Brain Institute works to accelerate the translation of fundamental discoveries into cutting-edge treatments for a broad spectrum of brain disorders," said Dr. W. P. Andrew Lee, Executive Vice President for Academic Affairs, Provost, and Dean of UT Southwestern Medical School, who holds the Atticus James Gill, M.D. Chair in Medical Science.

Dr. Dauer was previously on the faculty at the University of Michigan as Director of the Movement Disorders Group and Director of the Morris K. Udall Center of Excellence for Parkinson's Disease Research. For nearly two decades, Dr. Dauer's groundbreaking research has been focused on the molecular basis of dystonia and the mechanisms of neurodegeneration in Parkinson's disease. His findings have elucidated the critical role of the torsinA protein in the progression of dystonia, which is marked by disabling, involuntary movements. Studies taking place under his direction at the Udall Center explaining the neurobiologic basis of falls in Parkinson's disease are being used to pioneer a novel therapy for this currently untreatable symptom.

Building teams across disciplines, among both scientists and clinicians, will be a key focus of the O'Donnell Brain Institute as it seeks to uncover the fundamental causes of brain disease and translate discoveries into treatments.

"UT Southwestern has a uniquely outstanding scientific culture," said Dr. Dauer, who holds the Lois C.A. and Darwin E. Smith Distinguished Chair in Neurological Mobility Research. "It's really the perfect place to bring together the best minds in the country, or even the world, to work on brain science with the important goal of improving the lives of people with brain diseases."

Established in 2015 with a gift from the O'Donnell Foundation, the O'Donnell Brain Institute brings together doctors and researchers from various disciplines to better understand the molecular workings of the brain and apply those discoveries to the prevention and treatment of brain, spine, nerve, and muscle disorders.

Artificial intelligence moves into clinical spaces to improve patient care

Imagine a future in which a patient's wristband can nudge his or her doctor by indicating they've been in the exam room for half an hour. Or where the clinic is wired for sensors that recognize patients as they walk in the door, getting temperatures, blood pressures, heights, and weights.

Far from science fiction, these clinic scenarios are real AI projects currently being developed at UT Southwestern's Medical Artificial Intelligence and Automation (MAIA) Laboratory.

"AI is going to transform health care. Nothing is comparable," said Dr. Steve Jiang, Professor of Radiation Oncology, Director of the MAIA Lab, Vice Chair of Radiation Oncology, and Director of the Division of Medical Physics and Engineering. "Almost everything we do in health care will be impacted by artificial intelligence – to improve the efficiency and quality of the work. AI helps humans do a better job, faster."

AI will never replace doctors – who will continue to provide the warm, human touch – but it will enable new physicians to work hand in hand with the latest technology to improve patient care and research.

"The reality is when one of our current medical students hits his or her professional life – AI is going to be in the clinic," said Dr. Gaudenz Danuser, Chair of the Lyda Hill Department of Bioinformatics, Professor of Bioinformatics and Cell Biology, and holder of the Patrick E. Haggerty Distinguished Chair in Basic Biomedical Science.

To stay on top of this trend, a committee of faculty and administrators convened in late 2018 to evaluate adding AI to the UT Southwestern Medical School curriculum.

At a campus lecture last year, Dr. Danuser explained how companies like Facebook and Google are using AI to create profiles of users and their needs. In a similar way, he said, AI in medicine will help doctors process and understand data faster than a human brain can calculate such information.

In January 2019, the University added a lecture series to the Medical School curriculum introducing students to the basic concepts and applications of AI. A few months later, a Grand Rounds lecture series for the entire campus launched that brings in speakers to discuss AI topics.

"UT Southwestern is already developing sophisticated computer algorithms to guide diagnosis and treatment in oncology, cardiology, and other fields. AI has helped detect subtle patient abnormalities through imaging and can analyze large datasets to draw conclusions and predict likely patient outcomes," Dr. Danuser said.

"AI can learn from human experience and by itself by interacting with the environment," added Dr. Jiang, who holds the Barbara Crittenden Professorship in Cancer Research. "AI can improve patient safety by automatically detecting and preventing errors. The machine is never tired and will check everything, every detail. And it will learn from data from previously treated patients and become smarter and smarter from learning continuously."

Incorporating the latest teaching about artificial intelligence to benefit UTSW students, trainees, and fellows, and pursuing research using AI have become major focuses for Drs. Gaudenz Danuser (left) and Steve Jiang.

"Almost everything we do in health care will be impacted by artificial intelligence – to improve the efficiency and quality of the work." – *Dr. Steve Jiang*

Looking to the Future

The sky is the limit. Or so it seems as UT Southwestern expands on all fronts to support its mission of promoting health and a healthy society. Unprecedented success and growth, made possible in part through philanthropic support, have led to several major capital projects, including construction of a third tower at William P. Clements Jr. University Hospital and expansion into Frisco – not to mention advances in educational programs to arm future caregivers with the skills and knowledge needed to effectively perform their jobs.

Medical School curriculum launched in 2015 graduates first class

In August 2015, UT Southwestern Medical School launched an innovative new curriculum – called the *Foundation for Excellence* – and now, four years later, the first class that studied under that curriculum has graduated.

"As the first group of students to experience the new curriculum, we all learned about how to advocate for our interests as learners, how to give feedback, and how to adapt," said Dr. Kylie Cullinan, a 2019 graduate and current UTSW resident in internal medicine-pediatrics. "The freedom of the new curriculum gave me the push to find personal interests outside of the standardized curriculum and provided time to actively pursue them. I was able to identify strong mentors, spend a month learning about nutrition, and work at a camp for children with diabetes – all experiences that I think will make me a stronger physician."

The curriculum condensed material traditionally taught in the first two years of medical school into an integrated 18-month pre-clerkship block, giving students earlier exposure to clinical activities and adding considerable flexibility and breadth to each student's educational experience. This reduction in course time in the pre-clerkship phase was facilitated by minimizing content redundancy through coordination of all respective disciplines teaching each topic.

Dr. Angela Orlino talks with UTSW residents Drs. Lindsey West (left) and Kylie Cullinan, both of whom she mentored as medical students educated under the new curriculum.

"During the pre-clerkship period, students gain important scientific knowledge, attitudes, and skills, along with a common vocabulary shared by the medical profession, all of which are vital elements in building a foundation of excellence," said Dr. Angela Mihalic, Dean of Medical Students, Associate Dean of Student Affairs, Distinguished Teaching Professor of Pediatrics, and a 1995 UTSW Medical School graduate herself. "All classes during the pre-clerkship period are measured on a pass/fail basis so that students can concentrate on learning the material in a team-oriented environment."

In addition to traditional lectures, this pre-clerkship block is focused on building knowledge in basic and clinical sciences through team-based learning experiences in the classroom, laboratories, simulation environments, and small-group settings.

"Initially, as a new student at a very large medical school, these team-based learning groups allowed for closer interactions and friendships with fellow students," added Dr. Cullinan, who received a Dr. Richard Mays Smith Award as a graduate last year. "I think this approach reflects the evolving practice of medicine – it truly is a team sport. I need to communicate clearly with the other residents on my team, attending specialty physicians, and my patients."

Clerkships start in the middle of the second academic year. By starting clerkships sooner, medical students can explore more clinical fields to help them choose their specialty. For those students who have already decided on a discipline, they can explore a selected topic in greater depth or broaden clinical experiences with other opportunities.

To prepare students for residency and beyond, the expansion of clinical training under the new curriculum provides more opportunities for unique and tailored experiences. Then as students embark on the final phase of their medical school experience, the post-clerkship period allows them to explore innovative science and medicine in subject areas related to their future careers as well as gain mastery of clinical skills through simulation.

> "During the pre-clerkship period, students gain important scientific knowledge, attitudes, and skills, along with a common vocabulary shared by the medical profession."
> *– Dr. Angela Mihalic*

Dr. Lindsey West, a resident in dermatology who also graduated last year, experienced both the new and earlier curriculum. She had taken a year off for a research fellowship after her third year of medical school.

"The new curriculum allowed students to gain exposure to all of the specialties earlier on with increased elective time and the scholarly activity, and also helped students gain skills in how to work and communicate as a team," Dr. West said. "Working with their class during my fourth year, I noticed how the students seemed to be very comfortable and proactive when working in group settings in the classroom and on clerkships."

Graduate School gains international stature as member of elite Amgen Scholars Program

Sixteen select college undergraduates spent this past summer in UT Southwestern labs, working on dynamic and leading-edge research projects, as part of the initial class of Amgen Scholars here.

Lauren Duan, a junior at Johns Hopkins University, benefited as one of those Scholars who worked alongside UTSW faculty members and postdoctoral researchers. Her focus was on cardiac regeneration and investigating how cardiomyocytes can be programmed to regenerate and resist cell death.

"I knew that I wanted to gain a research experience unlike any other, to make big strides in my science, but also to contribute to answering big questions," said Ms. Duan, who plans to eventually apply to an M.D./Ph.D. program.

Ms. Duan's experience was made possible by a four-year grant awarded to UT Southwestern in 2018 from the Amgen Foundation. The program provides laboratory experience for undergraduates who may not otherwise be able to engage in research at the world's top educational and research institutions.

Only 13 institutions across the U.S. were selected to host these budding biomedical scientists. Last year, UT Southwestern – along with Duke, Johns Hopkins, and Yale universities – joined the California Institute of Technology, Columbia, Harvard, the National Institutes of Health, Stanford, UC-Berkeley, UCLA, UC-San Francisco, and Washington University in St. Louis in the network. More than 4,200 Amgen Scholars – representing more than 700 colleges and universities worldwide – have participated in this undergraduate program since its inception 12 years ago.

"Designation as an Amgen Scholars institution reaffirms UT Southwestern's international stature as an elite biomedical research institution," said Dr. Andrew Zinn, Dean of the Graduate School of Biomedical Sciences. "It also augments our highly successful Summer Undergraduate Research Fellowship Program, which plays a key role in our efforts to recruit outstanding undergraduates nationally to do their Ph.D. or M.D./Ph.D. training here and become future leaders in biomedical science."

Dr. Zinn, himself a graduate of UTSW's Medical School and Graduate School who holds the Rolf Haberecht and Ute Schwarz Haberecht Deanship of the UT Southwestern Graduate School of Biomedical Sciences, said the payoff for UT Southwestern has been just as high in terms of name recognition – one of the principal challenges in recruiting top U.S. undergraduates.

"I expect even Amgen Scholars who ultimately train elsewhere will come away impressed by UT Southwestern and tell others about us," Dr. Zinn said.

Dr. Jeffrey Zigman (center) discusses research data with Amgen Scholars Anna Patterson and Julian Maceren. The Scholars were among 16 who received hands-on laboratory experience at UT Southwestern this past summer.

School of Health Professions celebrates 50 years, grows to meet needs for health care professionals

The School of Health Professions, which marked its 50-year anniversary in 2018, continues to adapt and evolve in response to changes in higher education and the health care industry. Over the next half-century, that transformation will continue in efforts to optimally prepare tomorrow's health care professionals.

The School offers training in seven distinct areas: applied clinical research, physician assistant studies, clinical nutrition, prosthetics-orthotics, clinical rehabilitation counseling, radiation therapy, and physical therapy. Each year, more than 300 students enroll to pursue studies at master's and doctorate levels.

"Over the past 50 years, the School of Health Professions has successfully served its mission by training outstanding health care professionals, providing the highest quality patient care, and producing innovative health care research," said Dr. Jon Williamson, Dean of the School. "While we are proud of our accomplishments, we must continually strive for improvement to ensure we can continue to serve our mission, the institution, and our community."

The School has been recognized for the quality of its programs and a commitment to diversity and inclusion. The Physician Assistant Studies Program, for example, is ranked seventh in the nation by *U.S. News & World Report* in "America's Best Graduate Schools 2020," while *INSIGHT Into Diversity* magazine recognized the School in 2018 for demonstrating excellence in diversity and inclusion.

In 2019, the School of Health Professions started a new Ph.D. program in applied clinical research, which provides rigorous research training specifically for health professionals.

In response to demand for a wider variety of health care workers, the then-School of Allied Health Professions was established in 1968 and opened the next year. The first full academic year had 57 students. In 1983, the School moved to its current location on Harry Hines Boulevard, in the heart of the UTSW campus.

A distinguishing characteristic of the School is teaching and training by the outstanding faculty found only at an academic medical center, which provides students firsthand access to advanced clinical care and research. This is evident in the first-time licensure/certification student pass rates that top 97 percent. In addition, all programs report 100 percent employment of graduates within the first six months following graduation.

"The School of Health Professions has worked hard over the years to maintain high-caliber academic programs with quality faculty and integrated academic and clinical training," said Dr. Kim Hoggatt Krumwiede, Associate Dean for Academic Affairs.

In August, the School started a new Ph.D. program in applied clinical research that provides rigorous research training specifically for health professionals.

"The primary goal of the program is to develop and cultivate a new generation of health professionals pursuing careers as independent clinician-scientists," said Dr. Scott Smith, Associate Dean for Research. "Through participation in the program, individuals will acquire the skills and breadth of experience needed to contribute to the advancement of their respective fields through research in a substantive and impactful way."

Dr. Carolyn Bradley-Guidry instructs physician assistant students Chinonso Nnaji (left) and Aila Soomro in casting and splinting.

Simulation Center becomes national leader in quality and effectiveness of medical training

UT Southwestern's $40 million Simulation Center, one of the largest in the country, has quickly evolved since its opening in late 2018 into a national leader in simulation training as well as an integral factor in the quality of education and training provided to UTSW health care students and professionals.

"Patients should know that we embrace the most rigorous standards of training available today, and we're actually setting those standards. We are a dedicated campus for medical education, patient care, and research, and we're enhancing all three within the Simulation Center," said Dr. Daniel Scott, Assistant Dean of Simulation and Student Integration.

In September 2018, the institution opened the 49,000-square-foot facility on West Campus that includes specialized training laboratories for all specialties on campus. It also features high-tech instruments such as virtual reality equipment. Simulators in the Center closely replicate diseases, conditions, and other real-life patient scenarios, such as childbirth, orthopedic operations, trauma resuscitations, and more. The realistic medical settings allow learners to become familiar with the diagnostic and treatment processes and equipment, work in medical teams, and learn proper communication and bedside skills.

Health care educators are trying to achieve better patient care – and simulation is part of the solution. Over the past 20 years, a growing body of literature has linked simulation-based training to improved patient safety and clinical outcomes.

"Students are getting hands-on clinical exposure in the simulation environment where there are no untoward effects to actual patients," said Dr. Scott, who holds the Frank H. Kidd, Jr., M.D. Distinguished Professorship in Surgery. "There's also the aspect of psychological safety. Students are not afraid of making mistakes and can explore different decision-making options without having any real-life repercussions."

UT Southwestern medical students start training at the Center their first year. By the time they graduate, the goal is for students to have developed a "learner portfolio" of competencies verified through simulation training. The Center also trains students from UT Southwestern's Graduate School of Biomedical Sciences and School of Health Professions.

Faculty, residents, and fellows are among the other learners utilizing the Center for continuing education activities that allow them to fulfill certification requirements or potentially develop new treatment methods.

"What I hope to achieve, both within and outside the program, is institutionalizing simulation throughout health care education, including residency and medical education and also within interprofessional education," said Krystle Campbell, Director of Simulation Center Operations. "I would love to see a lot more interprofessional education events happen, along with instilling competency-based testing using simulation for both pre- and post-licensure students."

The Sim Center averages up to 2,500 learner visits per month. Moving forward, development priorities include further integrating simulation training into the Medical School curriculum, emphasizing advanced techniques for practicing providers, increasing the number of scholarly projects, and connecting simulation training data to actual clinical outcomes.

"We view the Simulation Center as a fantastic resource that not many places in the country have anything close to," Dr. Scott said. "This will allow our faculty to continue pioneering new educational methods, publish their innovative work, and bring excellence and recognition to UT Southwestern as a major leader in simulation."

Students and other UT Southwestern learners now benefit from practicing medical techniques on high-tech, lifelike manikins in the Simulation Center, which opened in late 2018.

President Dr. Daniel K. Podolsky (left) and Dr. Mack Mitchell discuss plans for the new UT Southwestern Medical Center at Frisco at a topping-off event for the project in late 2018.

UT Southwestern reaches into Frisco to offer specialized care

One of the most striking features of the new UT Southwestern Medical Center at Frisco – which opened in December – is the pedestrian bridge that connects it to Texas Health Hospital Frisco. It's a fitting metaphor for the remarkable relationship between UT Southwestern and Texas Health Resources, partners in the Southwestern Health Resources network.

The new facility represents a unique opportunity to grow UT Southwestern's clinical operations. The four-story structure offers on-site medical care for adults and children in a dozen specialty areas, along with a retail pharmacy and imaging and lab services.

Inpatient and surgical services take place right next door at UT Southwestern's partner site – the new 73-bed Texas Health Hospital in Frisco. Together, the two facilities comprise a 20-acre collaborative medical campus dedicated to providing a seamless patient experience.

"Our faculty physicians, together with Texas Health's community physician colleagues, serve the needs of the Frisco community through a coordinated network, ranging from primary care to the most specialized expertise," said Dr. Daniel K. Podolsky, President of UT Southwestern and holder of 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. "In addition, patients have the opportunity to go beyond even leading-edge treatments through access to participation in innovative clinical trials. This facility brings to Collin County some of the best that UT Southwestern Medical Center has to offer."

The city of Frisco, located 25 miles north of UT Southwestern, is undergoing significant growth. It is among the fastest growing cities in the country, with 37 new residents every day, according to U.S Census Bureau statistics. The city is also a key bridge between UT Southwestern's main campus in Dallas to more rural areas such as Prosper, Celina, and Little Elm.

Our Frisco physicians at the UT Southwestern Medical Center at Frisco are members of the UT Southwestern Medical Group, one of the largest, most comprehensive physician practices in Texas.

The Frisco project marks the fifth UT Southwestern regional medical center, joining others in Las Colinas, Park Cities, Richardson/Plano, and Fort Worth.

Celebrating a Clements University Hospital expansion milestone

After 19 months of construction, the first major expansion of William P. Clements Jr. University Hospital marked a significant milestone last year with the top-floor exterior framework completion. The project, necessitated by increasing patient demand and population growth that exceeded initial forecasts, is on schedule to be completed by September 2020.

The $480 million, 12-story tower will add operating rooms and an expanded Emergency Department to the existing 460-bed Clements University Hospital and become the inpatient home to the Peter O'Donnell Jr. Brain Institute. It will also increase the number of inpatient rooms, allowing consolidation of patients now treated at Zale Lipshy Pavilion to all be treated under one roof at Clements University Hospital.

Dr. John Warner, EVP for Health System Affairs and CEO of UT Southwestern University Hospital, signs a painted metal beam kept as a memento of the "topping-off" event.

In March 2019, less than five years after opening the hospital, UT Southwestern officials, physicians, nurses, and clinical staff gathered with architects, construction executives, and descendants of the hospital's namesake, the late Texas Gov. Clements, to celebrate the "topping off" of the third tower.

"This new 12-story tower will allow us to bring together all of our University inpatient services in one location on the UT Southwestern campus," said UTSW President Dr. Daniel K. Podolsky, who 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. "It will allow health professionals to work more closely together as they care for patients."

The construction milestone came just a few months before UT Southwestern was named the No. 1 hospital in Dallas-Fort Worth and the No. 2 hospital in Texas for the third consecutive year by *U.S. News & World Report.* In 2018, Clements University Hospital received a national Rising Star Award for improved quality and safety efforts, ranking it within the country's top 25 academic medical center hospitals.

Zale Lipshy began UT Southwestern's legacy of service to patients when it opened in 1989, said Dr. John Warner, Executive Vice President for Health System Affairs and holder of the Jim and Norma Smith Distinguished Chair for Interventional Cardiology, and the Nancy and Jeremy Halbreich, Susan and Theodore Strauss Professorship in Cardiology.

Architectual rendering of the completed William P. Clements Jr. University Hospital

The additional space in the new Clements University Hospital tower will allow for "the coming together of these two excellent clinical care communities," Dr. Warner said.

Event attendees Nancy Seay and her granddaughter, Nancy Neuhoff – both members of the UTSW art selection committee – have been searching to find the hundreds of pieces needed for public areas and patient rooms.

Ms. Seay is the daughter of Gov. Clements, who donated $100 million to UT Southwestern in 2009. As one of many who added their signatures to the construction beam at the topping-off ceremony, she included a special note: "Hey Dad, the hospital is wonderful. Nancy."

> "This new 12-story tower will allow us to bring together all of our University inpatient services in one location on the UT Southwestern campus." – *Dr. Daniel K. Podolsky*

North Campus expansion plan kicks off

Growth of brain research, cancer treatment programs drives new building project

A new building with two towers designed to serve UT Southwestern's ongoing growth in the high-priority areas of brain research and cancer patient care – the Outpatient Cancer Care Tower of the Harold C. Simmons Comprehensive Cancer Center and the Research Tower of the Peter O'Donnell Jr. Brain Institute – is expected to open in the fall of 2022.

The nine-story towers – approximately 300,000 square feet each – will stand adjacent to the C. Kern Wildenthal Research Building on North Campus.

At a June 2019 groundbreaking ceremony, UT Southwestern President Dr. Daniel K. Podolsky, who 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, spoke to donors, administrators, clinicians, researchers, and supporters.

"We're here to begin the next great project on the UT Southwestern campus – a building that will expand our ability to respond to those in need of cancer care. Our researchers, working with learners, will also be able to make discoveries to improve the treatment, cure, and prevention of all the forms of brain disease that affect 50 million Americans," Dr. Podolsky said.

He thanked event attendee Annette Simmons and her late husband, Dallas businessman Harold C. Simmons, for longtime, generous support that has furthered cancer research and care at UT Southwestern. He also thanked Edith and Peter O'Donnell Jr. for their decades of giving and generosity to help launch the O'Donnell Brain Institute to advance brain science.

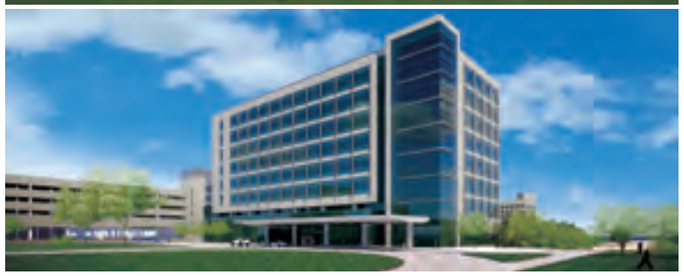
The Research Tower will help UT Southwestern attract the best and the brightest research talent, top-flight faculty, and the most outstanding Ph.D. students in the country, said Dr. Joseph Takahashi, Chair of Neuroscience and holder of the Loyd B. Sands Distinguished Chair in Neuroscience.

Dr. William T. Dauer, Director of the O'Donnell Brain Institute, said that the Research Tower will be the home of signature scientific initiatives of the Institute.

"Teams of scientists will pursue studies aimed at discovering the fundamental mechanisms of brain disease and repair and developing advanced technologies to therapeutically modulate brain function. We will target areas that hold great potential for clinical translation," said Dr. Dauer, who holds the Lois C.A. and Darwin E. Smith Distinguished Chair in Neurological Mobility Research.

Great strides are being made in treating and curing cancer, added Dr. Carlos Arteaga, Director of the Simmons Cancer Center, which will be expanding from the clinical buildings nearby. Dr. Arteaga, also Associate Dean of Oncology Programs, holds The Lisa K. Simmons Distinguished Chair in Comprehensive Oncology.

Dr. Arteaga said the new facility would triple current cancer care capabilities on campus.



Under construction on North Campus is a building with two towers to support UT Southwestern's growth in the high-priority areas of brain research (top) and cancer patient care (bottom).

Grateful families give back to advance breast cancer research

Three generations of Aaron women: (from left) Dawn, Morgan, and Carol

At the June 2019 groundbreaking of the Outpatient Cancer Care Tower of the Harold C. Simmons Comprehensive Cancer Center and the Research Tower of the Peter O'Donnell Jr. Brain Institute, Morgan Aaron and her mother, Dawn, shared how far UT Southwestern's cancer and brain treatments have already come.

Morgan was 28 years old in 2016 when she was diagnosed with stage 4 breast cancer that had spread to her brain, resulting in five brain tumors. Because triple-negative breast cancer is not fueled by hormones, it does not respond to hormonal therapy medicines, making treatment options limited.

Within days of her diagnosis, Morgan's UT Southwestern care team – Dr. Barbara Haley, Professor of Internal Medicine, who holds the Charles Cameron Sprague, M.D. Chair in Clinical Oncology; Dr. Toral Patel, Assistant Professor of Neurological Surgery, Neurology & Neurotherapeutics, and Radiation Oncology; and Dr. Robert Timmerman, Professor of Radiation Oncology and Neurological Surgery, who holds the Effie Marie Cain Distinguished Chair in Cancer Therapy Research – had performed the treatment that saved her daughter's life, Dawn said. "Today Morgan is healthy. She is cancer-free."

The families of Todd and Dawn Aaron and Steven L. and Carol Aaron made a combined gift of $250,000 to support triple-negative breast cancer research at the Simmons Cancer Center.

"Reason and logic say I should not be standing here before you all today," Morgan said at the groundbreaking. "You brought me back to life."

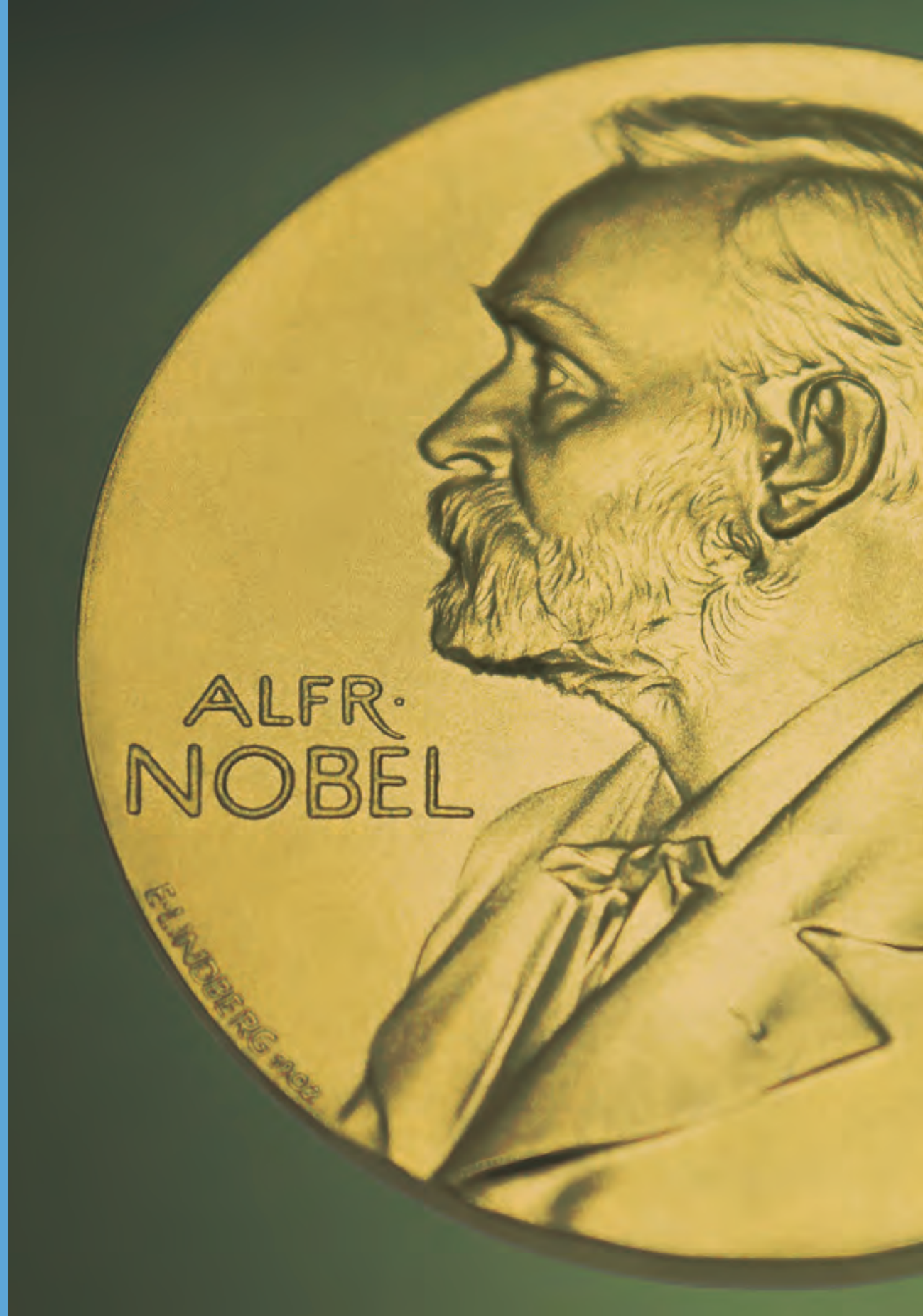
The Aaron families are passionate about supporting the research to develop new, more effective treatments that will change the future for others diagnosed with the disease.

"How do you thank someone for saving your daughter's life?" Dawn asked. "We are thankful to UT Southwestern and for the incredible work of her medical team. We were in such fine hands – such capable, compassionate, brilliant hands. It was with a human touch the entire way."

Strengthening Reputational Excellence

UTSW faculty, staff, students, and community supporters are making an impact – through exceptional work that has led to high-profile awards bolstering the institution's reputation for excellence and through efforts that engage the community in innovative outreach programs.

UT Southwestern faculty members have been awarded Nobel Prizes in 1985, 1988, 1994, 2011, and 2013.



UT Southwestern heightens community outreach efforts

"You guys want to hold a brain?"

In any other context, it might seem a strange question. But this was UT Southwestern Science Saturday, and guests gathered for just this kind of experience – a chance to hold a model brain, amplify their own heartbeat, or don a safety suit and boots.

Nearly 1,700 visitors attended Science Saturday, the first event of its kind. Open to the public, and promoted via community partners such as *The Dallas Morning News* and the Perot Museum of Nature and Science, the fall 2018 event on McDermott Plaza attracted visitors of all ages, ranging from those just beginning to show interest in science to some with a long history of work in research.

"This kind of open discussion with our community is part of us giving back and what makes me enthusiastic for the future of science and medicine, especially at UT Southwestern," said Dr. Stuart Ravnik, Associate Dean of the UT Southwestern Graduate School of Biomedical Sciences.

These outreach initiatives connect UT Southwestern directly with various stakeholders – thought leaders, decision-makers, potential donors, key influencers, and other community leaders.

For more than seven decades, UT Southwestern has been an integral part of the Dallas community. The institution's impact is broad in the health care industry and significant for its economic impact in North Texas. These outreach initiatives connect UT Southwestern directly with various stakeholders – thought leaders, decision-makers, potential donors, key influencers, and other community leaders – who can support the work and mission of the institution in a myriad of ways. It is also an opportunity to introduce others to the UT Southwestern mission by bringing them to campus for the first time.

UT Southwestern engages the Dallas community with outreach initiatives to promote awareness of its mission in myriad ways, some of which include: **A.** Science Saturday **B.** Black Men in White Coats **C.** Conquering Cancer **D.** Soluna: Music and the Brain **E.** Science in the City **F.** Carnaval de Salud

In addition to Science Saturday, UT Southwestern's high-priority areas of brain research and cancer care were the focus of several other outreach initiatives during the year. In February 2019, the Harold C. Simmons Comprehensive Cancer Center partnered with former Dallas Mayor Mike Rawlings and Fort Worth Mayor Betsy Price to launch Conquering Cancer, a campaign aimed at raising cancer awareness and increasing screening.

The program kicked off at the Dallas Mavericks game against the Indiana Pacers, with UT Southwestern, the mayors, and the Mavericks asking the community to make time for mammograms, stop smoking, get screened for hepatitis C and colon cancer, vaccinate teens and preteens against HPV, and learn about cancer risk through genetic testing.

In April 2019, UT Southwestern and *The Dallas Morning News* again joined forces to open the doors of research labs to the Dallas-area community with the second annual Science in the City, a community initiative to allow the public inside the research labs that are changing the world of science and health care.

Only 10 days later, UT Southwestern's Peter O'Donnell Jr. Brain Institute partnered with the Dallas Symphony Association for Soluna: Music and the Brain, which featured world-renowned brain scientists and clinicians coming together to discuss interaction, improvisation, and cross-cultural communication through music. During the pre-event reception and intermission, UT Southwestern volunteers from the O'Donnell Brain Institute showed guests an actual brain and answered questions.

In late April, UT Southwestern produced the annual Carnaval de Salud at Thomas J. Rusk Middle School. The event, organized and run by UT Southwestern students, faculty, and staff volunteers, is in its 15th year of providing free health care services, information, and lifestyle strategies to hundreds of families from underserved populations in Dallas.

This is only the beginning: Expect to see even more outreach by UT Southwestern going forward. It's all connected to fulfilling the mission of promoting health and a healthy society that enables individuals to achieve their full potential.

Each year, as part of the United to Serve campaign, UTSW students, faculty, and staff participate in Carnaval de Salud, a community health fair at Thomas J. Rusk Middle School.

Beyond borders: Physician-scientist fights infectious diseases worldwide

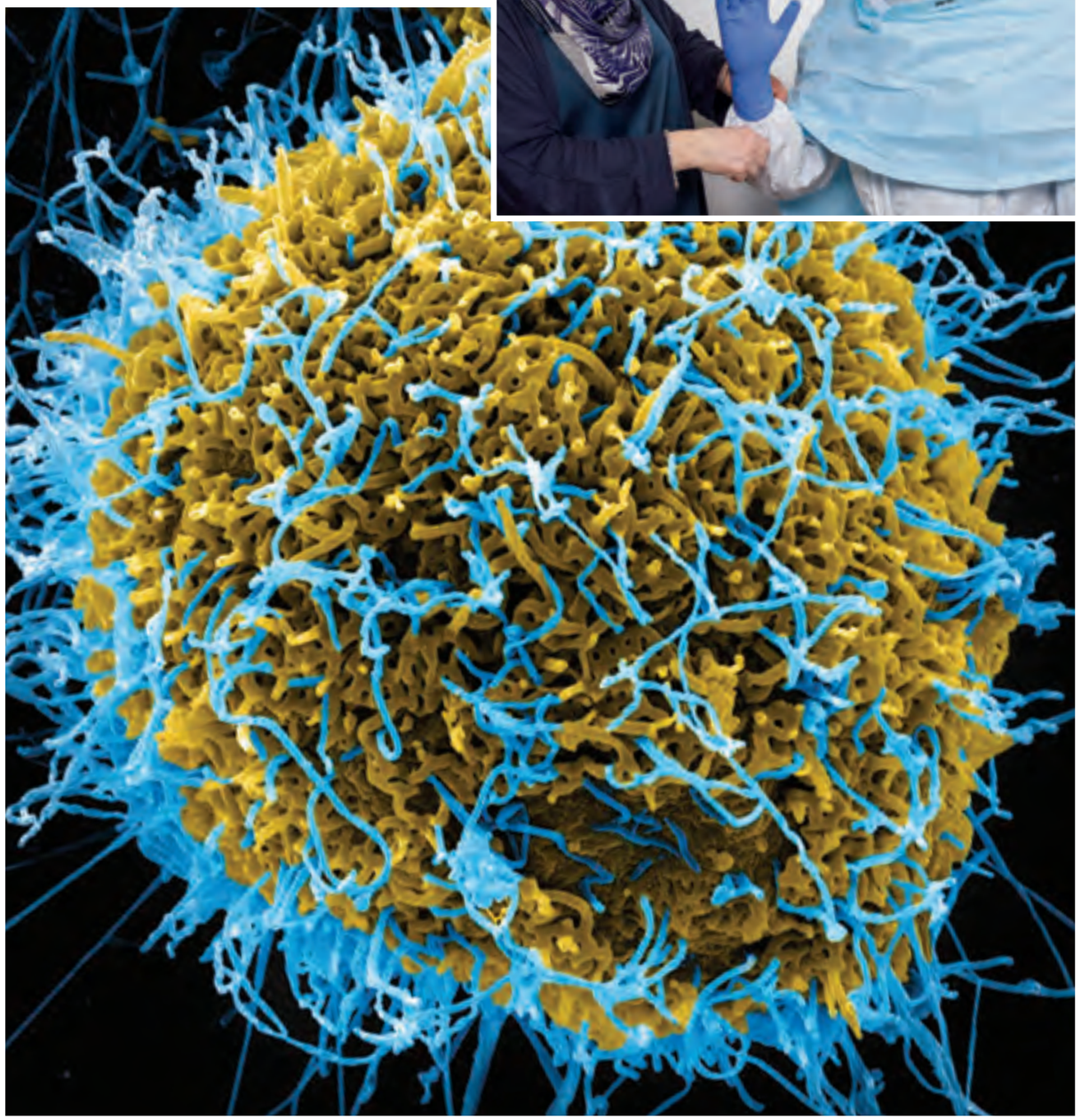
An Ebola outbreak in West Africa hit close to home for North Texas in late 2014 – one patient who died of the disease in the U.S. was treated in Dallas, and two local health care workers acquired the infection but recovered. Worldwide, hospitals and the public were on high alert.

Since then, UT Southwestern has stepped forward in national and international efforts to reduce the chances of such deaths and infections happening again on American soil or elsewhere in the world, and to minimize the severity of new outbreaks.

Dr. Trish Perl, a UT Southwestern infectious diseases specialist who has worked with the World Health Organization (WHO), led an effort to create guidelines for personal protective equipment standards for health care workers treating Ebola patients. The guidelines were published in late 2018.

Dr. Perl, Chief of the Division of Infectious Diseases and Geographic Medicine, and the international team working with her found that some strategies designed to protect workers – such as taping their gloves to their gowns – may have added to their risk by making it more difficult for them to safely take the gowns off. There also was evidence

Dr. Trish Perl demonstrates proper use of protective gear for clinicians working with Ebola patients with the help of UTSW medical student Michael Ji.



Shown budding from an infected cell are filamentous Ebola virus particles (colored blue).

that the bleach used to spray down the equipment may have led to breakdowns in the material, she said.

While there is evidence to support the need for goggles, coveralls, and a respirator, her subcommittee found that removing these pieces of gear – not engineered to work together – may have led to transmission among health care workers. Risks were associated with the combination of the gear.

"Health care workers were actually fainting from the heat because of the lack of breathability of the protective equipment used at the time," she said. Other workers then had to rush to suit up and pull them out of the room. Her group's guidelines suggest that fluid-resistant gowns and clear plastic shields that hang in front of the face, along with gloves and thick-soled boots, provide effective protection.

If adopted, the new guidelines could help during the current African outbreak that began in 2018, Dr. Perl said. And if a case were to arise here now, she added, the American health care system would be in a much better position to handle it.

This is important locally because North Texas is at risk of experiencing other emerging infections. Dallas Fort Worth International Airport – the nation's fourth-busiest airport – receives travelers from around the globe and is making North Texas become increasingly hospitable to disease-carrying vectors due to climate warming.

For example, in 2012, Dallas was the epicenter of the largest West Nile outbreak in the country. Then, in 2016, Dallas reported the nation's first sexually transmitted case of Zika, another viral infection most often seen in South America and also spread by mosquitoes.

As more and more infectious diseases emerge, and reemerge, academic institutions like UT Southwestern will need to play an increasingly important role in helping with investigations, running diagnostics, developing treatments, and providing potential prevention strategies, Dr. Perl said.

With these growing threats, UT Southwestern has taken action. Staff members at William P. Clements Jr. University Hospital receive special training to assess and diagnose Ebola patients, joining a network of highly skilled medical centers across the country designated either as assessment or treatment centers.

"I think we have a better understanding now of what the potential risks are and an understanding of how difficult it is to treat Ebola patients successfully," added Dr. Perl, a Professor of Internal Medicine who holds the Jay P. Sanford Professorship in Infectious Diseases.

"I think we have a better understanding now of what the potential risks are and an understanding of how difficult it is to treat Ebola patients successfully." – *Dr. Trish Perl*

UTSW reaches out with vision of hope in Ethiopia

Local healers suspected Bisrat Sisay was possessed by evil spirits. They could offer no other explanation for the boy's violent convulsions that would throw him to the ground and turn his eyes ghostly white.

Now 14 years old, Bisrat is beginning a new stage of his life, one where he can logically explain to others that epilepsy – not an evil spirit – causes his convulsions. Although he was diagnosed with the condition several years ago, his parents didn't know how to manage the seizures until UT Southwestern started a medical outreach program in Ethiopia that is elevating the care provided by the local hospital.

Bisrat's story is disturbingly common in Ethiopia, where a shortage of neurologists leaves large swaths of the country without doctors to treat common brain conditions such as epilepsy and autism. But a recent groundswell of international collaborations between developing countries and U.S. medical centers is helping to address the scarcity, in particular in several sub-Saharan Africa nations where the situation is most dire.

Bisrat Sisay

UT Southwestern Drs. Karen Kowalske (right) and Mehari Gebreyohanns (in glasses) conduct multidisciplinary teaching rounds at Ethiopia's Tibebe Ghion Bahir Dar University Hospital.

Bahir Dar University, Ethiopia

In one of the newest efforts, UT Southwestern established a partnership in the Ethiopian city of Bahir Dar where a hospital serving a region of several million people has no neurologist and lacks basic brain-scanning equipment. UTSW clinicians teach medical personnel there the basics of neurology and each summer send physicians and doctors-in-training to help with patients like Bisrat.

"This is how we develop a new breed of doctors," said Dr. Mehari Gebreyohanns, a UT Southwestern neurologist from Ethiopia who spearheads the collaboration endorsed by Bahir Dar University and the local government. "We are training the next generation of leaders who believe they can improve the quality of life, not just in the U.S., but in countries thousands of miles away."

The need is great. One survey found that 23 African nations average one neurologist per 5 million people, while 12 nations have no neurologists, added Dr. Gebreyohanns, Assistant Professor of Neurology & Neurotherapeutics.

The UT Southwestern program, endorsed by Ethiopia's health minister, is part of the Medical Center's Global Health Initiative that aims to help developing countries improve their health care infrastructure while offering international training opportunities for its resident doctors.

Dr. Mehari Gebreyohanns (at right in glasses) conducts teaching rounds in the ICU of Ethiopia's Tibebe Ghion Bahir Dar University Hospital in July 2019.

UT Southwestern's exceptional scientists and clinicians earn major honors

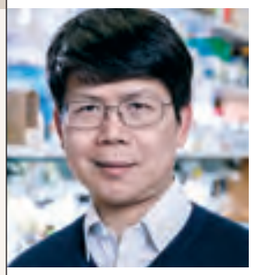
The discoveries of an enzyme that activates the body's immune defenses, a hormone released by fat cells (which expanded our understanding of diabetes), and the first mammalian gene controlling circadian rhythms are among the scientific achievements that led to prestigious honors for UT Southwestern faculty this past year. And in an example of clinical excellence, outstanding patient care and advocacy resulted in a department chair being named a Giant of Cancer Care. Highlighted on these pages are some of those extraordinary individuals whose work merited top honors in 2018-2019.

UT Southwestern's faculty has received six Nobel Prizes, and includes 22 members of the National Academy of Sciences, 17 members of the National Academy of Medicine, and 14 Howard Hughes Medical Institute Investigators.

The full-time faculty of more than 2,500 is responsible for groundbreaking medical advances and is committed to translating science-driven research quickly to new clinical treatments.

UT Southwestern physicians provide care in about 80 specialties to more than 105,000 hospitalized patients, nearly 370,000 emergency room cases, and oversee approximately 3 million outpatient visits a year.

Dr. Zhijian "James" Chen – *Breakthrough Prize in Life Sciences*



Biochemist Dr. Zhijian "James" Chen won the prestigious 2019 Breakthrough Prize in Life Sciences for his discovery of the cGAS enzyme that launches the body's immune defense system. That enzyme patrols the cell's interior and triggers the immune system in response to DNA.

The international award program, founded in 2013, is sponsored by Sergey Brin, Priscilla Chan and Mark Zuckerberg, Ma Huateng, Yuri and Julia Milner, and Anne Wojcicki. Winners receive $3 million each.

Dr. Chen is Professor of Molecular Biology and Director of the Center for Inflammation Research as well as a Howard Hughes Medical Institute Investigator. He holds the George L. MacGregor Distinguished Chair in Biomedical Science.

Dr. Chen's discovery of the enzyme cyclic GMP-AMP synthase (cGAS) solved a longtime medical mystery. In 1908, a Nobel Laureate noted that surgeons in Europe treated patients with DNA to boost their patients' defense against infections. Dr. Chen's investigations revealed the mechanism underlying that response.

Dr. Philipp Scherer – *Manpei Suzuki International Prize for Diabetes Research*

Dr. Philipp Scherer last year became the first scientist to win what could be called the "Triple Crown" of recognition for diabetes research breakthroughs. Dr. Scherer, Director of the Touchstone Center for Diabetes Research, was awarded the 2018 Manpei Suzuki International Prize for Diabetes Research in recognition of his discovery of adiponectin, a hormone released by fat cells, and for his subsequent research into the hormone's role in fending off diabetes.

His research has "deepened and widened our understanding of diabetes, obesity, and energy homeostasis," according to the Manpei Suzuki Diabetes Foundation.

Dr. Scherer was recognized in 2017 with what is considered the top European award in diabetes research, the EASD-Novo Nordisk Foundation Diabetes Prize for Excellence, given by the Germany-based European Association for the Study of Diabetes and the Novo Nordisk Foundation of Denmark. And in 2015, he received the prestigious Banting Medal for Scientific Achievement from the American Diabetes Association. Collectively, these three awards are considered the highest honors for achievement in diabetes research.

Dr. Scherer, a Professor of Internal Medicine and Cell Biology, holds the Gifford O. Touchstone, Jr. and Randolph G. Touchstone Distinguished Chair in Diabetes Research.

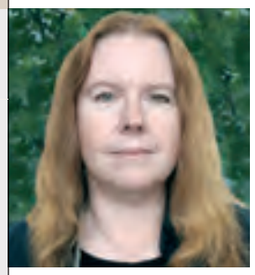
Dr. Joseph Takahashi – *Gruber Neuroscience Prize*

Dr. Joseph Takahashi, Chair of Neuroscience, won the Gruber Neuroscience Prize last year for his pioneering work on the molecular and genetic bases of circadian rhythms in mammals.

The international award – which honors scientists for major discoveries that advance the understanding of the nervous system – recognized Dr. Takahashi's discovery of Clock, *the first mammalian gene controlling circadian rhythms. Subsequent research has established* Clock *as a prominent regulator of many genes and a key target to better understand the primary underpinnings of human physiology.*

A cascade of other findings has stemmed from his lab's work over the years, helping scientists understand the important role biological clocks have in some of the most crucial functions in the human body – from sleep and mental health to metabolism and defending against deadly diseases such as cancer.

Dr. Takahashi is also an Investigator with the Howard Hughes Medical Institute and a member the National Academy of Sciences, the National Academy of Medicine, and the American Academy of Arts and Sciences. He holds the Loyd B. Sands Distinguished Chair in Neuroscience.



Dr. Melanie Cobb – *American Academy of Arts and Sciences*

Dr. Melanie Cobb, Professor of Pharmacology and Associate Director of Basic Research for the Harold C. Simmons Comprehensive Cancer Center, was elected to membership in the American Academy of Arts and Sciences, one of the most prestigious honorary societies in the world.

She joins the ranks of Thomas Jefferson, Alexander Graham Bell, Bruce Springsteen, Jonas Salk, and other Americans who have been elected to the Academy for distinguished, enduring contributions over a wide range of disciplines. Founded in 1780, the American Academy of Arts and Sciences includes more than 250 Nobel Laureates and 60 Pulitzer Prize winners among its members.

Dr. Cobb leads UT Southwestern's Cancer Cell Networks Program and headed a team that discovered one class of protein kinase enzymes that play critical roles in cancer development. She identified the first mammalian mitogen-activated protein kinases in the early 1990s. She purified them, isolated cDNAs encoding these proteins, and named them ERK1, ERK2, and ERK3, or ERKs. It was a meaningful breakthrough because Ras, an important protein involved in cell growth and differentiation, has an intimate relationship with these kinases. The misregulated or inappropriate functions of ERKs, in partnership with Ras, can contribute to cancer development.

Dr. Cobb, also a member of the National Academy of Sciences, holds the Jane and Bill Browning, Jr. Chair in Medical Science.

Dr. Sean Morrison – *National Academy of Medicine*

Dr. Sean Morrison, Director of the Children's Medical Center Research Institute at UT Southwestern and a UTSW Professor of Pediatrics, was elected in late 2018 to the National Academy of Medicine (NAM). The recognition is one of the highest honors in health and medicine.

The NAM – formerly known as the Institute of Medicine – recognizes individuals who have demonstrated outstanding professional achievement and a commitment to service. Along with the National Academy of Sciences and the National Academy of Engineering, the NAM advises the nation and the international community on critical issues in health, medicine, and related policies.

Dr. Morrison identified a series of genes required for stem cell self-renewal, which is necessary for stem cells to persist throughout life and regenerate tissues after injury. His research showed that stem cell self-renewal mechanisms change over time to match the varying growth and regeneration demands of tissues during development and aging.

Also an Investigator with the Howard Hughes Medical Institute, Dr. Morrison holds the Kathryne and Gene Bishop Distinguished Chair in Pediatric Research at Children's Research Institute at UT Southwestern and the Mary McDermott Cook Chair in Pediatric Genetics.

Dr. David Johnson – *Giant of Cancer Care*

Dr. David Johnson was honored last year as one of 15 Giants of Cancer Care by OncLive.com, the website for the Oncology Specialty Group.

Dr. Johnson, who holds the R. Ellwood Jones, M.D. Distinguished Professorship in Clinical Education, was recruited to UT Southwestern in 2010 to serve as Chair of Internal Medicine. He is an oncologist who has been on all sides of cancer: as an attending physician, as a leading expert in clinical trials, as an enthusiastic supporter of cancer research, and as a former cancer patient.

In his early 40s, while on the faculty at Vanderbilt University School of Medicine, Dr. Johnson was treating cancer patients in Tennessee when he was diagnosed with lymphoma, which led him to connect with patients on a level that few other doctors could match.

Meanwhile, he pushed forward with clinical trials for several new drugs that would later become staples in lung cancer treatment. This clinical research was a significant contribution to cancer care, and his achievement was one of the reasons he was selected to become UT Southwestern's fourth Chair of Internal Medicine. During his tenure as Chair, Dr. Johnson hired 150 new faculty members and played a role in opening the new, 460-bed William P. Clements Jr. University Hospital.

This annual review is a publication of the Office of Communications, Marketing, and Public Affairs at The University of Texas Southwestern Medical Center, a component of The University of Texas System.

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