CenterTimes

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IN MEMORIAM

W.A. "Tex" Moncrief Jr.: Generosity extended academic medical care, research efforts

From Staff Reports

W.A. "Tex" Moncrief Jr., whose extraordinary generosity has and will benefit many generations of Texans by expanding UT Southwestern programs in Dallas, Fort Worth, and surrounding communities, died Dec. 28 at age 101.

Tex Moncrief and the Moncrief family, longtime supporters of academic medicine, helped facilitate the expansion of cancer care services through the Moncrief Cancer Institute in Fort Worth, more than a dozen primary and specialty services at the Monty and Tex Moncrief Medical Center at Fort Worth, as well as brain cancer research through philanthropy that began in the 1960s.

"W.A. 'Tex' Moncrief Jr. was passionate in wanting to ensure that the communities of Fort Worth and North Texas more broadly had access to outstanding health care. There was never an individual more decisive in pursuing his passion. His vision and remarkable generosity – always in honor of his admired father – has enabled UT Southwestern to serve legions of those in need," said Daniel K. Podolsky, M.D., UTSW President. "In planning the Moncrief Cancer Institute and the UT Southwestern Monty and Tex Moncrief Medical Center at Fort Worth, he

W.A. "Tex" Moncrief Jr.

was determined that they not only provided facilities enabling access to medical expertise but lifted the spirits of those in need of help."

In 2017, UT Southwestern dedicated the Monty and Tex Moncrief Medical Center at Fort Worth, providing access to more than a dozen areas of specialty care from cardiology to neurology in the heart of Fort Worth's Medical District. (See related story on page 3.) The three-story, 110,000-square-foot multidisciplinary outpatient facility, which was UT Southwestern's first named campus outside of Dallas, complements UTSW's cancer presence at the neighboring Moncrief Cancer Institute. The precursor to the Institute, Moncrief Radiation Center, was started by W.A. Moncrief in 1958 when his son, Tex Moncrief, lost his 8-year-old daughter to leukemia. The Moncrief Cancer Institute's mission is to make cancer prevention, patient treatment, clinical trials, and a variety of cancer-related research more accessible to Fort Worth-area citizens.

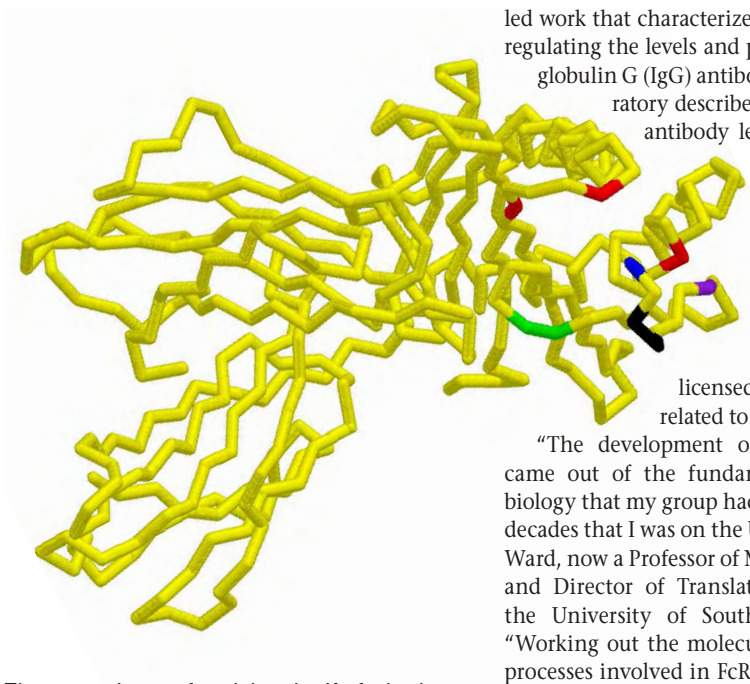
"My family has been touched by cancer, and we therefore take the fight against cancer very personally and very seriously. We want to defeat this horrible disease while in the meantime ensuring our community has every resource necessary to offer the best cancer care and treatment for our fellow citizens," Tex Moncrief said during dedication ceremonies for the Moncrief Cancer Institute.

Over the years, the Moncrief family has contributed nearly $14 million from the William A. and Elizabeth B. Moncrief Foundation and from Tex Moncrief in direct support of UTSW programs and facilities on its Dallas campus, including the W.A. Monty & Tex Moncrief Radiation Oncology Building. In 2003, Tex and Deborah Moncrief contributed $7.5 million to UT Southwestern's Innovations in Medicine campaign for the Moncrief Radiation Oncology Center in Dallas to complement the UT Southwestern Moncrief Radiation Center in Fort Worth, housing state-of-the-art radiation therapy and research equipment. This is in addition to the $75 million given to the Moncrief Cancer Foundation to support the Moncrief Cancer Institute.

Thanks to gifts totaling $3.2 million from Tex Moncrief and affiliated family foundations, a collaborative research team at UT Southwestern's Harold C. Simmons Comprehensive Cancer Center is testing new therapies that offer hope to those diagnosed with glioblastoma, an aggressive form of brain cancer. That gift, made in honor of Tex's late son, Charlie, initiated the Charlie Moncrief Glioblas-

Please see MONCRIEF on page 3

Decades of UTSW research pave way for new drug to treat rare muscle disease



The new drug, efgartigimod alfa-fcab, is an engineered fragment of a human antibody that binds to a cell surface receptor known as the neonatal Fc receptor, or FcRn. This figure shows the structure of FcRn, with amino acids that contact Fc/IgG shown in colors. Note: The figure was drawn using RasMol (Roger Sayle, Bioinformatics Research Institute, University of Edinburgh, Edinburgh, U.K.).

By Christen Brownlee

A first-in-kind immune-modulating drug that arose from decades of basic research at UT Southwestern has received approval from the Food and Drug Administration as a new treatment for adults with a form of myasthenia gravis. This rare and chronic autoimmune disease is characterized by debilitating and potentially life-threatening muscle weakness.

The new drug, efgartigimod alfa-fcab (to be marketed as Vyvgart), is an engineered fragment of a human antibody that binds to a cell surface receptor known as the neonatal Fc receptor, or FcRn. Between 1990 and 2015, former UTSW Professor of Immunology E. Sally Ward, Ph.D., led work that characterized this receptor's role in regulating the levels and persistence of immunoglobulin G (IgG) antibodies. In 2005, her laboratory described an approach to lower antibody levels by blocking FcRn activity, and subsequently demonstrated preclinical proof-of-concept to treat antibody-mediated autoimmune disease. The global immunology company argenx has licensed exclusive patent rights related to this drug from UTSW.

"The development of this FcRn inhibitor came out of the fundamental work on FcRn biology that my group had worked on during the decades that I was on the UTSW faculty," said Dr. Ward, now a Professor of Molecular Immunology and Director of Translational Immunology at the University of Southampton in England. "Working out the molecular and cell biological processes involved in FcRn biology and its regulation and transport of antibody molecules was a major focus of our work at UTSW over more than two decades, starting when I was an Assistant Professor there."

Clinical trials that led to the recent FDA approval found that 68% percent of patients with anti-acetylcholine receptor antibody positive myasthenia gravis responded to efgartigimod, compared with 30% of those taking a placebo. The company is exploring possible uses for the agent in other conditions mediated by IgG.

Efgartigimod represents Dr. Ward's second commercial success based on fundamental research conducted at UTSW. That work also led to technology that can extend the half-life of therapeutic antibodies and currently is used in the FDA-approved drug ravulizumab (Ultomiris) and two antibody therapies against COVID-19, as well as another antibody in development to treat respiratory syncytial virus (RSV).

It is also the second first-in-kind drug developed from basic research at UTSW to be approved by the FDA in the past year. Less than six months ago, belzutifan (Welireg), a HIF-2α inhibitor, received

Please see DRUG on page 2

Scientists find first-in-human evidence of how memories form

The study identified 103 memory-sensitive neurons in the brain's hippocampus and entorhinal cortex (colored portion in illustration above) that increase their rate of activity when memory encoding is successful.

By Patrick McGee

In a discovery that could one day benefit people suffering from traumatic brain injury, Alzheimer's disease, and schizophrenia, UT Southwestern researchers have identified the characteristics of more than 100 memory-sensitive neurons that play a central role in how memories are recalled in the brain.

Bradley Lega, M.D., Associate Professor of Neurological Surgery, Neurology, and Psychiatry, said his findings published in *NeuroImage* may point to new deep brain-stimulation therapies for other brain diseases and injuries.

"It sheds important light on the question, 'How do you know you are remembering something from the past versus experiencing something new that you are trying to remember?'" said Dr. Lega, a member of the Peter O'Donnell Jr. Brain Institute.

The most significant finding was that firing of neurons occurs with different timing relative to other brain activity when memories are being retrieved. This slight difference in timing, called "phase offset," has not been reported in humans before. Together, these results explain how the brain can "reexperience" an event but also keep track of whether the memory is new or something previously encoded.

"This is some of the clearest evidence to date showing us how the human brain works in terms of remembering old memories versus forming new memories," Dr. Lega said.

His study identified 103 memory-sensitive neurons in the brain's hippocampus and entorhinal cortex that increase their rate of activity when memory encoding is successful. The same pattern of activity returned when patients attempted to recall these same memories, especially highly detailed memories.

This activity in the hippocampus may have relevance to schizophrenia because hippocampal dysfunction underlies schizophrenics' inability to distinguish between

Please see MEMORIES on page 5

UT Southwestern creates interdepartmental diversity team

By Carol Marie Cropper

The Office of Faculty Diversity & Development has established a Departmental Diversity Leaders initiative to promote diversity, equity, and inclusion (DEI) across UT Southwestern's departments.

Each department chair will appoint a diversity leader – a faculty member who will serve as an adviser on DEI issues – to sit on the department's executive leadership team. Members will also meet regularly with each other to share ideas and expertise and promote best practices to advance DEI at UTSW, said Quinn Capers IV, M.D., Associate Dean for Faculty Diversity, who will guide the effort.

"The leaders will be the local champions that help diffuse DEI initiatives across campus," Dr. Capers said. The goal, he said, is to make UT Southwestern "a national exemplar of diversity, equity, and inclusion" in academic medicine.

"This includes not only enhancing the compositional diversity of the faculty and trainees," he explained, "but promoting a climate of inclusion, and ensuring that principles of equity are upheld in our clinical, research, and education missions."

The 33 leaders appointed to the group from UT Southwestern departments will be given protected time to work on the effort, with dedicated funding set aside by President Daniel K. Podolsky, M.D.; W. P. Andrew Lee, M.D., Executive Vice President for Academic Affairs, Provost, and Dean of UT Southwestern Medical School; and UT Southwestern departments.

Appointed diversity leaders will meet regularly as a collaborative group to discuss challenges and opportunities they have identified around DEI, then guide the development and implementation of initiatives to address them, Dr. Capers said. This approach to DEI recognizes that enhancing diversity in medicine and science is an effort that requires strategic planning, cross-departmental engagement, and institutional support to succeed, he said.

Research shows that developing DEI competencies improves the quality of health care delivery and science, he said.

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Dr. Capers holds the Rody P. Cox, M.D. Professorship in Internal Medicine.

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

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.

Quinn Capers IV, M.D., Associate Dean for Faculty Diversity

UT-FOCUS provides support to retain physician-scientists

By Jan Jarvis

Five early career physician-researchers are the first awardees to receive support from the UT Southwestern Fund to Retain Clinical Scientists (UT-FOCUS) program.

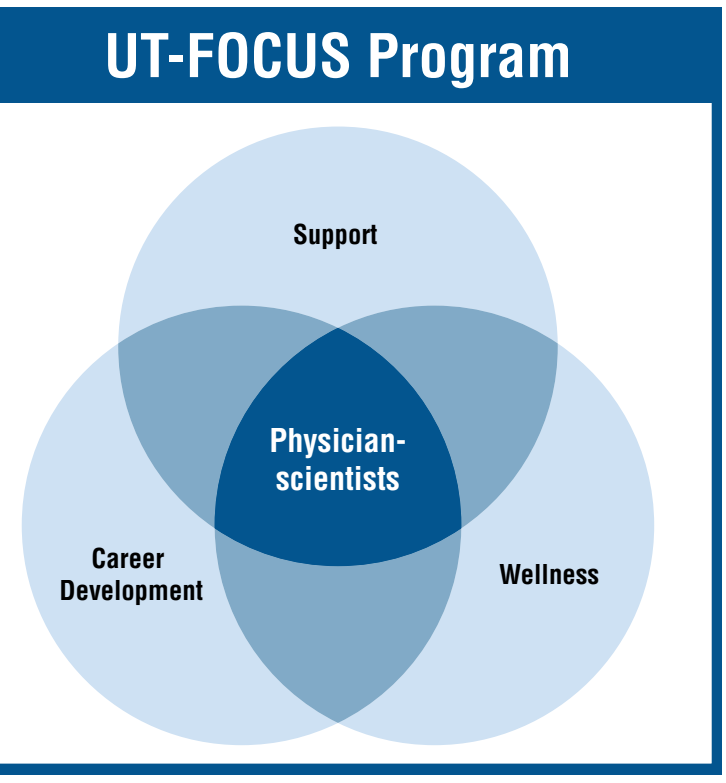
The UT-FOCUS program provides financial, career development, and wellness support to retain early career physician-scientists who need additional assistance due to caregiving responsibilities exacerbated by COVID-19, according to the program's Director, Susan Hedayati, M.D., M.H.S., Professor of Internal Medicine in the Division of Nephrology and Associate Vice Chair for Research.

UT Southwestern is one of only a few institutions nationwide to be selected for the award. The program is funded by a grant from the Doris Duke Charitable Foundation, the American Heart Association, and support from the UT Southwestern Dean's Office.

"I am so delighted to say that this is the first such program funded at our institution, and now we are among only a handful of academic institutions nationwide with this award from the American Heart Association," Dr. Hedayati said. "As both a clinician and researcher, I have observed firsthand the toll that the COVID-19 pandemic has taken on our clinical and research faculty, not only on the hospital COVID front lines, but also at home with additional caregiving responsibilities inflicted by the pandemic. We are so fortunate to be able to somehow contribute some support to faculty who diligently continue our institutional missions of research and patient care."

The first recipients are Emily Adhikari, M.D., Assistant Professor, Obstetrics and Gynecology; Andrew Day, M.D., M.P.H., Assistant Professor, Otolaryngology – Head and Neck Surgery; Jenny Francis, M.D., M.P.H., Associate Professor, Pediatrics; Kara Goss, M.D., Assistant Professor, Internal Medicine and Pediatrics; and Rachel Leon, M.D., Ph.D., Assistant Professor, Pediatrics.

Each awardee gets $50,000 in supplemental flexible funds. Additionally, they receive access to a personal wellness coach for support specific to caregiving responsibilities; networking opportunities and group coaching around work-life balance; and additional resources to support their research programs. The wellness program is organized by Susan Matulevicius, M.D., program co-Director, Associate Professor of Internal Medicine, and Assistant Dean of Faculty Wellness.



The UT-FOCUS program combines support, wellness, and career development resources for UTSW physician-scientists.

Since the program is designed to support academic faculty facing caregiving challenges, funding is flexible and can be used to pay for extra research support, salaries, services, and other needs. Biostatistical services, database development, phlebotomy, and human sample processing and storage are examples of resources and services covered.

To be eligible, program applicants must be physician-scientists with an M.D., M.D./Ph.D., or equivalent degree who are full-time Instructors, Assistant Professors, or Associate Professors at a rank of one year or less with at least 50% effort allocated to research with a high potential to improve human health. The next round of applications opens in June. For more information on eligibility and to apply, go to utsouthwestern.edu/research/programs/ut-focus.

■

Dr. Day is a Eugene P. Frenkel, M.D. Scholar in Clinical Medicine.

Dr. Hedayati holds the Yin Quan-Yuen Distinguished Professorship in Nephrology.

NEWS

MAKER

DeBerardinis receives Paul Marks Prize for contributions to cancer research

Ralph DeBerardinis, M.D., Ph.D., a Professor at UT Southwestern in the Children's Medical Center Research Institute at UT Southwestern (CRI), is one of three researchers awarded the 2021 Memorial Sloan Kettering Paul Marks Prize for Cancer Research. The award recognizes outstanding early and midcareer investigators who have made significant contributions to increase the understanding of cancer or improve the treatment of the disease through basic or clinical research.

Dr. DeBerardinis, who is also a Howard Hughes Medical Institute (HHMI) Investigator and member of the National Academy of Medicine, is known for his discoveries in cancer metabolism and research into genetic conditions in children known as inborn errors of metabolism. At UT Southwestern, he is co-Leader of the Cellular Networks in Cancer Program at the Harold C. Simmons Comprehensive Cancer Center.

Ralph DeBerardinis, M.D., Ph.D.

"I am honored to receive this award and follow in the footsteps of many other amazing cancer researchers," said Dr. DeBerardinis, who is Chief of the Division of Pediatric Genetics and Metabolism at UT Southwestern and an attending physician at Children's Health.

Dr. DeBerardinis' achievements include helping to pioneer a new way to study altered metabolism directly in cancer patients. This has allowed his team to uncover the mechanisms by which tumors use nutrients to produce energy and to identify metabolic pathways that allow tumors to grow and spread. The approach provides researchers with insights about cancer metabolism in the human body, which differs in some ways from the metabolism of the same cells growing in laboratory dishes. This method is now being used to study metabolism in patients with nearly a dozen forms of cancer. The long-term goal of this research is to develop new drugs that destroy cancer cells by targeting metabolic differences between cancer cells and normal cells.

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Dr. DeBerardinis, also a Professor of Pediatrics who holds an appointment in the Eugene McDermott Center for Human Growth and Development, holds the Joel B. Steinberg, M.D. Distinguished Chair in Pediatrics and is a Sowell Family Scholar in Medical Research.

Drug Continued from page 1

approval as a treatment for familial kidney cancer.

"Considered together, these approvals mark UTSW as one of the major sources of breakthrough medicines for previously untreatable diseases. We are indeed a center for biotechnology," said Michael Brown, M.D., Director of the Erik Jonsson Center for Research in Molecular Genetics and Human Disease and joint recipient of the 1985 Nobel Prize in Physiology or Medicine with research partner Joseph Goldstein, M.D., Chair of Molecular Genetics. Dr. Brown helped recruit Dr. Ward to UTSW in 1990.

UT Southwestern receives financial compensation from argenx for the newly approved drug's foundational intellectual property. Dr. Ward also receives compensation related to the licensing of the technology and research funding from the company.

E. Sally Ward, Ph.D., at UT Southwestern in 2004

Efgartigimod is the second first-in-kind drug developed from basic research at UTSW to be approved by the FDA in the past year.

■

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

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

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Hibbs receives Hackerman Award for brain receptor research

By Christen Brownlee

Structural biologist and neuroscientist Ryan Hibbs, Ph.D., has received a 2022 Norman Hackerman Award in Chemical Research. The prize recognizes his work investigating the structure and function of receptors on the surfaces of brain cells and how they interact with drugs, such as nicotine or general anesthetics.

Dr. Hibbs, Associate Professor of Neuroscience and Biophysics and a member of the Peter O'Donnell Jr. Brain Institute, is one of two Hackerman Award winners this year and the ninth UT Southwestern researcher to receive the prestigious prize since its establishment in 2002. The other recipient is Dr. Guihua Yu of UT Austin, selected for his work in nanomaterial science.

The Welch Foundation, one of the nation's oldest and largest sources of private funding for basic research in chemistry, presents the $100,000 award annually to a rising star at a Texas institution. The award is named after the late Norman Hackerman, Ph.D., an internationally known chemist, former President at UT Austin and Rice University, and longtime Chair of the foundation's Scientific Advisory Board.

"I was blown away and extremely grateful to find out that I had won one of this year's Hackerman Awards. I know some of the previous awardees and their work, and it is an honor to be considered a part of that exceptionally high caliber of scientists," Dr. Hibbs said.

Neuroscientist Ryan Hibbs, Ph.D., has been honored for his work on structure and function of receptors in the brain.

"My very first research grant came from The Welch Foundation, and it allowed me to take more risks, hire a postdoctoral fellow, and do more in my lab, but it also gave me assurance that an external committee thought my work was exciting enough to support. The Welch Foundation has been immensely helpful in supporting me financially and giving me confidence to succeed," he added.

The award recognizes Dr. Hibbs' important contributions to better understand synaptic ligand-gated ion channels, types of cell-surface receptors present on neurons. These protein receptors act as locks that are opened by molecular keys, either natural chemicals or synthetic pharmaceuticals. In particular, the Hibbs lab has studied receptors that bind nicotine – the addictive component in tobacco – as well as general anesthetics and the benzodiazepine class of anti-anxiety drugs. He has also studied receptors that bind natural neurotransmitters.

"Ryan Hibbs is clearly one of the rising stars in the structural biology and biophysics of neuronal ionotropic receptors. His recent discoveries solving the structures of the nicotinic acetylcholine receptors and the $GABA_A$ receptor are landmark accomplishments. Perhaps most stunning historically is the structure of the native nicotinic receptor from the fish electric organ, which was the very first neurotransmitter receptor to be described by neuroscience pioneer Jean-Pierre Changeux over 50 years ago," said Joseph Takahashi, Ph.D., Chair of Neuroscience and a Howard Hughes Medical Institute (HHMI) Investigator.

An important first step in understanding the workings of these channels is to visualize them at high magnification and resolution, Dr. Hibbs explained. He added that UT Southwestern's decision to invest in cryo-electron microscopy, or cryo-EM – an imaging system that allows visualization of proteins at the atomic level by freezing them in place – has been key to his lab's success in this field. Dr. Hibbs' wife, Colleen Noviello, Ph.D., is a Senior Research Scientist at UT Southwestern and has collected most of the cryo-EM data for the Hibbs lab.

"Ryan possesses a powerful combination of creativity, fearlessness, technical excellence, and superb scientific taste. These have allowed him and his group to determine some of the most important structures in molecular neuroscience," said Michael Rosen, Ph.D., Chair of Biophysics and an HHMI Investigator. "His work has deepened our understanding of basic functions of the brain and opened the door to improved therapeutics for human conditions spanning mental illness to insomnia."

■

Dr. Hibbs is an Effie Marie Cain Scholar in Medical Research.

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

Dr. Takahashi holds the Loyd B. Sands Distinguished Chair in Neuroscience.

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

Moncrief Continued from page 1

toma Mouse Program to find better treatments and to improve survival rates for patients with glioblastoma.

"Our family is committed to making a significant positive impact in the world around us, and we are confident our gift to UT Southwestern can make a profound difference in the way glioblastoma is treated in the future," Tex Moncrief said at the time.

W.A. "Tex" Moncrief Jr. was born on March 27, 1920, the son of William Alvin and Elizabeth Bright Moncrief. He graduated from the Culver Military Academy in 1937 and from UT Austin with a Bachelor of Science degree in petroleum engineering in 1942. After working as an engineer in the East Texas oil fields, he received a commission in the U.S. Naval Reserve and was trained at Harvard as a communications officer before serving in the Pacific. After the war, he returned to Fort Worth and went into the oil business with his father. Tex Moncrief made huge discoveries of natural gas in Wyoming, as well as major discoveries on the Gulf Coast, in Texas and Louisiana.

In 1983, he was honored as a Distinguished Engineering Graduate by UT Austin, to which he provided support ranging from athletics to computer labs. In 1987, he was appointed to a six-year term on the Board of Regents of the UT System by then-Gov. William P. Clements Jr., for whom UT Southwestern's hospital is named. He was named to the Texas Philanthropy Hall of Fame in 2001 and was honored as a Distinguished Alumnus by the University of Texas Exes in 2008.

"Tex Moncrief leaves an indelible imprint on North Texas through his generosity of spirit," Dr. Podolsky said.

■

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.

Moncrief Cancer Institute


Daniel K. Podolsky, M.D., President of UT Southwestern, left, visits with W.A. "Tex" Moncrief Jr. at the opening in 2015 of the Monty and Tex Moncrief Medical Center at Fort Worth.

UTSW expands primary care at Moncrief Medical Center in Fort Worth

Monty and Tex Moncrief Medical Center at Fort Worth

By Patrick Wascovich

To meet growing demand for primary and preventive health care in Fort Worth, Tarrant County, and the surrounding region, UT Southwestern has launched a primary care clinic in the UT Southwestern Monty and Tex Moncrief Medical Center at Fort Worth.

The new clinic – located on the third floor – is one of a dozen clinics housed at the Monty and Tex Moncrief Medical Center, a multispecialty outpatient facility designed to meet the medical needs of area residents with services ranging from neurology to urology. The clinic offers well visits and physicals; pediatric and adolescent care; care for common and chronic illnesses, including diabetes, high blood pressure, high cholesterol, and arthritis; women's health care; preventive health services; on-site labs and pharmacy; and imaging services at the neighboring Moncrief Cancer Institute.

The primary care physicians will have access to referrals to UTSW specialists in Fort Worth and across the Health System. Eleven UT Southwestern specialties are currently housed at the Monty and Tex Moncrief Medical Center. In addition, UT Southwestern offers more than a dozen cancer care programs along with prevention screenings and other services through the Moncrief Cancer Institute, which is part of the Harold C. Simmons Comprehensive Cancer Center.

"Our family physicians at the new primary care clinic will serve patients from the western part of the metroplex, providing comprehensive care for chronic medical conditions, acute needs, and preventive health," said David Schneider, M.D., Professor and Chair of Family and Community Medicine.

Opened in 2017 and located in the heart of Fort Worth's burgeoning medical district, the 106,000-square-foot Monty and Tex Moncrief Medical Center at Fort Worth was designed and built to meet the medical needs of the area.

Primary care appointments are available by calling 817-882-2590. The UT Southwestern Monty and Tex Moncrief Medical Center at Fort Worth is located at 600 S. Main St., Third Floor, Suite 500, Fort Worth, Texas 76104.

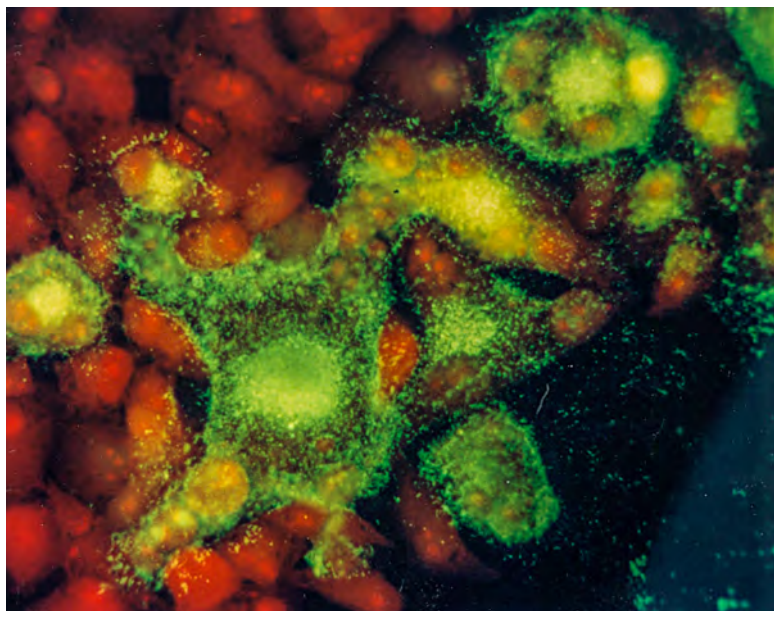
■

Dr. Schneider holds the Perry E. Gross, M.D. Distinguished Chair in Family Medicine.

FOCUS: FIGHTING VIRAL INFECTIONS

UTSW researchers take new approach to fight viral infections

Inhibiting proteins in cellular pathway stems replication of childhood pathogen RSV and coronaviruses



An immunofluorescence micrograph of cells infected by RSV (RSV is green; cells are red).

By Christen Brownlee

A new approach that targets the cellular machinery that viruses need to reproduce – rather than the virus itself – appears to stem replication of a common childhood pathogen known as respiratory syncytial virus (RSV), UT Southwestern researchers report. The findings, published in *Scientific Reports*, could offer a novel strategy to fight this virus and others, including SARS-CoV-2.

"RSV is far and away the major respiratory pathogen in infants and children," said study leader Jeffrey Kahn, M.D., Ph.D., Professor of Pediatrics and Microbiology, Chief of the Division of Pediatric Infectious Disease at UT Southwestern, and Director of Infectious Diseases and Medical Director of Research at Children's Medical Center Dallas. "The approach we've discovered turns the tables on this virus and potentially others in a whole new way."

RSV is a leading cause of pediatric deaths worldwide, killing an estimated 160,000 children each year, according to the National Institute of Allergy and Infectious Diseases. Despite the fact that 65 years have passed since its discovery, there are still no effective treatments or a vaccine. Although some promising antiviral drugs have been explored that target components of this and other viruses, Dr. Kahn explained, viruses inevitably evolve to develop resistance against these compounds.

Taking a completely new approach, Dr. Kahn and his colleagues used genetic and pharmacological inhibition to search for vulnerable cellular pathways that RSV hijacks to replicate itself. Their experiments showed that inhibiting various components of a protein network known as the mechanistic target of rapamycin (mTOR) pathway prevented RSV from replicating in human cells. They also showed that this same strategy inhibited OC43, a human coronavirus in the same viral subfamily as SARS-CoV-2.

Because some of the drugs shown to inhibit mTOR components and block viral replication in this study are already approved by the Food and Drug Administration, they could offer hope for quick approval as antivirals against RSV, SARS-CoV-2, and other viral infections if further research confirms their utility, Dr. Kahn said.

■

Dr. Kahn holds the Sarah M. and Charles E. Seay Chair in Pediatric Infectious Diseases.

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

Blocking TLR2 could calm COVID-19's cytokine storm

By Christen Brownlee

Although COVID-19 is known for its respiratory symptoms, people with the disease sometimes launch an overwhelming immune response, called the cytokine storm, which can also be deadly. UT Southwestern scientists are closing in on the mechanism for this hyperinflammatory response.

In an *eLife* study, Hasan Zaki, Ph.D., Assistant Professor of Pathology, and his colleagues explored a cell surface protein called toll-like receptor 2 (TLR2) and its relationship to the flood of inflammatory molecules, or cytokines, released during COVID-19 infection. Shahanshah Khan, Ph.D., a postdoctoral fellow in the Zaki lab, was lead author.

"The cytokine storm is a major cause of cell death and organ damage in SARS-CoV-2-infected patients," Dr. Zaki explained. "Understanding how the hyperinflammatory response is activated during SARS-CoV-2 infection could ultimately help define new strategies for treating COVID-19."

To better understand COVID-19's cytokine storm, Dr. Zaki and his colleagues exposed human and mouse immune cells to each of the four major structural proteins that make up SARS-CoV-2: the spike protein, which allows the virus to infect and enter cells; the membrane protein, which is essential for viral replication; the envelope protein, which is important for assembly, release, and virulence; and the nucleocapsid protein, which packages the viral genome. Of these, only the spike protein caused these immune cells to produce inflammatory cytokines.

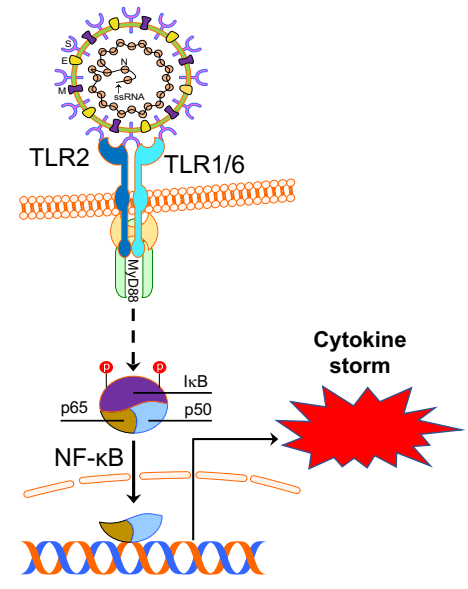
Hasan Zaki, Ph.D.

They observed that TLR2, working with one of two other proteins – TLR1 or TLR6 – acts as the sensor on cell exteriors that responds to the spike protein. Digging deeper, they found that immune and lung epithelial cells isolated from animals genetically altered to lack TLR2 didn't produce inflammatory cytokines when exposed to the spike protein. The same was true with cells exposed to chemical agents that blocked TLR2 or had undergone a genetic editing technique to disable this protein. Recognition of the spike protein by TLR2 leads to the activation of the cell-signaling molecules, resulting in the activation of the transcription factor NF-κB, which is responsible for the expression of cytokines and other inflammatory molecules constituting the cytokine storm.

Dr. Zaki noted that if further research confirms this finding, COVID-19 therapies may eventually include drugs that block TLR2 to prevent or treat the cytokine storm.

"Cytokines play important roles in the immune system, but in excess, they can be very detrimental," Dr. Zaki said. "By carefully selecting patients for treatments that suppress TLR2 function, we may be able to significantly improve COVID-19 outcomes and reduce death."

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



Researchers found that the SARS-CoV-2 spike protein is recognized by TLR2, in association with TLR1 or TLR6, leading to activation of a transcription factor that induces inflammatory molecules.

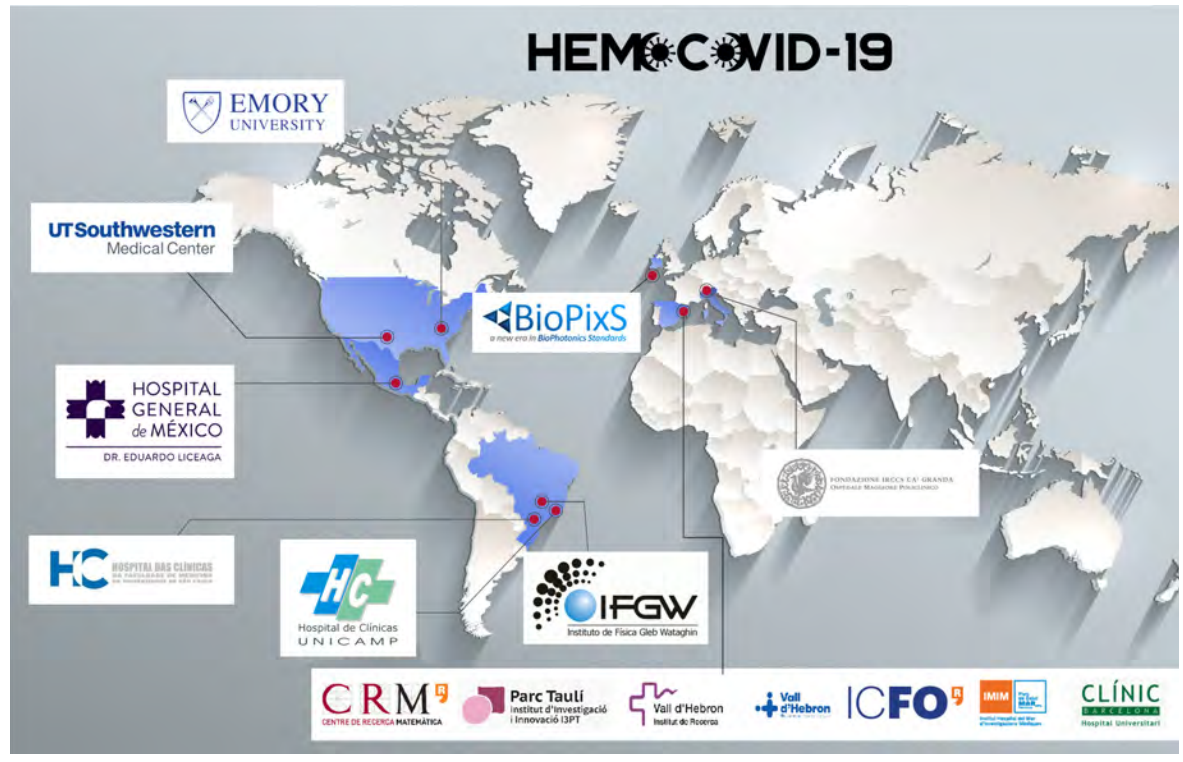
Study indicates severe COVID-19 impairs microvascular function

By Christen Brownlee

COVID-19 impairs the function of the body's microvascular system with an intensity that corresponds to the severity of disease, suggests a new study by an international consortium that includes Southwestern.

Developing a better understanding of COVID-19's impact on individual patients' microcirculation could lead to personalized therapies as well as better predictions of patient outcomes, explained co-author David Busch, Ph.D., Assistant Professor of Anesthesiology and Pain Management and Neurology at UT Southwestern. The findings, reported in *Critical Care*, may explain some clinical features of severe COVID-19 and eventually help identify new ways to monitor the course of an infection.

"Our findings reinforce the idea of a systemic microvascular involvement in severe COVID-19 patients," said Dr. Busch, a member of the international HEMOCOVID-19 consortium led by Turgut Durduran, Ph.D., Professor and Medical Optics Group Leader at ICFO. This group brings together researchers from the U.S., Mexico, Spain, Ireland, Italy, and Brazil to study alterations in tiny blood vessels in COVID-19 patients and the associated consequences for patient outcomes. The Busch lab develops optical technologies for noninvasive and minimally invasive bedside assessment of microvascular blood flow and oxygen saturation, allowing continuous assessment of oxygen metabolism during critical care.



UT Southwestern investigators are members of the HEMOCOVID-19 consortium, an international effort testing biophotonics tools in intensive care units to help manage severely ill COVID-19 patients. Credit: HEMOCOVID-19 consortium

Other UTSW faculty members participating in this consortium include Christopher Choi, M.D., Siddharth Dave, M.D., and Peiman Lahsaei, M.D., all Assistant Professors of Anesthesiology and Pain Management; Sreekanth Cheruku, M.D., Associate Professor of Anesthesiology and Pain Management; and DaiWai Olson, Ph.D., RN, Distinguished Teaching Professor of Neurology and Neurological Surgery.

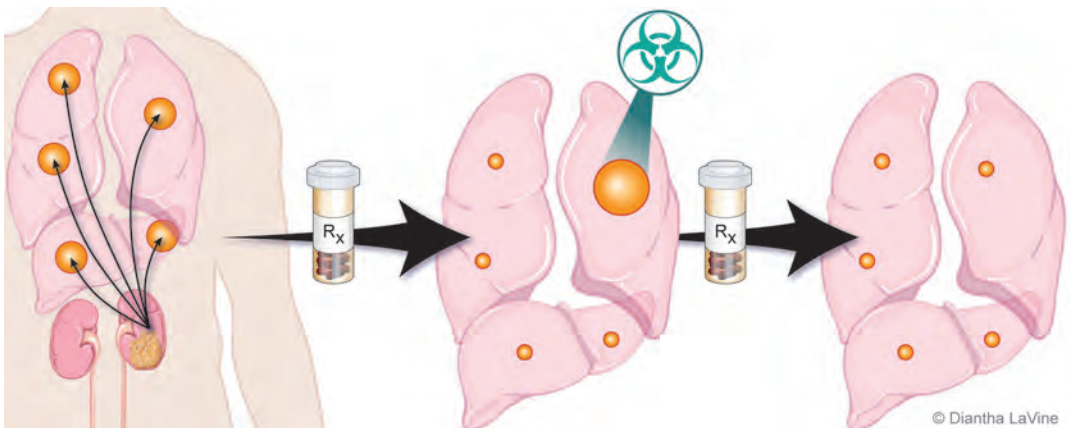
Although COVID-19 is often considered primarily a respiratory syndrome, several studies have shown it also affects the circulatory system. However, its effect on microcirculation – the movement of blood in the body's smallest blood vessels that supplies the bulk of oxygen and nutrients to organs and tissues – hasn't been well characterized, explained Dr. Busch, a Fulbright and Whitaker Scholar.

Using near-infrared spectroscopy, the researchers measured local oxygen saturation and hemoglobin concentration in tissues and blood before and after restricting blood flow. The COVID-19 patients had lower oxygen metabolism saturation and microvascular reactivity after blood flow restriction that corresponded to the severity of their acute respiratory distress syndrome, a key feature of COVID-19 infection. These findings and those from other studies suggest that COVID-19 may damage the endothelium, the lining of blood vessels that controls their dilation and constriction.

Early results from the HEMOCOVID-19 project led to support from both the National Institutes of Health (NIBIB R21EB031261) and EU (Vasocovid) to develop improved instrumentation and analysis.

This study, one of more than 250 COVID-related studies at UTSW, was funded by grants from the CELLEX Foundation of Barcelona, Spain; Mir-Puig Foundation; Barcelona City Hall; State Research Agency (PHOTOMETABO, PID2019- 06481RB-C31/10.13039/501100011033); the Severo Ochoa Program for Centers of Excellence in R&D (CEX2019-000910-S); the "La Caixa" Foundation (LlumMedBcn); Government of Catalonia (CERCA, AGAUR-2017-SGR-1380, RIS3CAT-001-P-001682 CECH); and European Commission Horizon 2020 (FEDER, 688303/LUCA, 101016087/VASCOVID, 87114/LASERLAB-EUROPE V). The study authors also acknowledge collaboration and an instrument loan from Artinis (Netherlands).

Clinical trials show stereotactic radiation slows kidney cancer



As illustrated here, the Kidney Cancer Program study showed that stereotactic ablative radiation (SAbR) controlled isolated progressive metastasis in a kidney cancer clinical trial.

Raquibul Hannan, M.D., Ph.D.

By Michelle Parish

A study from the Kidney Cancer Program (KCP) at UT Southwestern's Harold C. Simmons Comprehensive Cancer Center shows that highly focused radiation to isolated metastases that progress, despite drug therapy, can prolong treatment in kidney cancer patients, saving the few other drugs for treating kidney cancer for future use. This study and a recently published Canadian study support an expanding role for radiation therapy in renal cancer.

Metastatic kidney cancer is largely incurable. Despite recent advances, most patients eventually succumb to the disease. Resistance develops to each line of therapy, which is followed by the next with progressively lower returns, and some patients run out of drug treatment options.

With one exception, little is known about how drug resistance arises. There is equally little understanding about patterns of progression. For example, while progression occurs at multiple sites in some patients, in others only a few growing sites are observed.

"The current standard of care for metastatic progression is to change systemic (drug) therapy," said lead author Raquibul Hannan, M.D., Ph.D., Associate Professor of Radiation Oncology and KCP Radiation Oncology co-Leader, "but there's no guarantee that the next line of therapy will be effective."

The KCP study found that highly focused stereotactic ablative radiation (SAbR) was an effective strategy for controlling metastatic disease when it progressed at just a few sites, known as oligoprogression. The phase two clinical trial showed that SAbR extended ongoing systemic therapy by a median of 11.1 months.

The Canadian study, also a phase two trial that involved multiple institutions across the country, showed similar results, with SAbR extending systemic therapy by 12.6 months.

Both studies deployed sequential SAbR over time while the disease remained oligoprogressive, which is a new approach, and both showed that SAbR successfully controlled radiated lesions (>90% local control rates). Additionally, the KCP study showed that SAbR did not undermine patients' quality of life. These findings build on a pioneering report from KCP investigators published in 2013 and retrospective studies by KCP and other investigators showing promise of SAbR for oligoprogression.

Localized therapies such as SAbR, which are generally associated with minimal toxicity, are an attractive option to complement systemic therapies that are otherwise working and well tolerated. For those who respond to systemic therapy, the development of a few "rogue" drug-resistant metastases may not demand a change of treatment. Eradicating progressing sites with high-dose, pinpoint radiation may extend the window when drugs can provide effective cancer control.

"While both clinical trials involved a small number of patients, the concordant positive results suggest that the approach has merit. These studies support larger trials that may introduce SAbR in routine patient care," said co-corresponding author James Brugarolas, M.D., Ph.D., Professor of Internal Medicine, Division of Hematology and Oncology, and Director of the KCP.

■

Dr. Brugarolas holds the Sherry Wigley Crow Cancer Research Endowed Chair in Honor of Robert Lewis Kirby, M.D.

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

UTSW's ECMO program achieves Platinum status

By Catherine Gara

UT Southwestern has provided extracorporeal membrane oxygenation (ECMO) to patients in need since 2012, supporting heart and lung transplant teams that rank among the top 25 in volume nationally.

So during the pandemic, to treat patients whose lungs were failing due to COVID-19, UTSW had the infrastructure in place to serve the needs of the Dallas community. In recognition of these achievements, and following a review of the program's systems of care by the Extracorporeal Life Support Organization (ELSO), UTSW was named a Platinum Center of Excellence.

Under Amy Hackmann, M.D., Surgical Director of the ECMO program, protocols for patient care have been refined to improve consistency. Each patient has a bedside nurse who has received classroom and hands-on training for managing the ECMO machine. Patients are also assigned an ECMO nurse specialist who has additional training, especially for responding to emergencies.

"Stellar nursing involvement in patient care is a big part of why we received ELSO's Platinum Center of Excellence recognition this year," said Dr. Hackmann, Associate Professor of Cardiovascular and Thoracic Surgery.

Other members of the team include perfusionists, intensivists, hematologists, infectious diseases specialists, gastroenterologists, pulmonologists, and cardiologists, as appropriate, said Fernando Torres, M.D., Professor of Internal Medicine, and Medical Director of Lung Transplantation at UT Southwestern.

ECMO program team members celebrate recognition as a Platinum Center of Excellence by the Extracorporeal Life Support Organization.

Jennifer Thibodeau, M.D., Medical Director of UTSW's Heart Failure and ECMO programs and Associate Professor of Internal Medicine, added, "We have also built a formal cardiogenic shock team to expedite assessment of patients with cardiogenic shock, evaluate their need for temporary mechanical support, and optimize their care in order to improve outcomes."

Already, the team's survival rates are better than ELSO benchmarks for both respiratory and cardiac support. The most important hallmarks of a platinum ECMO program are the patients who wouldn't be alive without it, such as one former patient in his 60s. According to Dr. Torres, COVID-19 had destroyed this man's lungs; he couldn't oxygenate, and he had major bleeding in his chest. ECMO was his only hope. It took a few months on ECMO, but the team was eventually able to convert him to mechanical ventilation. Then, he went through several months of rehabilitation until he was strong enough to undergo a lung transplant. Today, Dr. Torres said, the man is doing well.

Amy Hackmann, M.D., is Surgical Director of the ECMO program.

Bradley Lega, M.D.

Memories Continued from page 1

memories and hallucinations or delusions. The neurons identified by Dr. Lega are an important piece of the puzzle for why this happens, said Carol Tamminga, M.D., Chair of Psychiatry and a national expert on schizophrenia.

"Hallucinations and delusions in people with a psychotic illness are actual memories, processed through neural memory systems like 'normal' memories, even though they are corrupted. It would be important to understand how to use this 'phase offset' mechanism to modify these corrupted memories," Dr. Tamminga said.

An opportunity to learn more about human memory that arose from surgeries in which electrodes that were implanted in epilepsy patients' brains to map their seizures could also be used to identify neurons involved in memory. In this study, 27 epilepsy patients who had the electrodes implanted at UT Southwestern and a Pennsylvania hospital participated in memory tasks to generate data for brain research.

The data analysis does not conclusively prove, but adds new credibility to an important memory model called Separate Phases at Encoding And Retrieval (SPEAR) that scientists developed from rodent studies.

"It's never been nailed down. It's one thing to have a model; it is another thing to show evidence that this is what's happening in humans," Dr. Lega said.

> "This is some of the clearest evidence to date showing us how the human brain works in terms of remembering old memories versus forming new memories."
>
> – Bradley Lega, M.D.

The SPEAR model, which predicts the "phase offset" reported in the study, was developed to explain how the brain can keep track of new-versus-old experiences when engaged in memory retrieval. Previously, the only evidence in support of SPEAR came from rodent models.

This study was supported by National Institutes of Health grants R01NS125250 and R01NS106611.

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Dr. Tamminga holds the Stanton Sharp Distinguished Chair in Psychiatry.

Students honored for community service at MLK event

By Carol Marie Cropper

Three UT Southwestern students were honored for their community service at this year's Martin Luther King Jr. Commemorative Celebration, held virtually Jan. 19. The annual campus event honors the legacy of Dr. King, a champion for civil rights and community service.

Second-year medical student Dalia Mitchell won the top award, which includes a $5,000 scholarship. Receiving $500 each as runners-up were third-year medical student Robert Treviño Jr. and third-year neuroscience graduate student Daniela Barbosa.

Shawna Nesbitt, M.D., Associate Dean in the Office of Student Diversity and Inclusion, and Daniel K. Podolsky, M.D., President of UT Southwestern, provided opening and congratulatory remarks to this year's scholarship recipients.

First-year medical student Banahene Glover performed a beautiful rendition of "Lift Every Voice and Sing" on the keyboard.

Keynote speaker at the event was Keith C. Norris, M.D., Ph.D., Professor of Medicine at UCLA's Division of General Internal Medicine and Health Services Research, and Executive Vice Chair for Equity, Diversity, and Inclusion in UCLA's Department of Medicine. His talk, "Race, Race Consciousness, and Health Equity," outlined the goals of valuing all individuals and populations equally; recognizing and rectifying historical injustice; and providing resources according to need.

The event was hosted by the Office of Student Diversity and Inclusion and the Office of Institutional Equity and Access.

Scholarship Winner
Dalia Mitchell
Second-year medical student and Master of Public Health candidate

Dalia Mitchell's commitment to increasing health care equity and breaking down barriers that prevent families from receiving the care they need began early in life. While still in elementary school, the London native who was raised in Plano, Texas, volunteered to help children with special needs. Then, as an undergraduate at the University of Rochester, she provided art therapy to children with Down syndrome. Now at UT Southwestern, Ms. Mitchell has worked with the Dallas County Juvenile Department to launch a program called Therapeutic Arts Relieving Adverse Childhood Experiences (TRACE) to train medical and health professions students in the use of art to mentor children in juvenile detention – children who have often experienced trauma but might lack access to art activities and their therapeutic benefits. Ms. Mitchell has also volunteered to help homeless patients and worked at Agape Multidisciplinary Clinic, providing pediatric and family medicine services. Ultimately, Ms. Mitchell said, she hopes to treat children as a pediatric surgeon while continuing her efforts to promote health equity and make specialized care more accessible to children and their families.

Finalist
Daniela Barbosa
Third-year graduate student

Daniela Barbosa, from Brownsville, Texas, benefited from a full scholarship to a rigorous private middle school serving bright South Texas children with limited financial means. Later, a college professor whose lab she worked in took her under her wing, encouraging Ms. Barbosa to become a researcher. She has not forgotten the doors and dreams those experiences opened up for her. Giving back by mentoring students from disadvantaged backgrounds has become a life mission. Ms. Barbosa has mentored students from her former middle school, Guadalupe Regional Middle School, and appeared on panels at the hometown university she attended, UT Rio Grande Valley, describing what it is like to be a Ph.D. candidate. Now in North Texas, Ms. Barbosa goes to an area high school every month to give freshmen insights into career possibilities and, as part of the ScholarShot program, mentors a Hispanic UT Austin student considering medical school.

Finalist
Robert Treviño Jr.
Third-year medical student

A self-described "military brat" from San Antonio, Texas, Robert Treviño Jr. took health care for granted – something guaranteed. Over the years, as he visited relatives in the small Texas town where his Hispanic grandparents lived, he came to realize that wasn't the case. Mr. Treviño's passion to provide care to those he saw struggling without it led him to the decision to become a doctor. It's also the reason he volunteered as president of the medical student-run Monday Clinic that provides free care to uninsured patients in Dallas, and why he came up with the idea for an online resource called Successful Service to provide information to those who want to open their own free clinic. Improving access to educational opportunities is another mission for Mr. Treviño. He speaks to elementary students in underprivileged areas of Dallas, and two years ago started a podcast called "¡Con Ganas!," in which he interviews medical professionals from underrepresented minority groups. Mr. Treviño hopes to promote health equity in underserved populations as a physician practicing at an academic institution.

■

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: Read each student's essay and learn, in their own words, what inspires them on *Center Times Plus* at **utsouthwestern.edu/ctplus**.

NEWS

MAKERS

McBrayer gets Sontag Foundation Distinguished Scientist Award

Sam McBrayer, Ph.D., an Assistant Professor of Pediatrics in the Children's Medical Center Research Institute at UT Southwestern (CRI), is one of six winners of the 2021 Distinguished Scientist Award, presented by the Sontag Foundation. The award is given annually to extraordinary scientists with the potential to make a significant impact in the field of brain cancer research.

"The generous support of the Sontag Foundation will accelerate our research and allow us to pursue innovative, high-yield approaches to studying how altered metabolism promotes brain cancer development and progression," said Dr. McBrayer, who is also a member of the Harold C. Simmons Comprehensive Cancer Center.

Sam McBrayer, Ph.D.

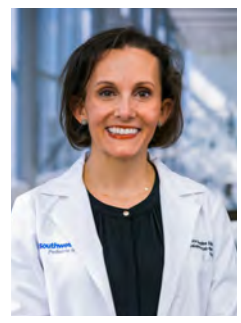
The McBrayer laboratory focuses on understanding how changes in metabolism control cell fate and cell function in the setting of brain cancer, particularly for gliomas. A significant portion of gliomas are driven and initiated by mutations that affect *IDH* genes. These genes encode metabolic enzymes and cause profound metabolic reprogramming when acquired in brain tumor cells. One of the major roadblocks to understanding how changes in metabolism influence cancer risk is the lack of genetically engineered mouse models that are driven by alterations in metabolism. To address this roadblock, Dr. Brayer's laboratory recently developed a new mouse model of brain cancer that is driven by an *IDH* mutation. This model creates new opportunities to dissect the molecular changes that link altered metabolism with brain tumor formation.

"We're hoping this new model will help us address a critical unmet need for new brain tumor therapies," said Dr. McBrayer, a Cancer Prevention and Research Institute of Texas Scholar and an Abeloff V Foundation Scholar. "Essentially, standard of care for brain tumor patients hasn't changed since 2005. The new insights that we're gaining into the altered metabolic state of these brain tumors will point the way to new therapeutic targets and ultimately allow us to develop more effective therapies. This work would not be possible without the Sontag Foundation's generous support."

Dr. McBrayer and the other winners received $600,000 each to support their research and joined past awardees at a scientific summit in February 2022 hosted by the Sontag Foundation.

Bordes Edgar honored with diversity award for mentorship

Veronica Bordes Edgar, Ph.D., has been awarded the 2021 Tony Wong Diversity Award for Outstanding Work Related to Diversity as a Mentor, given to a National Academy of Neuropsychology member who has made a significant contribution to the field of multicultural neuropsychology.



Veronica Bordes Edgar, Ph.D.

"I am very humbled by this honor. Several of my former students nominated me for this award. It was touching to hear their words of how I impacted their lives, because each mentee also leaves an impact on my life as well," said Dr. Bordes Edgar, Associate Professor of Psychiatry and Pediatrics.

She said her own experience of being nurtured by outstanding mentors proved how valuable such encouragement is to achieve success.

"I am here because I was fortunate enough to have mentors along my journey who pushed me beyond what I thought I was capable of. It allowed me to break barriers and confront challenges that came my way. I hope that my mentoring of future psychologists and physicians will encourage them to do the same," Dr. Bordes Edgar said.

She first discovered a passion for mentoring in graduate school. Dr. Bordes Edgar's own research revealed the powerful impact that mentoring had on Latinx college students' drive to graduate. She also studied the mentoring experiences of female graduate students and identified key variables that they found impactful – findings that have helped in her own mentoring efforts.

"Now I am fortunate to get to mentor trainees at multiple levels, including undergraduate students, graduate students, fellows in psychology and neuropsychology, and medical residents. I also get to mentor junior faculty here at UT Southwestern and nationally," said Dr. Bordes Edgar, also President of the Hispanic Neuropsychological Society. "In addition, I work with the Women in Medicine group here at UTSW, but also I work with men and with mentees who are struggling through issues of racism and diversity."

Black History Month Celebration spotlights wellness, resiliency

Keynote speaker Altha Stewart, M.D.

UT Southwestern's annual Black History Month Celebration highlighted the importance of wellness and resiliency for health care providers. Keynote speaker Altha Stewart, M.D., Senior Associate Dean for Community Health Engagement at the University of Tennessee Health Science Center, talked about "Burnout in African Americans: From Measurement and Mitigation to Prevention and Thriving," aligning with the 2022 national theme for Black History Month, "Black Health and Wellness."

Due to an upswing in COVID-19 cases, the Feb. 24 event hosted by the Office of Institutional Equity & Access and the African-American Employee Business Resource Group (AAE-BRG) was held virtually this year.

Dr. Stewart, Associate Professor of Psychiatry and Director of the Division of Public and Community Psychiatry and the Center for Health in Justice Involved Youth at UTHSC, is currently a member of the Governor's Juvenile Justice Reform Implementation Council. From 2018-2019, she served as the American Psychiatric Association's first African American President in its history. Dr. Stewart received her medical degree from what is now the Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, and completed her residency at Drexel University College of Medicine, also in Philadelphia.

"We're learning more and more each day about the responsibility for addressing burnout in health care workers, certainly no time than ever before, since the pandemic. So it's important that we understand that our systems of care … play a contributing role in the evolution of burnout in individuals," Dr. Stewart said. "No matter what your role in the organization, the shared responsibility for how burnout develops and what we can do to address it resides not only in the individual, but also in the institution."

"We've got to modify the learning environment," she added. "We've got to prioritize wellness and self-care over memorization and 'only tests matter.' And we've got to increase our understanding of the contributing factors to this rising rate of resident and medical student suicide."

Following Dr. Stewart's presentation, Jennifer Okere, Ph.D., UTSW Assistant Professor of Psychiatry, spoke about work of the Dallas-Fort Worth Association of Black Psychologists. "Our mission is to support the mental health needs of the African American community in the DFW area, through a combination of education, advocacy, and volunteer work," said Dr. Okere, a founding member of the group.

The event also featured cultural performances by UTSW's own Brittanny Anderson from Human Resources, remarks by Marc Nivet, Ed.D, M.B.A., UTSW Executive Vice President for Institutional Advancement, and a presentation on resources available within the UTSW community to support mental and physical health.

Biochemistry Post-Baccalaureate Program aims to inspire minority college grads

By Jan Jarvis

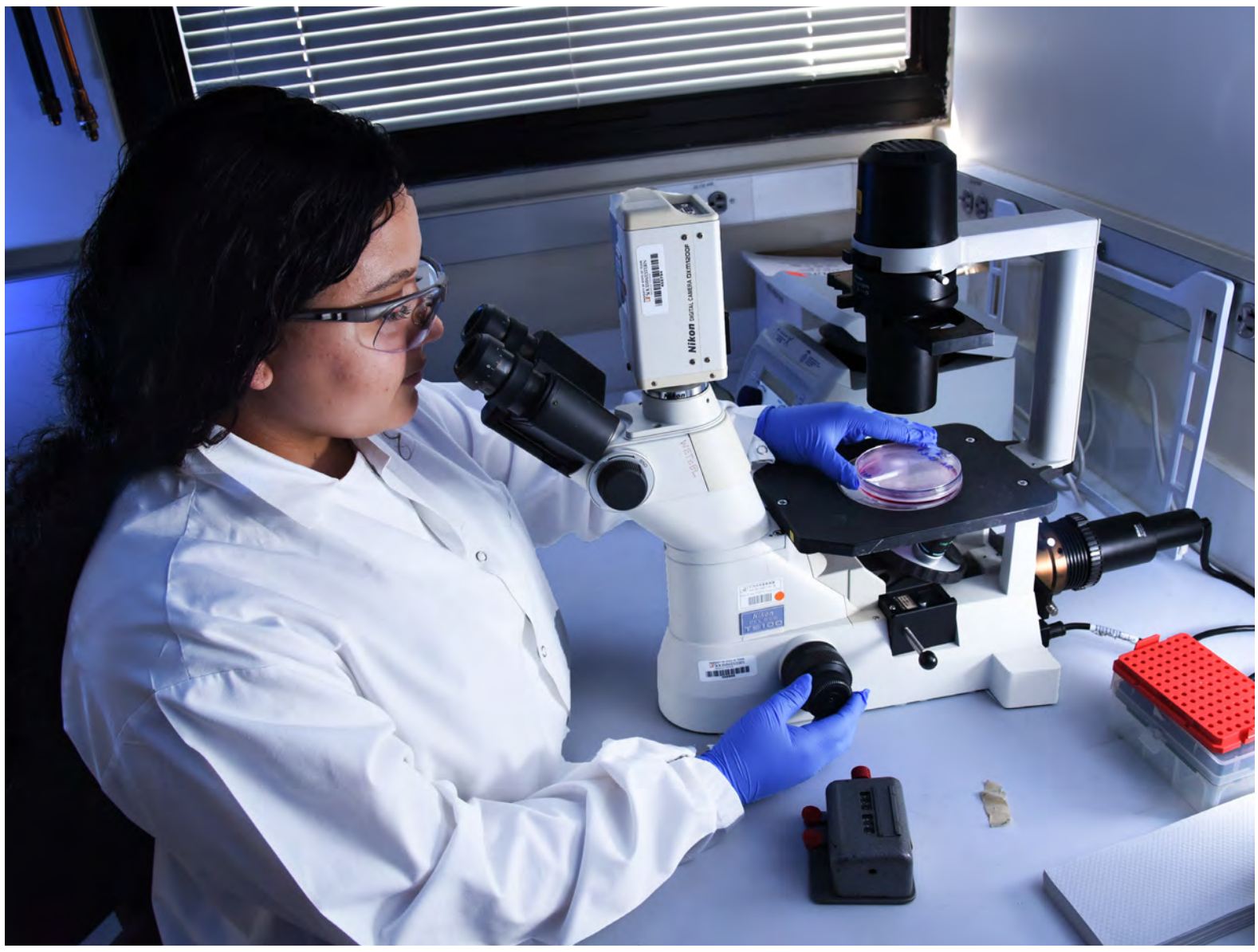
Alyza Roman knew becoming a scientist would be challenging, especially as the first member of her family to attend college.

Although she had worked in a lab as an undergraduate, Ms. Roman wanted more experience. The Department of Biochemistry's Post-Baccalaureate program at UT Southwestern offered the exact type of research exposure she needed. Launched last year, the program offers biochemistry and chemistry laboratory experience to recent college graduates from underrepresented populations.

"Conducting research full time for one to two years would give me a taste of what my future in this career would look like," said Ms. Roman, one of the first participants in the program.

The Biochemistry Department's Post-Baccalaureate Program gives students from underrepresented minority groups support to pursue a career in science, said Uttam Tambar, Ph.D., Professor of Biochemistry, Director of Diversity for Biochemistry, and Chair of the Organic Chemistry Ph.D. program in the UT Southwestern Graduate School of Biomedical Sciences. The goal is to increase diversity among students and faculty involved in biochemistry and chemistry research.

"The number of students from underrepresented populations who earn a bachelor's degree is small, but the number who seek a Ph.D. is even smaller," Dr. Tambar said. "We hope to increase the number of Ph.D.s who are from underrepresented populations."



Alyza Roman examines a sample under the microscope.

Improving diversity in science

The Diversity and Inclusion Committee in the Biochemistry Department created the program to reach out to undergraduate students who showed an interest in becoming scientists. Participants, who receive a $35,000 annual stipend, get a taste for life as a graduate student, Dr. Tambar said.

The program is co-led by Robyn Cooper, Administrative Associate in the Biochemistry Department, and Arnaldo Díaz Vázquez, Ph.D., Assistant Dean for Diversity in the Graduate School. The Department received a contribution from the Chilton Foundation to fund two post-baccalaureate scholars a year for the next two years. The first A.L. Chilton Foundation Post-Baccalaureate Scholars are Grant Showell and Ms. Roman.

The program is a key component to promote the inclusion of a more diverse group of young scientists in the Department, said Margaret Phillips, Ph.D., Chair of Biochemistry.

"We are really excited about the potential of this program to provide mentorship and training to support the career aspirations of underrepresented minority students interested in scientific careers while also providing our faculty and institution an opportunity to attract these bright and motivated students to our campus," she said. "We are grateful to the Chilton Foundation for their generous support, which has been instrumental in helping us get the program off the ground."

In August, three recent college graduates – including Andres Delarosa, who received funding through UT Southwestern – became the first to join the two-year program. They were selected from a pool of exceptional post-baccalaureate applicants from around the country. The database was made available to UT Southwestern after it was officially designated as an American Chemical Society Bridge Partner, which highlights the University's commitment to prepare students from underrepresented minority groups for graduate school.

Biochemistry Post-Baccalaureate Program participants include (from left) Andres Delarosa, Ms. Roman, and Grant Showell.

"The program gives young scientists an opportunity to do research and find out what area of science they are passionate about," Dr. Tambar said. "Seventy-five percent of what they do while they are here is research. Long term, these students will end up being successful scientists, and they'll be able to say UT Southwestern played an important role in making that happen."

Developing a passion for science

Mr. Delarosa, who graduated from the University of California, San Diego, said he was attracted to UT Southwestern's program because it offered an opportunity to focus on research.

"I applied to the program because I wanted to gain more experience in laboratory research and all that entails, like lab techniques, literature research, and exposure to the kind of work one would do in pursuing a Ph.D. and running a research-driven project," he said.

Since starting the program, Mr. Delarosa is convinced he made the right choice.

"It has made me more certain that obtaining a Ph.D. is something that I want," he said. "The program allows you to do research on something otherwise unknown and to hopefully contribute a small bit of knowledge to the scientific community."

Ms. Roman said the program has strengthened her commitment to a career in research as well.

"I hope to conduct research in many areas, including microbiology and neurobiology, combating diseases and disorders disproportionately affecting underserved populations," she said. "Programs that support underrepresented minority students, like me, are a critical step in addressing health disparities."

The program encourages participants to pay it forward – something Ms. Roman plans to do. One of her goals is to introduce science as a career to underserved communities.

"In the future, I wish to run my own lab at one of the top research institutions in the nation, supporting and teaching underrepresented minority students, as many have done for me," she said. "I wish to convince underrepresented minorities who suffer from imposter syndrome to believe in themselves. Ethnicity is not a measure of intelligence, but rather hard work and perseverance."

■

Dr. Phillips holds The Sam G. Winstead and F. Andrew Bell Distinguished Chair in Biochemistry.

Dr. Tambar holds the Bonnie Bell Harding Professorship in Biochemistry and is a W.W. Caruth, Jr. Scholar in Biomedical Research.

Mr. Showell transfers a solution with a pipette.

Mr. Delarosa is shown here using a rotary evaporator.

Broader post-baccalaureate effort to launch this summer

In 2021, the Department of Biochemistry launched its Post-Baccalaureate Program to bring underrepresented minorities to laboratories in that Department.

This year, a separate program called the UT Southwestern Postbaccalaureate to PhD (PB2PHD) Program will be introduced campuswide. Although the newer initiative shares many features similar to the Biochemistry Department's endeavor, PB2PHD was designed to attract students to all departments at UT Southwestern.

PB2PHD, which began accepting applications in November, will serve recent college graduates interested in research training in the biomedical sciences with a faculty-mentored research experience. The program begins in June and will place students in laboratories that match their scientific interests.

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

Pak Center founder donates $1M for research and patient care

Career of innovation drives decades of support for mineral metabolism work at UT Southwestern

Charles Pak, M.D., with his late wife, Jane Riechers Pak, in 2019

By Andrew Marton

As founding Director of the Charles and Jane Pak Center for Mineral Metabolism and Clinical Research, Charles Pak, M.D., helped distinguish UT Southwestern as a national leader in preventing, diagnosing, and treating bone and mineral disorders. His discoveries paved the way for pioneering therapies that continue to be used to treat patients with kidney stones and osteoporosis.

Equally impressive is his long-standing support of the institution.

"My goal in giving has always been to build a top-notch international center in mineral metabolism in both research and patient care," said Dr. Pak, Professor of Internal Medicine. "I believe the Center can be stellar by seeking out as many clinical research opportunities as possible wherever it is engaged in patient care."

Recently, Dr. Pak made a $1 million gift to UT Southwestern for the Pak Family Support Fund for Clinic-Based Research and Patient Care. His latest act of generosity continues his family's decadeslong support of mineral metabolism care and research.

In 1995, gifts from Dr. Pak helped establish the Center, which is named for him and his late wife, Jane Riechers Pak. He also plans to support the Center through estate gifts via the Charles Y.C. Pak Foundation.

Orson Moe, M.D.

> "What is exceptional about Dr. Pak is that he takes excellent research and – within a short time frame – turns it into drugs that make people's lives better."
>
> – Orson Moe, M.D.

Dr. Pak credits his wife for having the philanthropic vision to invest in the institution. A lifelong educator and civic volunteer, Mrs. Pak, who died last year from breast cancer, remained a constant partner in the couple's support of UT Southwestern.

"Without my wife, Jane, none of this would have been possible," Dr. Pak said.

He holds patents for therapeutic drugs and diagnostic tests developed from his research, including Citracal, a calcium supplement that helps ward off osteoporosis. He also developed Urocit-K and THIOLA, which are prescribed to help prevent kidney stones, and the StoneRisk Profile, a diagnostic kit used to determine the causes of kidney stones by analyzing a 24-hour urine sample.

Dr. Pak's sustained giving has supported several of the Center's key initiatives, including a collaborative research fund that provides annual support to jump-start forward-looking collaborative research in mineral metabolism. Recipients are selected through a competitive process from the 12 faculty members who hold endowed professorships established by Dr. Pak's personal foundation. According to Dr. Pak, the program has resulted in more than 60 peer-reviewed journal articles. Another breast cancer/bone initiative supported by Dr. Pak's generosity provides competitive grants to two faculty members, selected each year from across the institution, to pursue research of breast cancer that has spread to a patient's bones.

"I intend to continue this program in memory of my wife, who suffered from this dreadful disease," he said.

In 2003, Dr. Pak transitioned the Center's leadership to Orson Moe, M.D., Professor of Internal Medicine and Physiology, who continues the Center's momentum today.

"What is exceptional about Dr. Pak is that he takes excellent research and – within a short time frame – turns it into drugs that make people's lives better," Dr. Moe said. "The independent funds made available by Dr. Pak's generosity help the Center pursue early, innovative research that may not be ready to compete for outside funding."

For Dr. Pak, his giving is part of a career devoted to UT Southwestern.

"It is a culmination of a lifelong effort and dream," Dr. Pak said. "As I am reaching closure of my career and with this latest gift, I feel satisfied that the future of the Center for Mineral Metabolism and Clinical Research is assured. I'm pleased to have been able to return some of the rewards reaped from opportunities that UT Southwestern has given me."

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Dr. Moe holds The Charles Pak Distinguished Chair in Mineral Metabolism, and the Donald W. Seldin Professorship in Clinical Investigation.

Dr. Pak holds the Alfred L. and Muriel B. Rabiner Distinguished Academic Chair for Mineral Metabolism Biotechnology Research.

Helping those with a rare disease find the right treatment

Multidisciplinary team strategy aids Ehlers-Danlos syndrome patients, who are often misdiagnosed

By Jan Jarvis

As a child, Kimberly Bertrand, O.D., injured more easily than others and would pass out frequently. As an adult, plantar fasciitis made walking difficult, and spinal stenosis caused recurring neck and back pain.

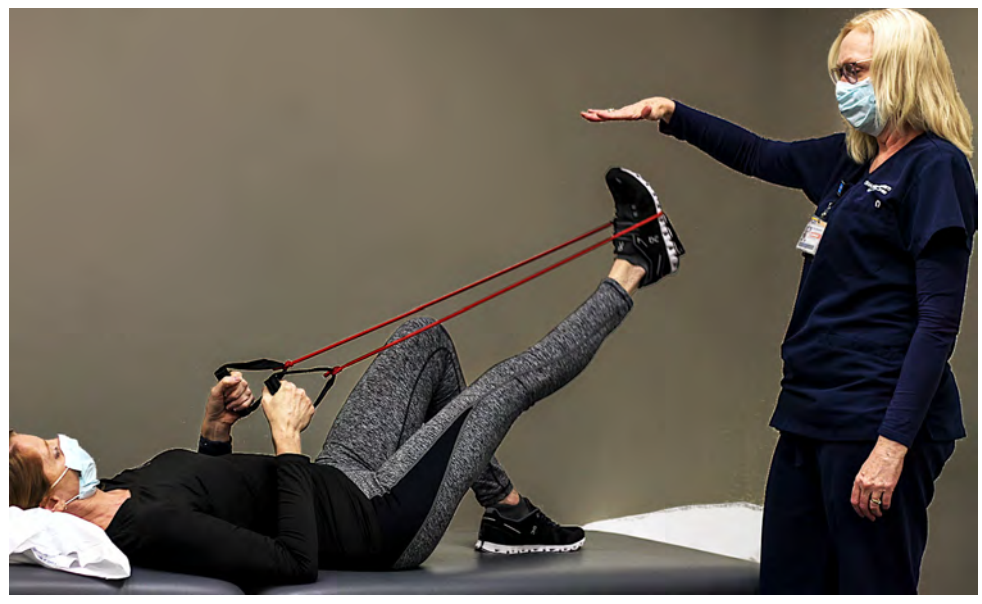
"I have always felt more fragile than everyone else," said Dr. Bertrand, an optometrist and Dallas resident. "In my childhood and teenage years and into my mid-30s, most of my issues were with strength and coordination."

Dr. Bertrand had lived with symptoms for decades before she was diagnosed.
Credit: Traci Schwomeyer, Metroplex Headshots

The 46-year-old, who practices in Southlake, grew increasingly desperate for answers. Last May, she sought treatment at UT Southwestern and was diagnosed with hypermobility Ehlers-Danlos syndrome, or EDS.

"Patients with this genetic disorder struggle with pain, fatigue, and other symptoms that make simple tasks like cooking or getting dressed difficult," said her doctor, Isabel Huang, M.D., Assistant Professor of Physical Medicine and Rehabilitation.

"Ehlers-Danlos individuals may suffer from a multitude of symptoms that can affect joints, gastrointestinal, cardiovascular, and neurological systems," Dr. Huang said. "The connective tissue is the issue, which is found everywhere in the body."



Kimberly Bertrand, O.D., (left) had tried physical therapy in the past, but working with UT Southwestern's Michelle Munster, Sc.D., an expert in treating EDS patients, made all the difference.

By the time EDS patients come to UT Southwestern, many have already seen numerous doctors and are still searching for an accurate diagnosis and treatment plan. The UTSW Physical Medicine and Rehabilitation specialist team is well equipped to help patients with this rare condition, creating a customized treatment plan for each.

The disease, which affects about one in 5,000 people worldwide, can result in a range of symptoms including headaches; hypermobility (loose, flexible joints); mast cell activation (an allergic-type reaction to certain triggers, such as sunlight or stress); poor circulation; skin that stretches, tears, and bruises easily; digestive complications; lack of bladder control; dizziness; and extreme fatigue. There are 13 types of EDS, categorized by which areas of the body the disease affects. The disorder is often misdiagnosed as fibromyalgia.

When screening new patients for EDS, Dr. Huang starts with the joints.

"We discuss which joints are loose and any other joint-related symptoms they're experiencing," she said. "Then we discuss energy levels, chronic pain, and the cardiovascular, gastrointestinal, and muscle systems."

"We try to see if there is connection between what seems like random symptoms into one, cohesive diagnosis based on the characteristics of each type of EDS," Dr. Huang added. "The sooner we can diagnose the disorder, the faster we can help improve a patient's quality of life with personalized treatment."

Since EDS has no cure, the goal is to improve quality of life by increasing strength and decreasing pain, discomfort, and fatigue. Physical and occupational therapy can improve joint stability, splints can prevent hyperextension, and strengthening exercises also help. Other treatments include cognitive behavioral therapy, speech therapy to improve swallowing, and medication for pain, insomnia, anxiety, or depression. A daily home exercise routine often improves overall function.

For Dr. Bertrand, the diagnosis meant that at last she could put all her nonspecific symptoms into one category.

"Sometimes a diagnosis isn't helpful because getting it doesn't cure you or anything," she said. "But with the knowledge I now have, it gave me direction on where to find help."

Dr. Huang created a treatment plan that included adding more proteins and electrolytes to Dr. Bertrand's diet, modifying her activity, and adding a physical/occupational therapy program to strengthen her muscles. Dr. Bertrand noticed her energy levels increased after a couple of months. Today, she can run 3 miles in under 30 minutes, whereas before she could not walk 1 mile without pain.

"I feel younger than ever," she said. "My treatment plan and general awareness of EDS have improved my mental health as well, so I can devote more energy to my physical well-being."

Dr. Munster (left) works with Dr. Bertrand to help her build strength.