CenterTimes

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Shining a spotlight on UT Southwestern's Leaders in Clinical Excellence

By Jan Jarvis

At the Leaders in Clinical Excellence Awards on Dec. 1, which was held in person and livestreamed from the Tom and Lula Gooch Auditorium on South Campus, awards were issued in seven categories: Rising Star Award, Mentoring Award, Patient and Family Recognition Award, Program Development Award, Institutional Service Award, The President's Award for Diversity and Humanism in Clinical Care, and the Patricia and William L. Watson Jr., M.D. Award for Excellence in Clinical Medicine. Fourteen recipients won individual awards, and seven leaders represented two winning programs.

Presenting the awards were Daniel K. Podolsky, M.D., UTSW President; John Warner, M.D., Executive Vice President for Health System Affairs; and W. P. Andrew Lee, M.D., Executive Vice President for Academic Affairs, Provost, and Dean of UTSW Medical School.

Since 2018, the Leaders in Clinical Excellence Awards event has shone a light on UT Southwestern's commitment to excellence in patient care by recognizing clinical faculty. The many ways that UTSW's health care heroes sought to meet the needs created by COVID-19 were woven into speeches throughout the event. From caring for the babies born during the pandemic to consoling families who lost loved ones, UTSW honorees compassionately went above and beyond the call of duty when needed.

Padmaja Reddy, M.D., an Assistant Professor of Internal Medicine in the Division of General Internal Medicine, was

Please see AWARDS on page 2

Winners of UT Southwestern's 2021 Leaders in Clinical Excellence Awards

UT Southwestern and UT Dallas break ground on bioengineering facility

Building made possible by a gift from Texas Instruments will foster education and research innovations

Rendering of the Texas Instruments Biomedical Engineering and Sciences Building

From Staff Reports

Construction began in November for a new building on campus that catalyzes the launch of a unique partnership between UT Southwestern and UT Dallas, bringing the biomedical engineering programs of the two institutions together to foster innovative solutions for unmet medical needs.

The 150,000-square-foot Texas Instruments Biomedical Engineering and Sciences Building, located on the East Campus, is made possible by a transformative gift from Texas Instruments and funds from the Permanent University Fund of the University of Texas System. A groundbreaking ceremony took place Nov. 15 to celebrate the effort.

"This new facility will be a catalyst to deepen the collaboration between UT Southwestern and UT Dallas facilitating transformational bioengineering research to improve patient care. By integrating biomedical engineering with advances in related fields such as artificial intelligence, molecular imaging, robotics, and genetic engineering, the UTSW-UTD collaborations will further solidify North Texas as a hub for biomedical innovation," said Daniel K. Podolsky, M.D., President of UT Southwestern.

"Biomedical engineering and science are a major driver of UT Dallas' rapidly growing research portfolio," said Richard C. Benson, Ph.D., President of UT Dallas and the Eugene McDermott Distinguished University Chair of Leadership. "The already robust partnership between UT Dallas and UT Southwestern will take another huge step forward upon the launch of our shared facilities. This partnership will also provide students and faculty with more opportunities to create transformative technologies that will improve lives. We are grateful for the visionary support of Texas Instruments in this endeavor."

Scheduled for completion in 2023, the five-story building will support the work of dozens of faculty and their teams with both wet and dry laboratory space, as well as areas designated specifically to promote multidisciplinary interactions. A Biodesign Center will feature a large assembly/design studio, a metal fabrication shop, and rooms for 3D printing.

"Our gift reflects our confidence in the brilliant minds at UT Southwestern and UT Dallas – to combine medical and engineering talent and resources to solve problems that will advance patient care," said Rich Templeton, Chairman, President, and CEO of Texas Instruments. "What gets

Please see BIOENGINEERING on page 5

Achilefu recruited to lead new Department of Biomedical Engineering

Samuel Achilefu, Ph.D., new Chair of Biomedical Engineering

By Patrick Wascovich

Molecular imaging expert Samuel Achilefu, Ph.D., joined UT Southwestern in February as the first Chair of a new Department of Biomedical Engineering. Dr. Achilefu was recruited to UTSW from the Mallinckrodt Institute of Radiology at Washington University School of Medicine in St. Louis.

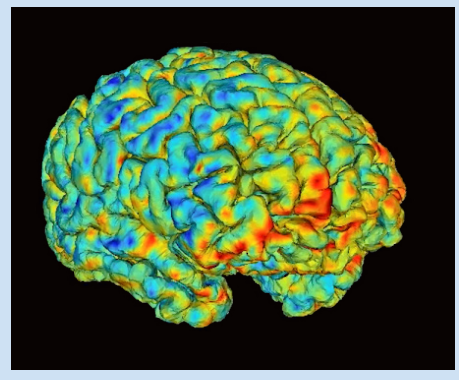
He worked at Washington University for more than 20 years, most recently as a Professor of Radiology, Medicine, Biomedical Engineering, and Biochemistry & Molecular Biophysics. He also served as Chief of the Optical Radiology Laboratory, Vice Chair for Innovation and Entrepreneurship at the Mallinckrodt Institute of Radiology, and co-leader of the Oncologic Imaging Program of the Siteman Cancer Center. Recently, Dr. Achilefu was elected to the National Academy of Medicine, considered one of the highest honors in the fields of health and medicine.

Born and raised in Nigeria, he studied chemistry and materials science at the University of Nancy in France before completing postdoctoral training in oxygen transport in biological systems and hematological science at Oxford University in the United Kingdom.

"With his demonstrated success in innovative research and clinical impact, Dr. Achilefu brings the leadership and vision needed to launch our newest department to foster transformational research in biomedical engineering

Please see ACHILEFU on page 5

Brain imaging biomarkers predict antidepressant response



UTSW-led research has identified new imaging biomarkers that predict antidepressant response.

By Patrick McGee

Research led by UT Southwestern has identified MRI brain imaging biomarkers that bring new levels of precision for prescribing the most effective antidepressants.

The outcome predictive models were developed in part using data from a large multicenter National Institute of Mental Health-funded study and published in *Biological Psychiatry*. The findings provide strong evidence that the current trial-and-error approach used in clinical practice for selection of the right antidepressant can be replaced with this new precision medicine approach.

"This is a significant advance. It's noninvasive. It can be and should be used immediately," said Madhukar Trivedi, M.D., Professor of Psychiatry and Director of the Center for Depression Research and Clinical Care, one of the pillars of the Peter O'Donnell Jr. Brain Institute.

The new biomarkers could spare patients with severe depression two to three months of taking the wrong medication, Dr. Trivedi said. The study tested the antidepressant drug sertraline against a placebo control group. Patients who did not respond to sertraline after eight weeks were switched to bupropion, another antidepressant. Researchers measured changes in brain circuit reactions

Please see BIOMARKERS on page 3

INSIDE THIS ISSUE

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Holly Crawford appointed Executive VP for Business Affairs

By Cathy Frisinger

Holly G. Crawford, M.B.A., a longtime financial leader at the University of Rochester, recently was hired as new Executive Vice President for Business Affairs, replacing Arnim Dontes, who left in July.

Holly G. Crawford, EVP for Business Affairs

UT Southwestern President Daniel K. Podolsky, M.D., said Ms. Crawford's experience made her an excellent choice for the position, which she assumed on Nov. 29.

"Ms. Crawford brings to UT Southwestern a deep understanding of academic medical centers and the complexities of a large, growing university such as our own," Dr. Podolsky said.

At the University of Rochester, which includes a medical school, dental school, and six hospitals, Ms. Crawford served for nearly six years as Senior Vice President for Administration, Chief Financial Officer, and Treasurer. In this role – her most recent at the institution – she was responsible for a $5.4 billion budget.

Now with UT Southwestern, Ms. Crawford oversees more than 15 departments, including Accounting and Fiscal Services, Budget and Resource Planning, Facilities Management, Information Resources, Supply Chain Management, Human Resources, and the UT Southwestern Police Department.

"This position aligned really well with my experience, and I am excited about the work that Dr. Podolsky and his team are doing and the trajectory that the University is on," said Ms. Crawford, who added that she is excited to become part of an institution on the cutting edge of so many scientific and medical achievements.

Ms. Crawford grew up in Northport, New York, and graduated from Long Island University with a bachelor's degree in accounting. She earned an M.B.A. from the University of Rochester's Simon Business School. Before her more than 20 years at the University of Rochester in upstate New York, she held management positions with ACC Telecommunications, Bausch + Lomb, and Arthur Andersen LLP.

Her proudest accomplishment at the University of Rochester, Ms. Crawford said, was building a strong team and collaboratively building relationships across the institution, and she expects that emphasis on work relationships and cohesion to continue at UTSW.

"To execute at the highest level, I believe that our Business Affairs team must have a twofold aim of stewardship and service – providing client-centric services of the highest quality to our faculty, students, staff, patients, and visitors while stewarding the human, financial, and physical resources of the University. As a leader, I am deeply committed to the professional development and morale of all my team members and always strive to provide supportive and clear leadership within a culture of integrity, inclusiveness, respect, collaboration, and accountability," she added.

Challenges she foresees in the near future at UTSW include continuing to cope with the obstacles created by the pandemic, learning the nuances of the UT Southwestern culture, and hiring and retaining employees in this dynamic employment market.

"I am looking forward to meeting and hearing from faculty, students, and staff in the coming months. Everyone I have met to date has been warm and welcoming, and there seems to be a collective pride in working here and excitement about the future of the institution," Ms. Crawford said.

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

Awards Continued from page 1

among three honorees of the Patient and Family Recognition Award that recognizes clinical faculty whose dedication to the compassionate, respectful delivery of care has garnered the highest degree of patient trust and satisfaction.

During the COVID-19 pandemic, Dr. Reddy became a lifeline of information for patients and their families facing the darkest days. At a time when the public was desperate for information, she spearheaded the COVID ICU Family Outreach Program at Parkland Memorial Hospital, providing daily virtual updates to relatives of every COVID-19 ICU patient. She also served on one of the UT Southwestern COVID-19 ICU Response Teams that was recognized with a Program Development Award.

Each of the evening's award recipients, such as Dr. Reddy, represent the very best of the Health System. Dr. Reddy emotionally recalled how her UT Southwestern colleagues have selflessly and continuously rallied to help throughout the pandemic.

"Time and again, they gave tiny pieces of themselves away to these families in order to shield the team in the unit, and in return for their tireless work, some got doughnuts, some got breakfast tacos, one got to jump in my pool to cool off in the middle of the July heat – but that was about it," she said. "They did it simply because of a desire to serve, a desire to do the right thing. They never failed to answer the call."

Earning the top honor of the evening was Diane Twickler, M.D., Professor of Radiology and Obstetrics and Gynecology, as recipient of the Patricia and William L. Watson Jr., M.D. Award for Excellence in Clinical Medicine.

Dr. Twickler, also a Distinguished Teaching Professor, is a pioneer in gynecologic imaging who has earned a reputation for outstanding patient care. The UTSW faculty member of more than 30 years expressed her gratitude to UT Southwestern and offered thanks to Parkland's Women & Infants Specialty Health (WISH) clinic for helping to build and maintain the specialized Ob/Gyn ultrasound. Medicine is a field in which working as a team is key, she said.

"There is no way I could have been able to do the type of research that I'm engaging in without the model of collaboration that exists here at UT Southwestern. I feel very, very fortunate and extremely honored," Dr. Twickler said.

Examples of exceptional clinical care in a variety of other areas were recognized, such as the heart for patient advocacy of Cindy Darnell Bowens, M.D. As Medical Director of the Pediatric Intensive Care Unit at Children's Medical Center Dallas, Dr. Bowens recognizes the challenges that underrepresented minorities face. She is a passionate champion for every family.

The audience gave a round of applause to Diane Twickler, M.D., (center) winner of the Patricia and William L. Watson Jr., M.D. Award for Excellence in Clinical Medicine, and all the 2021 Leaders in Clinical Excellence Awards recipients.

Dr. Bowens, the recipient of The President's Award for Diversity and Humanism in Clinical Care, said a good day at work involves knowing she did the best job she could to get every child a step closer to going home.

"When you're taking care of families who are having the worst day of their lives, and you can make that day just a little bit better, the gratification that comes with that is tenfold what you've given to them," said Dr. Bowens, Associate Professor of Pediatrics.

For William Turner, M.D., mentoring others has been rewarding. Over his nearly 50-year career, the Professor of Surgery in the Division of Burn, Trauma, Acute, and Critical Care Surgery has had thousands of operating-room interactions with postgraduate trainees and students.

The Mentoring Award recipient said he was inspired by his parents. He grew up on a farm where his father taught him how to use his hands, while his mother was a schoolteacher. Watching his residents make progress is priceless, he said.

"They may operate on me one day," Dr. Turner said. "To see them become those people is one of the most rewarding things that I do."

One after another, humble honorees took time to thank UT Southwestern, co-workers, patients, family members, and volunteers for the village it takes to deliver exceptional patient care.

"We've witnessed teamwork that you've heard about tonight at its finest – our colleagues on the front lines and behind the scenes in vital supporting roles have faced the challenges with urgency and resolute commitment," Dr. Warner said.

Dr. Podolsky recalled how different the community was in 2020 with the world immersed in fighting COVID-19 and the Leaders in Clinical Excellence event taking place virtually.

"This evening, I cannot help but recall that last year's circumstances necessitated a virtual celebration of our Leaders in Clinical Excellence Awards. However, that event still provided a bright positive light at a moment when everyone across UT Southwestern, our communities, and the world was in the midst of unprecedented challenge," Dr. Podolsky said. "And to have that moment last year to celebrate the selflessness, the dedication, the commitment, the excellence – certainly for me anyway – was sustaining.

"Now a year later, it's a special pleasure to be able to honor our remarkable colleagues in person and know that, despite what we have all faced together, these guiding values are lived every day by members of the UT Southwestern community, as exemplified by our awardees this year."

■

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

See the endowed chairs held by Dr. Podolsky above.

Dr. Turner holds the Alvin Baldwin, Jr. Chair in Surgery, and the Carla and Paul Bass Professorship in Medical Education Honoring Charles C. Sprague, M.D.

Dr. Twickler holds the Dr. Fred Bonte Professorship in Radiology.

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

More online: To watch a video replay of the program and videos on individual winners, go to *Center Times Plus* at **utsouthwestern.edu/ctplus**.

Congratulations to 2021 honorees

Patricia and William L. Watson Jr., M.D. Award for Excellence in Clinical Medicine
Diane M. Twickler, M.D., FACR
Professor of Radiology and Obstetrics and Gynecology

Rising Star Award
Emily H. Adhikari, M.D.
Assistant Professor of Obstetrics and Gynecology
Division of Maternal-Fetal Medicine
Reuben Arasaratnam, M.D.
Assistant Professor of Internal Medicine
Division of Infectious Diseases and Geographic Medicine
Dharam J. Kumbhani, M.D., S.M.
Associate Professor of Internal Medicine
Division of Cardiology
Nina Niu Sanford, M.D.
Assistant Professor of Radiation Oncology
Chief of Gastrointestinal Radiation Oncology Service
Harold C. Simmons Comprehensive Cancer Center

Mentoring Award
Lina Chalak, M.D., M.S.C.S.
Professor of Pediatrics and Psychiatry
Sunati Sahoo, M.D.
Professor of Pathology
William W. Turner Jr., M.D.
Professor of Surgery
Division of Burn, Trauma, Acute, and Critical Care Surgery

Patient and Family Recognition Award
Becky Ennis, M.D.
Associate Professor of Pediatrics
Nisa Kubiliun, M.D.
Associate Professor of Internal Medicine
Division of Digestive and Liver Diseases
Padmaja Reddy, M.D.
Assistant Professor of Internal Medicine
Palliative Medicine Section

Program Development Award
Breast Reconstruction Program
Sumeet S. Teotia, M.D.
Professor of Plastic Surgery
Nicholas T. Haddock, M.D.
Associate Professor of Plastic Surgery and Orthopaedic Surgery

COVID-19 ICU Response Teams
CUH COVID-19 ICU Team, led by
Kristina L. Goff, M.D.
Assistant Professor of Anesthesiology & Pain Management
Corey D. Kershaw, M.D.
Associate Professor of Internal Medicine
Division of Pulmonary and Critical Care Medicine

Parkland COVID Tactical Care Unit, led by
Matt Leveno, M.D.
Associate Professor of Internal Medicine
Division of Pulmonary and Critical Care Medicine

COVID ICU Communications Team, led by
Kala Bailey, M.D.
Assistant Professor of Psychiatry

Parkland COVID ICU Family Outreach Program, led by
Padmaja Reddy, M.D.
Assistant Professor of Internal Medicine
Palliative Medicine Section

Institutional Service Award
James D. Griffin, M.D.
Professor of Anesthesiology & Pain Management
Robin Novakovic-White M.D.
Associate Professor of Radiology and Neurology

The President's Award for Diversity and Humanism in Clinical Care
Cindy Darnell Bowens, M.D., M.S.C.S.
Associate Professor of Pediatrics
Pediatrics - Critical Care

CenterTimes

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Artificial intelligence successfully predicts protein interactions

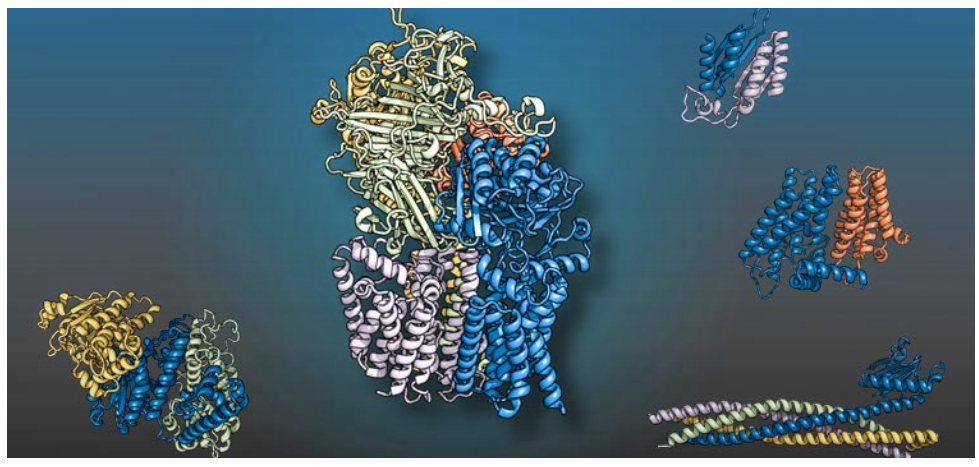
Research led by UT Southwestern and the University of Washington could lead to new drug targets

By Christen Brownlee

UT Southwestern and University of Washington researchers led an international team that used artificial intelligence (AI) and evolutionary analysis to produce 3D models of eukaryotic protein interactions. The study, published in *Science*, identified more than 100 probable protein complexes for the first time and provided structural models for more than 700 previously uncharacterized ones. Insights into the ways pairs or groups of proteins fit together to carry out cellular processes could lead to a wealth of new drug targets.

"Our results represent a significant advance in the new era in structural biology in which computation plays a fundamental role," said Qian Cong, Ph.D., Assistant Professor in the Eugene McDermott Center for Human Growth and Development with a secondary appointment in Biophysics.

Dr. Cong led the study with David Baker, Ph.D., Professor of Biochemistry and Dr. Cong's postdoctoral mentor at the University of Washington prior to her recruitment to UT Southwestern. The study has four co-lead authors, including UT Southwestern Computational Biologist Jimin Pei, Ph.D.



The yeast proteins shown in different colors come together as two-, three-, four-, and five-member complexes like 3D puzzle pieces to execute cellular functions. An international team led by researchers at UT Southwestern and the University of Washington predicted the structures using artificial intelligence techniques.

Proteins often operate in pairs or groups known as complexes to accomplish every task needed to keep an organism alive, Dr. Cong explained. While some of these interactions are well studied, many remain a mystery. Constructing comprehensive interactomes – or descriptions of the complete set of molecular interactions in a cell – would shed light on many fundamental aspects of biology and give researchers a new starting point on developing drugs that encourage or discourage these interactions. Dr. Cong works in the emerging field of interactomics, which combines bioinformatics and biology.

Until recently, a major barrier for constructing an interactome was uncertainty over the structures of many proteins. In 2020 and 2021, a company called DeepMind and Dr. Baker's lab independently released two AI technologies called AlphaFold (AF) and RoseTTAFold (RF) that use different strategies to predict protein structures based on the sequences of the genes that produce them.

In the current study, Dr. Cong, Dr. Baker, and their colleagues expanded on those AI structure-prediction tools by modeling many yeast protein complexes. Yeast is a common model organism for fundamental biological studies. To find proteins that were likely to interact, the scientists first searched the genomes of related fungi for genes that acquired mutations in a linked fashion. They then used the two AI technologies to determine whether these proteins could be fit together in 3D structures.

Their work identified 1,505 probable protein complexes. Of these, 699 had already been structurally characterized, verifying the utility of their method. However, there was only limited experimental data supporting 700 of the predicted interactions, and another 106 had never been described.

To better understand these poorly characterized or unknown complexes, the University of Washington and UT Southwestern teams worked with colleagues around the world who were already studying these or similar proteins.

Qian Cong, Ph.D.

By combining the 3D models the scientists in the current study had generated with information from collaborators, the teams were able to gain new insights into protein complexes involved in maintenance and processing of genetic information, cellular construction and transport systems, metabolism, DNA repair, and other areas. They also identified roles for proteins whose functions were previously unknown based on their newly identified interactions with other well-characterized proteins.

"The work described in our new paper sets the stage for similar studies of the human interactome and could eventually help in developing new treatments for human disease," Dr. Cong added.

■

Dr. Cong is a Southwestern Medical Foundation Scholar in Biomedical Research.

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

Potential cure identified for tropical parasitic disease

By Christen Brownlee

Combining two agents to block a parasitic worm's life cycle boosted survival from a potentially deadly tropical disease to 85% in animal models, according to a proof-of-concept study led by UT Southwestern pharmacologists.

The *Strongyloides* infestation – brought by tiny worms known as nematodes that can enter through your feet – can cause strongyloidiasis, a chronic infection found in some 600 million worldwide. While mostly found in tropical and subtropical regions, the parasite has recently been identified in Texas, Alabama, and the Appalachian Mountains region in the U.S. Mortality from complications with hyperinfection is up to 87% of reported cases, according to a 2020 modeling study.

"Parasitic nematodes that infect humans, animals, and plants are an enormous health and economic burden on society. We think the pathway we discovered could serve as a universal target for all parasitic nematode species," said David Mangelsdorf, Ph.D., Chair of Pharmacology. "This strategy could potentially offer a cure for the millions of people around the world who have strongyloidiasis – the disease caused by *Strongyloides stercoralis* – and points to a new way to fight many other parasitic nematode diseases."

Lab partners David Mangelsdorf, Ph.D., (left) and Steven A. Kliewer, Ph.D., discovered a nuclear receptor pathway in nematodes that may be targeted to develop drugs to fight a tropical parasitic disease.

Researchers studying gerbils initially found that administering dafachronic acid in drinking water for two weeks reduced fecal *S. stercoralis* larval output by 90%. In animals that became hyperinfected, which dramatically increases mortality, treatment with ivermectin or dafachronic acid alone increased survival to about 25% and 70%, respectively. But when combined, survival climbed to about 85% and *S. stercoralis* infection ended, representing a potential cure, said co-author Steven A. Kliewer, Ph.D., Professor of Molecular Biology and Pharmacology.

In this study published online in *eLife*, researchers targeted *Strongyloides stercoralis*, which can lead to a severe and potentially deadly hyperinfection syndrome for people who are immunocompromised, such as those taking glucocorticoids, a common steroid used to treat other medical conditions.

"Glucocorticoids were one of the first treatments used for severe COVID-19. WHO raised the concern that using steroids in countries where *S. stercoralis* is prevalent could set off a fatal hyperinfection in patients with chronic, subclinical strongyloidiasis. That possibility has elevated the urgency for finding new ways to treat the disease," said Dr. Mangelsdorf, a Howard Hughes Medical Institute Investigator and a member of the National Academy of Sciences.

Micrograph of a *Strongyloides stercoralis* parasite larva that expresses fluorescent markers showing the worm's cytoskeleton (red) and sensory neurons in the head and tail (green). Credit: Ariel Juno from the laboratory of James Lok, University of Pennsylvania

Drs. Mangelsdorf, Kliewer, and colleagues looked for vulnerabilities in the larval stage of *S. stercoralis*' life cycle. By purifying extracts of *S. stercoralis*, the team discovered that the parasite synthesizes the hormone dafachronic acid, which acts by binding to a receptor called DAF-12. Further research identified the enzymatic pathway that *S. stercoralis* uses to generate the hormone and showed that the DAF-12 receptor acts as an on-off switch controlling larval development based on the availability of dafachronic acid. Importantly, when the hormone is present at the wrong time, the parasite is unable to develop into the infectious form and dies.

Pure dafachronic acid in its present form may be unsuitable for treating humans because of its short half-life in the body, said Dr. Kliewer, also a member of the National Academy of Sciences. However, if chemistry techniques can be used to alter its structure, it could lead to a useful drug.

■

Dr. Kliewer holds the Diana K. and Richard C. Strauss Distinguished Chair in Developmental Biology.

Dr. Mangelsdorf holds the Alfred G. Gilman Distinguished Chair in Pharmacology and the Raymond and Ellen Willie Distinguished Chair in Molecular Neuropharmacology in Honor of Harold B. Crasilneck, Ph.D.

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

Biomarkers Continued from page 1

as more than 300 study participants performed a reward task in a functional magnetic resonance imaging (fMRI) scanner.

Madhukar Trivedi, M.D., Director of the Center for Depression Research and Clinical Care

The study used that data and innovations to construct new machine learning models that tell scientists and clinicians which specific brain regions and circuits are associated with prediction of treatment response to each medication.

"The signatures that we found are unique to each antidepressant's response," said Albert Montillo, Ph.D., Assistant Professor in the Lyda Hill Department of Bioinformatics, whose lab produced the 10,000 lines of code to efficiently tune new predictive models and sophisticated data cleaning methods to suppress fMRI head motion and achieve levels of accuracy unseen in other labs' tests.

"Due to the human brain's inherent complexity, neuroscientists typically find that brain activity can explain 15% of the variance in symptom relief," Dr. Montillo said. "In this study, we're able to explain 48% of the variance in the symptom relief from sertraline, 34% for bupropion, and 28% for placebo."

Dr. Trivedi said the results are highly credible because the underlying data the research utilized is broadly representative of the heterogeneity of clinical data, including data from Massachusetts General Hospital in Boston, Columbia University in New York, and the University of Michigan, as well as the rigor of the analytic approach with the use of deep learning models.

Albert Montillo, Ph.D.

The study is one of the first adaptations of deep machine learning to antidepressant outcome prediction for which Dr. Montillo developed methods to amplify the original fMRI data tenfold.

"The analytical approach we have developed can be readily adapted to identify biomarker signatures and predict outcomes for other treatments of depression, both pharmacological and nonpharmacological," Dr. Montillo said.

With a noninvasive approach and an abundance of evidence, Drs. Trivedi and Montillo said clinicians should switch to this approach now. They will seek additional funding to advance the research and see if it is compatible with blood biomarkers that Dr. Trivedi developed.

"It is a clear improvement from the standard prediction approaches currently used," Dr. Trivedi said. "We have also reached a point where our findings are stable and can provide a pathway for future work."

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Dr. Trivedi holds the Betty Jo Hay Distinguished Chair in Mental Health, and the Julie K. Hersh Chair for Depression Research and Clinical Care.

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

FOCUS: TRACKING COVID-19

UTSW lab identifies COVID-19 variants in North Texas

Researchers developed a process for delivering quick and accurate analysis of SARS-CoV-2 variants, allowing scientists to track the variant landscape over time

By Christen Brownlee

As 2021 began, the U.K.-originating Alpha variant of SARS-CoV-2 – the virus that causes COVID-19 – was the only significant variant circulating in the U.S. Since then, the World Health Organization has identified at least 11 important variants, different strains that arose through mutations to the original Wuhan strain's genetic code. These aren't just an academic curiosity, explained Jeffrey SoRelle, M.D., Assistant Professor of Pathology: Variants that stick around represent an evolutionary success, a way for the virus to more fruitfully spread and potentially produce a more severe infection.

To identify and track variants in North Texas, Dr. SoRelle partnered over the past year with Helen Hobbs, M.D., Professor of Internal Medicine and Molecular Genetics and an Investigator of the Howard Hughes Medical Institute. Combining a rapid, focused PCR-based test generated in the Once Upon a Time Human Genomics Center and genotyping test that Dr. SoRelle developed in the McDermott Next-Generation Sequencing Core, part of the Eugene McDermott Center for Human Growth and Development that Dr. Hobbs directs, these efforts have provided a wealth of data to show how SARS-CoV-2 has shifted and changed over time.

"Our combined work toward tracking variants has allowed us to follow in real time the changes in the viral strains causing disease in our own community," Dr. Hobbs said.

Tracking variants involves identifying differences in the nearly 30,000 nucleotides, or individual units, that make up the SARS-CoV-2 genome. Rather than starting with reading the entire sequence, a process that takes about a week and a half, Dr. SoRelle's genotyping method focuses initially on eight "hotspots" for mutation – areas of the genome that have proved rife for genetic changes over the course of the pandemic.

Dr. SoRelle began developing his test in January 2021, soon after the Alpha variant first spread to the U.S. from the United Kingdom, honing and perfecting his technique over the next several months. Since April 2021, every sample from patients within the UTSW system who tested positive for COVID-19 has been sent to the high-throughput COVID-19 lab in the Department of Pathology, where Dr. SoRelle genotypes it – a process that takes just six hours. Then, to verify his results and offer insight on more subtle changes in the sequence of the genome of the virus, Dr. Hobbs and her colleagues run the samples through the lengthier whole-genome sequencing process. The bioinformatics group in the McDermott Center then uses machine learning to digest this abundance of data, assigning a "lineage" to each specimen that signifies its variant or identifying new changes that could suggest a potentially novel variant.

Over the past year, the team has seen the prevalence of variants rise and fall, including the exponential spread of the Delta variant in recent months, and at least one case of the Omicron variant recently confirmed by the Texas Department of State Health Services.

"Through the data we generated, we were able to see the Delta surge coming before it happened," Dr. SoRelle said.

This data, which the team compiles into a weekly report, has proved extraordinarily useful to UTSW leadership, North Texas businesses, and public health departments as a nearly real-time read of variant trends and for developing forecasting models. Dr. SoRelle said he hopes his genotyping method might eventually be useful for research in public health labs, where it would vastly reduce the time it takes to receive variant results from weeks to hours and shrink costs to about a tenth of the current cost of $200 to $300 per sample.

Jeffrey SoRelle, M.D., developed a genotyping test that is used to identify COVID-19 variants.

Helen Hobbs, M.D., is working with Dr. SoRelle to study and track COVID-19 variants in North Texas.

"A major takeaway from our work is the importance of continuing to track variants over time, because we'll never be sure what we see in the future," Dr. SoRelle said. "The more we track, the more we learn."

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Dr. Hobbs holds the Philip O'Bryan Montgomery, Jr., M.D. Distinguished Chair in Developmental Biology, the Eugene McDermott Distinguished Chair for the Study of Human Growth and Development, and the 1995 Dallas Heart Ball Chair in Cardiology Research.

More online: To watch a video related to this story, go to *Center Times Plus* at **utsouthwestern.edu/ctplus**.

COVID-19 forecasting team keeps region apprised of virus's spread

By Patrick McGee

Mujeeb Basit, M.D., Assistant Professor of Internal Medicine, wanted his team's COVID-19 forecasting data to be helpful to North Texas citizens, government leaders, and school boards. Proof that the team reached the right audience came unexpectedly.

His wife was watching the Highland Park School Board meeting on her computer one day when suddenly she called out to him, "Oh, they're looking at your graph!" He looked over and saw his team's work on the screen as the school board discussed how to best protect students from the virus.

"It was so great to see real citizens using our data," Dr. Basit said. "We worked very hard to provide data that is clear, accurate, and without bias so that it can be used by a broad population."

This was the work of the data modeling team, a group of about 10 faculty and staff members who gathered in the onslaught of the COVID-19 crisis to help North Texas stay ahead of the pandemic. The team's goal was to share accurate, relevant data to keep the spread of COVID-19 as low as possible, said Seth Toomay, M.D., Associate Vice President and Chief Medical Officer at UT Southwestern.

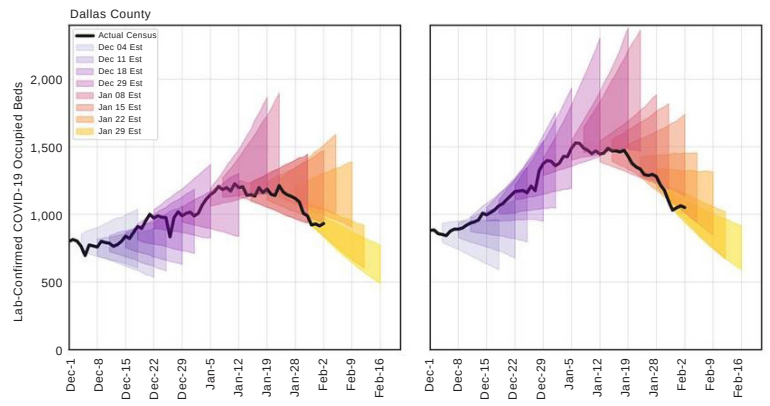
"There were patterns in the North Texas data that as physicians and scientists we were very concerned about. Positive tests lead to hospitalizations, hospitalizations to intubations, and intubations to deaths," Dr. Toomay said. "We wanted to communicate these concerns to the whole community in a way that was easy to understand and actionable, in the same way that we would talk to our friends and neighbors about where the pandemic was heading."

Mujeeb Basit, M.D., (left) and Trish Perl, M.D., look over COVID-19 modeling data used to produce virus spread forecasts for North Texas.

In the spring of 2020 during the initial onset of the pandemic in North Texas, the team's assembly was hurried, but UT Southwestern had been building expertise for years. UTSW leaders in bioinformatics, data modeling, clinical informatics, geospatial mapping, public health, data analytics and interpretation, surveillance, and infectious diseases convened with a sense of urgency and a shared mission.

"We were initially charged with helping the institution to anticipate and plan for needed resources. We soon recognized that there was a void in available and integrated information in the North Texas region that could provide the public with a view of how the pandemic was affecting the area," said Trish Perl, M.D., M.Sc., Professor of Internal Medicine in the Division of Infectious Diseases and Geographic Medicine. "Overall, this effort has been so impactful in helping understand, manage, and set the expectations for COVID in the region."

The team met at all hours – day and night if needed – initially utilizing data from Dallas and Tarrant counties, then from state and regional resources, national data from the Centers for Disease Control and Prevention and, most recently, North Texas data from UT Southwestern and Texas Health Resources. They harnessed UT Southwestern's expertise to accurately synthesize this massive data trove to make predictions on spread of the virus.



This data visualization depicting forecasts stacked over time with the actual trend shows that the range of UT Southwestern's data modeling was incredibly accurate. The colored bands show the forecasts, while the black line shows what was reported.

"At UT Southwestern, we tend to be more collegial, I would say, and we work really well together to bring a project to fruition," Dr. Basit said. "We check egos at the door of the meeting and make sure we are working toward a common goal."

They turned out meaningful reports on COVID-19 that included percent positivity of those tested, the evolution of cases and hospitalizations, vaccination rates, and mask-wearing. Mobility reports included details down to retail shopping, grocery shopping, and people's visits to the workplace and public parks. They also used this information to predict the trajectory of the pandemic – information that was used by many across the region.

Web traffic showed the data was heavily viewed by the media – and hindsight showed it was incredibly accurate.

"The predictions have performed well. Given data quality issues – especially retrospective changes to the data stream by state agencies – it is extremely hard to assess perfect accuracy, but the predictions have been within our error bars and extremely accurate in the near term," Dr. Basit said. "We will continue forecasting of COVID-19 and new variants. We will also work to package data so that more people can use it within the bounds of the data use agreements. If we are able to get funding, we hope to create a permanent advanced data analytics and do more innovative and creative solutions with our data."

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Dr. Perl holds the H. Ben and Isabelle T. Decherd Chair in Internal Medicine in Honor of Henry M. Winans, Sr., M.D.

More online: Read the latest COVID-19 forecast from the modeling team at **utsouthwestern.edu/covid-19**.

UTSW lung clinic helps former COVID-19 patients breathe easier

By Jan Jarvis

After spending nine weeks hospitalized for COVID-19 in a Richardson hospital, Diane Brouwer returned to her Plano home with an oxygen tank in tow.

"I had a lot of lung issues," said the mother of five, who was diagnosed with COVID-19 in January 2021 and suffered a collapsed lung. "Just walking across the room, I needed oxygen and had it on everywhere I went."

But thanks to the Post-COVID-19 Lung Clinic at UT Southwestern, Mrs. Brouwer, 54, got the help she needed to breathe on her own and is no longer tethered to supplemented oxygen.

Fernando Torres, M.D.

"I truly feel very blessed," she said. "It's very exciting to breathe."

Since the clinic opened in March, about 100 patients have been treated who range in age from 18 to their 80s. Although all of these patients recovered from COVID-19, they were still unable to breathe on their own, said Fernando Torres, M.D., Medical Director of Lung Transplantation, Head of the Pulmonary Hypertension Program, and Professor of Internal Medicine.

Diane Brouwer (left) is now able to breathe easier without supplemental oxygen thanks to care at UT Southwestern's Post-COVID-19 Lung Clinic. Dempsey Cluff (right) underwent a double-lung transplant at UTSW following an extensive recovery from COVID-19. He is another clinic patient now on the road to recovery.

"Patients who come to see me are on oxygen," Dr. Torres said. "The goal of the clinic is to get them off of oxygen and prevent them from needing a lung transplant."

To be treated in the clinic, patients must be 30 days post-COVID-19 and experiencing symptoms such as significant shortness of breath, an elevated heart rate, and inflammation in the lungs. These symptoms result from COVID-19 attacking the lungs, damaging tissue, and causing blood clots.

At the clinic, immune suppressant medications are often used to heal lung damage and restore breathing.

"We noticed a lung-injury pattern that is similar to what we see in immune disorders like lupus," Dr. Torres said. "An immune suppressant medication has been fairly successful at getting these patients off of oxygen."

When such medications fail, however, the next step is to put the patient on the waiting list for a lung transplant, Dr. Torres said.

One of those patients was Dempsey Cluff, a 60-year-old retired Dallas Area Rapid Transit supervisor who endured a yearlong struggle with COVID-19 that included hospitalization for post-COVID-19 complications at a Dallas-area hospital. He lost 100 pounds and could not breathe on his own. Mr. Cluff was at a rehabilitation facility in Houston when his sister heard about UT Southwestern's transplant program. Staff at the rehab facility got in touch with UTSW and worked on getting him stronger for a potential transplant. Mr. Cluff was placed on the transplant list at UT Southwestern, and when his condition worsened, he was flown to Dallas for the transplant.

More than once over his 15-month medical ordeal, Mr. Cluff's family had been told to prepare for the worst.

"The doctors said he had so much trauma, he would have never been able to get off the ventilator," said Kim Puckett, Mr. Cluff's sister.

In June, he became the first COVID-19 patient to undergo a double-lung transplant at UT Southwestern.

"According to my doctors, the match was perfect," Mr. Cluff said. "It could not have been any better."

About a month later, he returned home to Dallas, where he continues to recover and receive treatment at UT Southwestern.

"It is so good to be in my own home," he said. "I really never thought it would happen."

For Mrs. Brouwer, the clinic gave her the confidence she needed to rely on her lungs again instead of depending on supplemented oxygen.

"I realized I did not have to be scared anymore," she said.

For more information on the Post-COVID-19 Lung Clinic, call 214-645-5505.

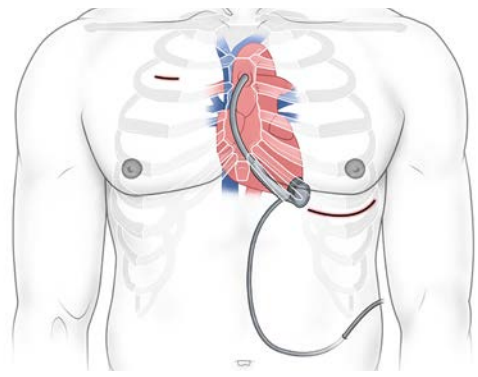
Improving LVAD outcomes with sternal-sparing surgery

By Catherine Gara

A less invasive approach to implanting a left ventricular assist device (LVAD), which leaves the flat bone protecting the chest called the sternum intact, has led to improved outcomes at UT Southwestern, including a four-year survival rate that is more than 30% higher than the industry average.

Ninety-five percent of patients who receive an LVAD at UT Southwestern now have the sternal-sparing surgery, which surgeons began using here in 2019. LVADs are a lifesaving therapy for patients awaiting a heart transplant or who have advanced heart failure. The battery-operated device helps the heart pump blood.

"I don't call sternal sparing 'minimally invasive,' because we do make an incision overlying the apex of the heart for implanting the pump, and then tunnel the graft and make another incision along the upper right chest to sew it to the aorta," said Matthias Peltz, M.D., Associate Professor and Surgical Director of Cardiac Transplant in the Department of Cardiovascular and Thoracic Surgery. "But we don't disrupt the stability of the chest wall, which significantly reduces the trauma of the surgery."



This diagram shows how the LVAD device is implanted in a minimally invasive procedure that keeps the sternum intact.

According to internal data, patients whose LVAD is implanted using the less invasive approach have shorter hospital stays, less need for transfusion, less time on ventilators, reduced risk of right-heart dysfunction, and a quicker return to normal activities compared with the traditional surgery.

To verify these apparent benefits and corroborate them with national data, UT Southwestern is participating in the SWIFT trial, a multi-institutional assessment of outcomes using the sternal-sparing approach compared with those of the clinical trial that first established the efficacy of the HeartMate 3 LVAD pump. To date, LVAD patients at UT Southwestern also have less bleeding, less early infection, and less renal dysfunction compared with the national average.

Matthias Peltz, M.D.

"Even though over 60% of our LVAD patients are in the sickest class categories, our current four-year survival rate is 78.9% – which is almost the same as the national average at only one year," Dr. Peltz said. "That's thanks in large part to the stellar care team that supports patients after implantation. We've also gotten better at identifying the right candidates for the procedure."

As Associate Medical Director of Mechanical Circulatory Support, Alpesh Amin, M.D., is a key part of the LVAD team. Dr. Amin, Associate Professor of Internal Medicine, agreed that the care team, especially its multidisciplinary makeup, is a large contributor to strong patient outcomes.

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Dr. Peltz holds the Sarah M. and Charles E. Seay Distinguished Chair in Thoracic Surgery.

Bioengineering

Continued from page 1

UT Southwestern and UT Dallas officials, plus invited guests, attended the Nov. 15 groundbreaking.

me personally excited is that semiconductor technology will be at the center of the medical discoveries that are made inside this new building."

UT Southwestern's Biomedical Engineering Program, part of the Graduate School of Biomedical Sciences, offers a Ph.D. degree in biomedical engineering. As part of the initiative, UT Southwestern is launching a Department of Biomedical Engineering, to be led by its first Chair, Samuel Achilefu, Ph.D. (See related story on page 1.)

Since starting its own Biomedical Engineering Department in 2010, UT Dallas' undergraduate bioengineering program has become the third largest in the U.S. based on enrollment, according to the American Society for Engineering Education, and its graduate program ranks third, according to *U.S. News & World Report*, among biomedical engineering programs at Texas public universities. In addition, support from TI, the UT System, and the O'Donnell Foundation made it possible for UTD to establish the Texas Biomedical Device Center in 2012.

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

More online: Learn more about programs planned for the new facility in a news story at **utsouthwestern.edu/newsroom**.

Achilefu

Continued from page 1

and related fields at UT Southwestern," said W. P. Andrew Lee, M.D., Executive Vice President for Academic Affairs, Provost, and Dean of UT Southwestern Medical School.

At UTSW, Dr. Achilefu leads the University's collaboration with UT Dallas that leverages the institutions' strengths in biomedical and engineering sciences. The Department of Biomedical Engineering (BME) eventually will be housed in the Texas Instruments Biomedical Engineering and Sciences Building on East Campus, a joint venture project with UT Dallas that is under construction and set to open in 2023. Below, Dr. Achilefu shared his vision for the new Department.

Why is this an exciting time for biomedical engineering?

The new era of technological revolution is transforming the world as we know it. From a biomedical engineering perspective, the merging of biological with medical engineering presents a unique opportunity to create innovative systems and methods to transform the current disease care system into a genuine health care enterprise.

I am inspired daily by our ability as scientists and engineers to make dreams a reality. But I am also a realist. I am aware of the challenges of venturing into the unknown. Perhaps one way to turn dreams into reality quickly is to train a future generation of researchers to think differently and develop solutions that are not constrained by roadblocks that our current understanding imposes on them.

What are the opportunities and challenges of building a new BME program at UT Southwestern?

Several factors have converged to support a viable and impactful BME Department at UT Southwestern, including the existence of a vibrant BME graduate program, outstanding faculty, motivated trainees, and exceptional resources to support innovation. In addition, the burgeoning infrastructure for clinical research creates diverse opportunities to engage in translational research.

Partnering with neighboring engineering schools in Dallas and Arlington serves as a pipeline to enrich student training and recruitment, as well as strengthens ongoing collaborations while establishing new ones. Along this line, I am particularly excited about the new Texas Instruments Biomedical Engineering and Sciences Building, which will house BME faculty members from UT Southwestern and UT Dallas. This level of programmatic integration will leverage UT Southwestern's institutional strength in medicine and biological sciences with UT Dallas' engineering prowess.

It also offers us a new platform to train well-rounded students equipped with knowledge and confidence. There is no better way to make inventions available to consumers than by partnering with industry to develop and commercialize innovative products from academia. Establishing this connection is critical for success.

Of course, there also will be challenges ahead. While institutional support is high and the opportunities for collaboration are enormous, the Department will not initially have the bandwidth to address many exciting medical and biological problems. We will strategically recruit faculty members while leveraging a pool of exceptionally talented engineers and scientists on campus to support the new BME Department's priorities. The impressive biomedical engineering graduate program at UT Southwestern has laid a solid foundation upon which we will build the new Department.

You are a recognized expert in applying molecular imaging to treat human diseases, with research interests in image-guided cancer surgery, portable imaging devices, and nanotechnology. With such varied interests, what is your vision moving forward?

I am excited about continuing some of my research projects at UT Southwestern, but my immediate priority as the inaugural BME Chair is to empower faculty members in the Department to transform ideas into technology-driven biomedical and clinical solutions. We need to provide valuable tools to clinicians and scientists to treat diseases effectively and understand the molecular and structural underpinnings of biological processes.

Development of portable, low-cost, and efficient devices will enable us to reduce health disparity and prevent the onset of diseases. While traditional engineering solutions will form a significant part of our research, I will encourage our faculty members to envision a world where our devices can help understand the healthy person so that deviations from the norm can be found early.

The cancer-detecting goggles you developed were partially inspired by tracers on cruise missiles in the Persian Gulf War. How can past experiences spark a potential solution for a seemingly unrelated problem?

I approach scientific problems by framing them into testable hypotheses. Then I explore different approaches to solve the problem. If additional expertise is needed, I search for the best collaborators to fill the gap. We then design the best experimental method to address the question, guided by our hypothesis. This strategy is not confining; it can be applied in diverse areas of life endeavors.

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

Dr. Achilefu holds the Lyda Hill Distinguished University Chair in Biomedical Engineering.

Seven researchers selected as newest UTSW Endowed Scholars

By Carol Marie Cropper

UT Southwestern's 2021 class of Endowed Scholars in Medical Science includes scientists searching for the following: a way to harness the central nervous system to control pain, to degrade pathological proteins found in neurodegenerative diseases such as Alzheimer's and Parkinson's, and to better understand the long-running battle between bacteria and the viruses that infect them.

As Endowed Scholars, they will receive five years of financial support from 2021-2025 to carry out independent, cutting-edge research as tenure-track Assistant Professors. The Program, established in 1998 with $60 million in philanthropic funds, is designed to support early career clinical or basic science research.

UT Southwestern is proud of this year's class of outstanding scientists, said David Mangelsdorf, Ph.D., Chair of the Endowed Scholar Committee.

"It was a banner year for the Endowed Scholars Program. UT Southwestern is excited to welcome seven of the most talented new investigators in the nation to our campus. Pay attention to these folks – they are the future of this institution," said Dr. Mangelsdorf, Chair of Pharmacology.

Learn more about each of the Endowed Scholars in their own words:

Seungwon (Sebastian) Choi, Ph.D., Assistant Professor of Psychiatry
Virginia Murchison Linthicum Scholar in Medical Research

What led to a career in research: I became interested in pursuing my career in biomedical research when I went through a liver transplant surgery as a donor for my father back in college. While it was a tremendously difficult time for my family, my experience sparked a passion for biomedical sciences, and since then my graduate and postdoctoral training has shaped my long-term interest in neuroscience research.

Research focus: Every day, we experience a variety of sensations of the physical world through our skin: a hug from a loved one, a warm shower, a mosquito bite, or touching a hot pan. These touch, temperature, itch, and pain signals are detected by peripheral sensory neuron terminals and end organs distributed throughout our body and propagated into the spinal cord where they are processed and transmitted to the brain via ascending spinal pathways. My research aims to define the functional organization of ascending somatosensory circuitry and to use this knowledge to reveal how internal states and disorders of the nervous system shape our sense of touch and pain. My lab will explore these exciting research areas by using new mouse genetic tools in conjunction with advanced molecular, anatomical, physiological, and behavioral approaches.

Ultimate career goal: I hope that my research will reveal new therapeutic substrates for treating disorders associated with dysfunction of the somatosensory system. I am also committed to collaborative science, teaching and mentoring young scientists, and promoting diversity and inclusion in science.

Kevin Forsberg, Ph.D., Assistant Professor of Microbiology
W.W. Caruth, Jr. Scholar in Biomedical Research

What led to a career in research: I took a high school course in biotechnology that motivated me to pursue biology as an undergraduate. In college, I was fortunate to find a fantastic research position at the Translational Genomics Research Institute, where I worked with bright, passionate, and empathetic people who showed me how creative, tangible, and rewarding a career in research could be. This motivated me to attend graduate school at Washington University in St. Louis with Gautam Dantas, Ph.D., whose excellent research environment gave me my first taste of professional success and provided me my first opportunity to mentor students. This combination proved to be an addictive elixir – I was hooked on research and set my vision squarely on making it my life's work.

Research focus: My lab studies the longest standing conflict on Earth – the one between bacteria and the viruses that infect them, called phages. To keep pace with their adversaries, both bacteria and phages must constantly adapt to their competitor's latest innovation, locking host and virus in a never-ending molecular arms race for survival. In many cases, however, it is difficult to predict whether the bacterium or phage will win this evolutionary tug-of-war, as the genes and systems that determine these outcomes are often poorly understood. The Forsberg lab aims to reveal many of these cryptic genes and mechanisms, using large-scale functional selections to find genes that influence phage-infection outcomes, followed by detailed experimentation to understand their mechanisms.

Ultimate career goal: When all is said and done, I'd like to end up like my postdoctoral mentor, Harmit Malik, Ph.D. (or, more reasonably, a poor approximation). In his group, there is a culture of support and empathy while, at the same time, a demand for rigor and celebration of ambition. He marks success both through scientific discovery and by the careers of those he has trained. He has his cake and gets to eat it, too. Because goals should be ambitious, I'd like a slice of what he's having.

Yuuki Obata, Ph.D., Assistant Professor of Immunology and Neuroscience
Nancy Cain and Jeffrey A. Marcus Scholar in Medical Research, in Honor of Dr. Bill S. Vowell

What led to a career in research: When I was an undergraduate, I was fascinated by the fact that gut microbiota have many beneficial effects on human health. This led me to study mucosal immunology and host-microbe interactions as a trainee at RIKEN, the large research institute in Japan where I learned how exciting the process of discovering the unknown can be. This experience made me realize that I wanted to work as a scientist.

Research focus: My research aims to understand how gut environmental factors (e.g., microbiota and diet) regulate neural circuits, immune responses, and neuroimmune crosstalk in health and diseases. We use a variety of experimental approaches, including viral tracing of gut nerves, in vivo and ex vivo physiological assays, gnotobiotic animal models, and multiomics technologies. I am also interested in understanding the molecular mechanisms of inter-organ communications such as the gut-brain axis.

Ultimate career goal: To pioneer and establish new areas of biomedical research and make discoveries that help people stay healthy.

Allan-Hermann Pool, Ph.D., Assistant Professor of Neuroscience, Anesthesiology & Pain Management, and in the Peter O'Donnell Jr. Brain Institute
Eugene McDermott Scholar in Biomedical Research

What led to a career in research: The initial spark that set me on this track was an introductory course in molecular and cell biology in high school that transformed the dull and messy discipline of biology into one of mesmerizing underlying logic and potential. What has enticed me about neuroscience is the chance to personally take a stab at understanding the mechanisms that provide a purpose to animal (including our own) behavior. A book that catalyzed my trajectory in this direction was Albert Camus' *The Myth of Sisyphus*, which underscored the essential lack of purpose to our existence. Although I still agree with the underlying premise, it is the biological imperative to survive and the basic biological drives that make our subjective experience of the world profoundly meaningful. Being able to study the biological substrate that brings this about is something that has made research highly enjoyable for me. Also, the fact that it is possible to get paid to do that is still fantastical to me.

Research focus: I am interested in how basic biological motivations are represented in the brain and how they determine the direction and content of animal behavior. In particular, my lab focuses on one of these biological drives – the mammalian pain and pain relief system. Specifically, we study how distinct pain modalities are encoded in the central nervous system and how the endogenous pain relief circuits can control the perception of pain. Furthermore, we seek to take advantage of the cellular identity of these central circuit nodes to design precision gene therapies to gain control of this system and make it therapeutically addressable.

Ultimate career goal: I will be happy, if as a result of my lab's work, we will understand both the cellular hardware and the operating principles of at least one of the basic drives, and generate a precise and simple means to reprogram cellular components of these systems outside specialized model organisms.

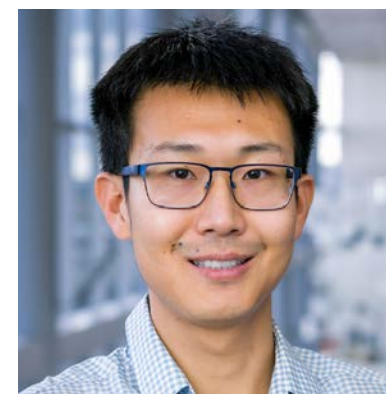
Courtney Schroeder, Ph.D., Assistant Professor of Pharmacology and Cell Biology
Deborah and W. A. "Tex" Moncrief, Jr. Scholar in Medical Research

What led to a career in research: My passion for research and the cytoskeleton was sparked by my time as an undergraduate working in the lab of Todd Stukenberg, Ph.D., at the University of Virginia. I studied a post-translational modification of microtubules, and I loved making discoveries, knowing I was treading new territory in biology. I also particularly enjoyed studying how proteins function at the molecular level. My Ph.D. adviser (Ron Vale, Ph.D.) and postdoctoral adviser (Harmit Malik, Ph.D.) further nurtured my love of academic research.

Research focus: My lab studies evolutionarily novel actin and tubulin proteins that span the animal kingdom. Given their essentiality, cytoskeletal proteins are commonly thought to be conserved throughout eukaryotic evolution, yet we have found many cytoskeletal genes are rapidly evolving – even between closely related species – and have adapted novel biological functions. We want to know what drives this genetic innovation and the biological consequences. We specifically use fruit flies and human tissue culture cells to study the functions of these unusual proteins, which appear to play important roles in both fertility and development. A subset of these proteins are misexpressed in cancer, and we will also explore how they may increase cancer cell survival.

Ultimate career goal: Scientifically, my career goal is to understand why cytoskeletal genes are diversifying. We know little about these novel actins and tubulins, and yet by studying them I think we gain insight into a number of biological processes that are under evolutionary pressure to diversify. Beyond the science, my goal is to mentor trainees to be successful and have fulfilling careers in or beyond academia.

Boyuan Wang, Ph.D., Assistant Professor of Pharmacology
Southwestern Medical Foundation Scholar in Biomedical Research



What led to a career in research: A career in research is a childhood dream that probably began from observing my dad collecting exhaust samples from autos for analysis. My favorite class in high school was chemistry, for the obvious sense of achievement from making new compounds. This interest gradually drifted to bacteriology, as I wanted to learn more about this domain of life with the simplest cellular structure but the most diverse chemistry. At the same time, I retained my identity as a chemist to synthesize chemical probes to provide creative approaches to biological problems.

Research focus: My latest research involves attempts to understand why bacteria, when challenged by nutrient starvation, tend to enter a "persistent" state featuring metabolic dormancy and a remarkable level of tolerance against chemotherapies. Interestingly, almost all bacteria produce the same second messenger, (p)ppGpp, also known as magic spot nucleotides, in response to starvation. Once we know how (p)ppGpp coordinates the downregulation of all major aspects of bacterial physiology to an onset of dormancy, we may be able to design therapeutics to combat persistent infection.

Ultimate career goal: My ultimate goal is to understand bacteria to the extent that we can communicate with them using their language to not only resolve infectious diseases but also make them versatile tools, faithful friends, and an endless source of inspiration for all human beings.

Haiyang Yu, Ph.D., Assistant Professor in the Center for Alzheimer's and Neurodegenerative Diseases, of Molecular Biology, and in the Peter O'Donnell Jr. Brain Institute
Effie Marie Cain Scholar in Medical Research

What led to a career in research: When I was in the fifth grade, I borrowed from the county library a charming book full of absorbing stories of chemists titled *Chemical Elements: The Fascinating Story of Their Discovery and of the Famous Scientists Who Discovered Them*. Particularly, I was fascinated by how Robert Bunsen and Gustav Kirchhoff discovered rubidium and cesium in the 19th century using cutting-edge equipment – the Bunsen burner and the Kirchhoff-Bunsen spectroscope. This book sparked the idea of becoming a scientist in my 11-year-old boy's mind. Graduating from high school, I decided to pursue a career in biological sciences, as I felt that this field was booming just like chemistry did at the beginning of the 20th century.

Research focus: My group has two closely related research directions. First, we will determine how liquid-liquid phase separation contributes to protein aggregation in neurons. Fibrils can form and propagate in several age-related neurodegenerative diseases, such as tau in Alzheimer's and frontotemporal dementia (FTD) and alpha-synuclein in Parkinson's. My previous work demonstrated that TDP-43, another aggregate-forming protein in FTD and ALS, forms liquid crystal condensates in cells. I plan to determine whether TDP-43 fibrils can arise from these liquid crystal condensates. Second, we will harness the cellular defense pathways to ameliorate pathological protein assemblies. In this direction, we plan to use conformation-specific antibodies to selectively degrade aggregated protein through proteasome-dependent or lysosomal pathways.

Ultimate career goal: Because of a growing older population, neurodegenerative diseases will be the next major health problem. I am devoted to elucidating the molecular mechanisms behind common dementia and to translating my findings into effective treatments for patients.

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Dr. Choi and Dr. Schroeder are both Cancer Prevention and Research Institute of Texas (CPRIT) Scholars.

Dr. Mangelsdorf holds the Alfred G. Gilman Distinguished Chair in Pharmacology, and the Raymond and Ellen Willie Distinguished Chair in Molecular Neuropharmacology in Honor of Harold B. Crasilneck, Ph.D.

New Postbaccalaureate to PhD Program launches this summer at UTSW

Initiative enhances research experience for undergrads to prepare them for graduate school

By Jan Jarvis

Recent college graduates who want to pursue biomedical research but need additional training can get support to achieve their goals through a new Postbaccalaureate to PhD (PB2PHD) Program launching this year at UT Southwestern.

The PB2PHD Program of one to two years focuses on recent college graduates who want to strengthen their skills and increase their competitiveness for admission to graduate school or an M.D./Ph.D. program, said Arnaldo Díaz Vázquez, Ph.D., Program Director and Assistant Dean for Diversity and Inclusion in the UT Southwestern Graduate School of Biomedical Sciences. Applications are currently being accepted for the PB2PHD Program, which begins in June.

Arnaldo Díaz Vázquez, Ph.D.

"The program targets students who need more experience in doing research before applying to graduate school," Dr. Díaz Vázquez said. "The goal is to help these students move into a Ph.D. or M.D./Ph.D. program and ultimately make the transition into the biomedical science workforce."

Funding the program is a $300,000 grant from the Communities Foundation of Texas, which since 1953 has provided more than $2 billion in grants to support education, health care, public safety, social services, animal care, and the arts.

"We're thrilled to be a part of diversifying the biomedical research field by investing in UT Southwestern's Postbaccalaureate to PhD Program," said Sarah Cotton Nelson, Communities Foundation's Chief Philanthropy Officer. "We know that supporting the development of medical professionals from all backgrounds helps to decrease health disparities and build thriving communities for all."

An applicant must be an American citizen or permanent U.S. resident with a baccalaureate degree in a biomedically relevant basic science from an accredited college or university that was awarded no more than 36 months prior to applying.

The Postbaccalaureate to PhD Program will provide research experience to help prepare participants for graduate school.

"Students from underrepresented populations in biomedical science as defined by the National Institutes of Health are encouraged to apply," Dr. Díaz Vázquez said.

A stipend/research assistantship of $35,000 per year allows students to focus on their research training rather than outside employment, Dr. Díaz Vázquez said. Individual health insurance, support to attend a scientific conference, and tuition and fees also will be provided. Students may apply for a second year in the program, contingent on performance during the first year and availability of funding.

Students in the program will work in a UTSW laboratory on research that matches their scientific interests, take graduate-level courses, and receive formal training in responsible research conduct. Academic and professional development activities tailored to the student's specific individual needs – such as scientific seminars, scientific writing, and interview skills – also will be offered. The program culminates with the students presenting their work at UT Southwestern and at a national scientific conference.

Students will have access to more than 350 full-time faculty at UTSW who maintain active research programs in disciplines that include genomics, cancer biology, computational biology, developmental biology, biomedical engineering, molecular genetics, structural biology, cell biology, chemical biology, systems biology, pharmacology, microbiology, neurosciences, immunology, and organic chemistry.

Candidates must complete and submit their online application by March 1. For more information, go to **utsouthwestern.edu/education/graduate-school/research-opportunities/post-baccalaureate/.**

Congratulations to School of Health Professions graduates of 2021

On Dec. 12, more than 100 students of the School of Health Professions celebrated their graduations at an in-person commencement ceremony in the Tom and Lula Gooch Auditorium on South Campus. It was the first live commencement ceremony for a class since the pandemic began. Eric Peterson, M.D., M.P.H., Vice Provost and Senior Associate Dean for Clinical Research and Vice President for Health System Research, delivered the commencement address. Below are a few photo highlights from the event.

Jon Williamson, Ph.D., Dean of the School of Health Professions, delivers welcome remarks.

Brittany Nicole Wright (left) and Chung Lin Kew wait to cross the stage to receive their Doctor of Philosophy degrees.

Master of Clinical Nutrition graduate Daileen Rodriguez (center) with Tad Campbell, M.C.N., RDN, LD, Instructor of Clinical Nutrition, (left) and Lona Sandon, Ph.D., RDN, LD, Associate Professor of Clinical Nutrition

Sarah Meng (left) and Yinying Wei, Master of Clinical Nutrition graduates

Master of Physician Assistant Studies graduate Kavia Gupta and her family

Doctor of Physical Therapy graduates (l-r): Shana John, Shraddha Bista, Shivani Patel, and Tricia Interino

Monica Yousef, Master of Physician Assistant Studies graduate, and her sister

Master of Physician Assistant Studies graduates (l-r): Nawal Suleman, Cameron Orme, and Niveen Joulani

Nine health professions students earn honors

The School of Health Professions honors students with four major awards each year. Nine outstanding students were recognized for their talents and service: Eight honorees won their awards this year, while the ninth was honored in 2020. All graduated with the Class of 2021.

Congratulations to the following honorees:

Raul Caetano, M.D., Ph.D., Student Research Award
Clayton Sue Benson
Brittany Nicole Wright (2020)

Gordon Green, M.D., Student Clinician Award
Margaret Tiye Lashay Hazelton

L. Ruth Guy, M.D., Student Leadership Award
Megan Broussard
Rebekah Lee Forshey
Nneka Odera Chisom Jermaine Nweke

John Schermerhorn, M.D., Student Service Award
Samantha Lauren Elizabeth Hickey
Tristine Lam
Abby Kathryn Wolf

More online: To learn more about the award winners, see the full story on *Center Times Plus* at **utsouthwestern.edu/ctplus**.

Increasing patient care and biomedical innovation needs drive expansion

By Patrick Wascovich

Unprecedented growth of UT Southwestern on campus is driving the institution toward even higher levels of real value in foundationally delivering on its mission to promote health and a healthy society that enables individuals to achieve their full potential.

Daniel K. Podolsky, M.D., President of UT Southwestern, said last year that ongoing construction "was not growth for growth's sake" but rather an opportunity to embrace what "epitomizes the essence of what is UT Southwestern. It is creating the opportunity for us to deliver on our mission through the care that we provide to our patients and their families, the research that is carried out in our laboratories, and through the training of the next generation of physicians, medical scientists, and other health care providers."

In 2021, the campus footprint was significantly adjusted with the operational launch of William P. Clements Jr. University Hospital's third tower in January and the opening of the newly expanded Radiation Oncology Building. Ongoing major construction projects include the North Campus Outpatient Cancer Care and Brain Research Towers, as well as the late-year groundbreaking for the Texas Instruments Biomedical Engineering and Sciences Building.

UT Southwestern's campus currently includes almost 15.5 million square feet of building space, with about 2.7 million square feet of capital or renovation projects under construction or in planning and design. This unprecedented institutional growth reflects burgeoning opportunities to serve patients while also addressing the need for additional research laboratories and educational facilities. In 2021, UT Southwestern had about 2.96 million square feet of construction approved by the UT System and underway, including 1.75 million square feet of future occupied buildings and more than 1.2 million square feet of garage space.

Juan M. Guerra Jr., Vice President for Facilities Management, leads these brick-and-mortar efforts. His docket in 2021 included nine current and five future capital improvement projects.

The most visible, completed campus project was the expansion of the 460-bed Clements University Hospital, which began in 2017 and was fully finished in mid-January 2021. The $502.1 million project added a 654,000-square-foot third tower that serves as the clinical home for the Peter O'Donnell Jr. Brain Institute and includes specialty care units for patients with diseases of the brain such as epilepsy, Alzheimer's, or stroke. The tower also includes more operating rooms, an expanded emergency department, and additional patient rooms that increased the hospital's bed count to about 875.

"We're really proud of the hospital expansion and the contribution that we'll make to the health of our community. We're also excited about the contribution it will make to our institutional priorities to educate, discover, and heal," said John Warner, M.D., Executive Vice President for Health System Affairs. "One of the great strengths at UT Southwestern is our physicians and other providers coming together to care for patients in a team-based multidisciplinary way. Particularly in a procedural environment, that's critically important as you integrate different types of physicians and also different types of technologies to make a big difference in how we improve outcomes for patients."

The addition of a third tower to William P. Clements Jr. University Hospital in January 2021 kicked off a year of rapid growth for UT Southwestern, with about 2.7 million square feet of new or renovated space under construction or in planning.

Juan M. Guerra Jr., Vice President for Facilities Management, leads campus expansion efforts, which in 2021 included nine current and five future capital improvement projects.

The Outpatient Care and Brain Research Towers on North Campus, scheduled to open in mid-2022, will house research efforts of the Peter O'Donnell Jr. Brain Institute and outpatient care and clinical trials space for the Harold C. Simmons Comprehensive Cancer Center.

UT Southwestern, a recognized leader in radiation oncology, also nearly doubled its facility dedicated to this specialty in 2021. The expansion brought the total combined space to more than 130,000 square feet that boasts 49 exam rooms, procedure rooms, patient-support rooms, two children's areas, a cafeteria, and a collection of the most sophisticated treatment machines. "Smart" treatment technologies provide a personalized patient experience through artificial intelligence-assisted radiation therapy adaptable to changes in the patient's anatomy, tumor size, and position, along with the ability to monitor treatment progress due to biological and functional changes.

Radiation Oncology is a key component of UT Southwestern's Harold C. Simmons Comprehensive Cancer Center – one of 51 designated comprehensive cancer centers in the U.S. by the National Cancer Institute – a member of the elite 30-member National Comprehensive Cancer Network with its cancer program nationally ranked among the top 25 by *U.S. News & World Report*.

And the future continues to look bright, thanks to ongoing construction projects.

The North Campus Outpatient Cancer Care and Brain Research Towers, scheduled to open mid-2022, will soon add volume to UT Southwestern's clinical and research initiatives. The $454.7 million towers, which broke ground in 2019, share a four-story footprint, each topped off by distinctive five-floor structures. One tower, recently named the Peter O'Donnell Jr. Biomedical Research Building in honor of the late philanthropist, will house research efforts of the O'Donnell Brain Institute and the other will provide outpatient care and clinical trials space for the Simmons Cancer Center. In all, this expansion adds more than 584,500 square feet of space to the North Campus.

"This building will more than double our current cancer care capabilities on campus," said Carlos L. Arteaga, M.D., Director of the Simmons Cancer Center. "It also will harbor our large infrastructure for clinical trials. We expect the Outpatient Cancer Care Tower not only to be the exceptional destination for cancer patients seeking the latest standards of care, but also a shining light for clinical investigations, innovation, and progress."

A 71,000-square-foot expansion in the summer of the Radiation Oncology building nearly doubled the size of the current facility, adding patient care areas as well as space for more advanced treatment machines.

"The new tower will allow us to nucleate unique groups of exceptional researchers in diverse disciplines required to comprehensively explore and advance brain science, with a focus on those areas that are ripe for human translation," said William T. Dauer, M.D., Director of the O'Donnell Brain Institute.

In November, ground was broken for construction of the Texas Instruments Biomedical Engineering and Sciences Building that will catalyze a unique partnership between UT Southwestern and UT Dallas, bringing their biomedical engineering programs together to foster innovative solutions for unmet medical needs.

The 150,000-square-foot, five-story facility on East Campus will support the work of dozens of faculty members and their teams with both wet and dry laboratory space, as well as areas designated specifically to promote multidisciplinary interactions when it opens in 2023. A Biodesign Center will feature a large assembly/design studio, a metal fabrication shop, and rooms for 3D printing.

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Dr. Arteaga holds The Lisa K. Simmons Distinguished Chair in Comprehensive Oncology.

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

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

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

Choy, Andersen named UT Southwestern Professors Emeritus

By Jan Jarvis

Two UT Southwestern faculty – one an internationally recognized leader in radiation oncology and the second a pioneer in his field and the first Chief of the Division of Pediatric Gastroenterology – have been appointed Professors Emeritus.

Hak Choy, M.D., former Chair of Radiation Oncology and now Professor Emeritus, is known for his research showing that chemotherapeutic agents and radiation can be used in combination to magnify benefits. Since he joined UT Southwestern as Chair in 2003, Dr. Choy has worked to improve the lives of patients by reducing the number of radiation treatments they undergo, improving therapy while decreasing side effects.

"Today we can treat with high doses and fewer treatments for better control of tumors. We can have a much bigger impact on cancer-killing technology," he said.

Through Dr. Choy's leadership, UTSW became one of the nation's leading centers in radiation oncology. Over 18 years, he built the Department of Radiation Oncology into a research powerhouse and one of the largest departments at UT Southwestern. Dr. Choy also helped UTSW gain a reputation as a trendsetter in radiotherapy, said Robert Timmerman, M.D., Professor and Interim Chair of the Department of Radiation Oncology.

Hak Choy, M.D.

"Dr. Choy recruited and nurtured a team that used technology and biology in novel ways, many that changed standards of care for cancer patients," Dr. Timmerman said.

As the Department grew, Dr. Choy remained steadfast in attracting highly qualified innovators who were determined to push the boundaries of science. In 2017, UT Southwestern became the first medical center in Texas to add GammaPod, the first stereotactic body radiation therapy system for treating breast cancer that has been shown to be more effective and efficient with fewer side effects.

After graduating from UT Medical Branch School of Medicine in 1987, Dr. Choy went on to become a Clinical Assistant Professor at Brown University's Warren Alpert Medical School. He joined Vanderbilt University School of Medicine as an Associate Professor and Clinic Director of its Radiation Oncology Center and in 1995 was promoted to Professor and Vice Chair of the Department of Radiation Oncology.

Since retiring in September, the father of four has moved to Colorado. Dr. Choy said he was fortunate to work at UT Southwestern, where he had so many opportunities to explore research and help the Department grow. He's grateful to have played a part in improving treatment for cancer patients and still hopes to see a day when single-day cancer treatment will become the standard of care.

"I don't think we'll see a day when cancer is cured," he said. "But I think people will live longer and, rather than die from cancer, live with it."

The second appointee is John Andersen, M.D., a guiding force in the Division of Pediatric Gastroenterology at UT Southwestern for over four decades. Dr. Andersen, the first Chief of that Division, helped grow UTSW's pediatric gastroenterology practice into a nationally recognized program. He also is one of the first to have completed and started a pediatric GI program, said Rinarani Sanghavi, M.D., Associate Professor of Pediatrics at UT Southwestern.

John Andersen, M.D.

"He is a clinician par excellence – and has referrals from all over the country," Dr. Sanghavi said. "He is a wonderful person and is a huge driving force behind why a lot of faculty came to Dallas to train and then stayed on."

When he became Chief of the Division in 1979, Dr. Andersen was UTSW's second pediatric gastroenterologist. He left for private practice for a period, then returned as Chief in 1992 to work on building the program. Under his leadership, the GI fellowship program was revived in 1994. That program proved to be fertile ground for development of future leaders as the Division expanded. By 2011, he was appointed Vice Chair of Clinical Operations for Pediatrics.

As an educator, Dr. Andersen emphasized letting people focus on their interests. "One thing I learned is you want to identify people's passions and then allow them to blossom," he said. "You want them to realize their dreams."

When he graduated from the University of Pennsylvania School of Medicine, Dr. Andersen did not envision a future in gastroenterology. Although he began his career as a pediatrician, research intrigued him. So when a fellowship in gastroenterology at UTSW became available, he jumped at the opportunity. He soon discovered that he enjoyed the challenge of treating children with liver disease, chronic abdominal pain, and other complex medical problems.

"Often I'm the third or fourth physician that the family has consulted with and it's a challenge to figure out what is going on," Dr. Andersen said. "I enjoy solving problems, and seeing someone get better – that's pretty validating."

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Dr. Timmerman holds the Effie Marie Cain Distinguished Chair in Cancer Therapy Research.

More online: Read the full stories on *Center Times Plus* at **utsouthwestern.edu/ctplus**.