CenterTimes

December 2020 / January 2021 — A Publication of The University of Texas Southwestern Medical Center — Campus Edition

Celebrating UT Southwestern's 'Leaders in Clinical Excellence'

By Carol Marie Cropper

As an anesthesiologist, Dr. Megan Maxwell spends her days helping to ease pain for patients – many of them women about to give birth. But in August, she found herself on the other side of that caring equation after her third child, a son, was born a month early at William P. Clements Jr. University Hospital.

"During the eight days he spent in the NICU (Neonatal Intensive Care Unit), they wrapped us in their arms and took care of us when we were at our most vulnerable," said Dr. Maxwell, recounting her experience Dec. 2 during the third annual Leaders in Clinical Excellence Awards ceremony.

"I was reminded why this job is so fulfilling," she said. "Be of service to others and that's where true happiness and fulfillment lies."

Dr. Maxwell, an Assistant Professor of Anesthesiology and Pain Management, was honored with one of four Rising Star Awards presented to promising early career physicians. One of her peers who nominated her for the award cited her "relentless energy and ability to solve problems."

In all, 19 physicians were recognized for outstanding clinical care. The Leaders in Clinical Excellence Awards program was established in 2018 to recognize the exceptional contributions of clinical faculty for the care of patients, the education of the next generation of health care professionals, and their service to UT Southwestern overall.

Due to the pandemic, this year's ceremony at UT Southwestern was presented virtually, with Dr. Daniel K. Podolsky, President; Dr. W. P. Andrew Lee, Executive Vice President for Academic Affairs, Provost, and Dean of the Medical School; and Dr. John Warner, Executive Vice President for Health System Affairs, announcing winners in seven categories.

Yet even in a virtual setting, the joy and pride felt by the honorees at being recognized by their peers was obvious – and sometimes overwhelming.

"It's just an honor that I will always remember," said Dr. Mark Drazner, Clinical Chief of Cardiology and Professor of

Please see AWARDS on page 4

Winners of UT Southwestern's 2020 Leaders in Clinical Excellence Awards

How the brain remembers right place, right time

Studies could lead to new ways to enhance memory for those with traumatic brain injury or Alzheimer's disease

By Christen Brownlee

Two UT Southwestern studies shed new light on how the brain encodes time and place into memories. The findings, published recently in *PNAS* and *Science*, not only add to the body of research on memory, but could eventually provide the basis for new treatments to combat memory loss from conditions such as traumatic brain injury or Alzheimer's disease.

About a decade ago, a group of neurons known as "time cells" was discovered in rats. These cells appear to play a unique role in recording when events take place, allowing the brain to correctly mark the order of what happens in an episodic memory.

Located in the brain's hippocampus, these cells show a characteristic activity pattern while the animals are encoding and recalling events, explained Dr. Bradley Lega, Associate Professor of Neurological Surgery at UTSW and senior author of the *PNAS* study. By firing in a reproducible sequence, they allow the brain to organize when events happen, Dr. Lega said. The timing of their firing is controlled by 5 Hz brain waves, called theta oscillations, in a process known as precession.

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Deciphering the method that cells use to degrade unwanted microRNAs

Discovery of mechanism that controls gene regulators could lead to new ways to fight disease

By Christen Brownlee

UT Southwestern researchers have discovered a mechanism that cells use to degrade microRNAs (miRNAs), genetic molecules that regulate the amounts of proteins in cells.

The findings, reported online in *Science*, not only shed light on the inner workings of cells but could eventually lead to new ways to fight infectious diseases, cancer, and a bevy of other health problems.

Scientists have long known that genes contain the instructions for making every protein in an organism's body. However, various processes regulate whether different proteins are produced and in what amounts. One of these mechanisms involves miRNAs, small pieces of genetic material that break down complementary pieces of messenger RNA (mRNA) in cells, preventing the mRNA sequence from being translated into proteins.

Since the discovery of miRNAs in 1993, researchers have amassed a wealth of knowledge about the hundreds of different miRNA molecules and their targets as well as mechanisms that control their production, maturation, and roles in development, physiology, and disease. However, explains Dr. Joshua Mendell, Professor and Vice Chair of Molecular Biology at UTSW, and postdoctoral fellow Dr. Jaeil Han, very little was known about how cells dispose of miRNAs when they're finished using them.

"As long as miRNA molecules stick around in a cell, they reduce the production of proteins from their target mRNAs," explained Dr. Mendell, a

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IN MEMORIAM

Edith Jones O'Donnell: Friend and transformative UT Southwestern supporter

Edith Jones O'Donnell

By Patrick Wascovich

Edith Jones O'Donnell, renowned for her commitment to arts and education and a pivotal figure in helping transform UT Southwestern Medical Center through extraordinary support from the O'Donnell Foundation she founded with husband Peter O'Donnell Jr., passed away on Nov. 14. She was 94.

Together and through the Foundation, Edith and Peter O'Donnell supported some of the most innovative and impactful programs at UT Southwestern. The O'Donnells' gifts have helped transform UTSW into an internationally recognized research leader through their support of educating new generations of physician-scientists, Nobel Prize-winning research, and recognizing the contributions to educational, training, and clinical care.

"Edith O'Donnell was a quiet visionary. While best known and appreciated for cultivating public appreciation and support for the arts and education, Mrs. O'Donnell also held a deep commitment to improving the health of the community she loved. UT Southwestern has lost a great friend. We are grateful for the trust and confidence she placed in our efforts," said Dr. Daniel K. Podolsky, President of UT Southwestern.

Mrs. O'Donnell, an Abilene native, graduated from The Hockaday School,

Please see O'DONNELL on page 8

Study finds low risk of pregnancy complications from COVID-19

The vast majority of pregnant women with COVID-19 infection had no adverse outcomes during their deliveries, according to a UTSW study.

By Lori Sundeen Soderbergh

Pregnant women who test positive for COVID-19 and their newborn babies have a low risk of developing severe symptoms, according to a UT Southwestern study.

The study, published recently in *JAMA Network Open*, shows that 95 percent of women who tested positive for COVID-19 during pregnancy had no adverse outcomes. Additionally, the study found that the virus was transmitted to the fetus in just 3 percent of the cases.

"Our findings are that approximately 5 percent of all delivered women with COVID-19 infection

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Recognized leader on diversity and inclusion appointed Associate Dean

By Lori Sundeen Soderbergh

Dr. Quinn Capers IV, a nationally recognized leader on diversity and inclusion in academic medicine, has been appointed Associate Dean for Faculty Diversity and the inaugural Vice Chair for Diversity and Inclusion in the Department of Internal Medicine. He joined UT Southwestern in December.

Dr. Capers, a cardiologist, came from The Ohio State University College of Medicine, where he served as Vice Dean for Faculty Affairs and Professor of Internal Medicine. During a decade as Associate Dean for Admissions, he led efforts to make Ohio State one of the most diverse medical schools in the U.S.

Dr. Capers was recently recognized with the Group on Diversity and Inclusion Exemplary Leadership Award from the Association of American Medical Colleges. The award recognizes innovative leadership in developing and implementing a highly effective program that demonstrates evidence-based best practices for enhancing diversity and inclusion in academic medicine and biomedical sciences.

"At UT Southwestern, I will be collaborating with a talented team to build on current efforts to enhance the diverse and inclusive climate of this world-class faculty," Dr. Capers said. "The spirit of innovation at UTSW is the perfect setting for launching novel strategies to recruit, support, and promote diverse physicians and scientists."

As Associate Dean, Dr. Capers oversees and will develop initiatives that expand faculty diversity and ensure inclusion and equity for faculty across all departments and mission areas. He will build on existing programs, working closely with Dr. Byron Cryer, Associate Dean for Faculty Development and Professor of Internal Medicine, and Dr. Helen Yin, Associate Dean for Women's Careers and Professor of Physiology. Dr. Capers also serves as a member of the UTSW President's Council on Diversity and Inclusion and is a Professor of Internal Medicine.

Dr. Capers' appointment reflects the commitment to diversity and inclusion at UT Southwestern, where the workforce is majority-minority with 38 percent identifying as white. UT Southwestern's Offices of Student Diversity & Inclusion and Faculty Diversity & Development are responsible for recruiting and retaining top students and faculty to campus, while also implementing strategies to promote the growth and presence of women and underrepresented minorities. At UT Southwestern Medical School, the percentage of underrepresented minorities is 27 percent for the Class of 2024, nearly double the national average of 14 percent.

"Diversity and inclusion are integral to UT Southwestern's mission of preparing a new generation of health care professionals to serve highly diverse communities in North Texas and beyond," said Dr. W. P. Andrew Lee, Executive Vice President for Academic Affairs, Provost, and Dean of the Medical School. "Dr. Capers will bring invaluable experience and perspective to our efforts to expand diversity and inclusion among our faculty and the entire UT Southwestern community."

Dr. Capers has led workshops across the country that have trained more than 1,000 physicians in strategies to reduce implicit racial bias. He is an inaugural member of the American College of Cardiology's Diversity and Inclusion Task Force.

In the new Vice Chair role, Dr. Capers will develop policies and practices consistent with the Department of Internal Medicine's goals to ensure equal opportunity for all faculty, trainees, and staff and to expand diversity within the Department. He will work to ensure that diversity and inclusion is an intrinsic component of all of the Department's clinical, research, and educational programs.

Dr. Quinn Capers IV

Dr. Capers will also see patients, both directly and during supervision of trainees at the UT Southwestern Clinical Heart and Vascular Center, William P. Clements Jr. University Hospital, and Parkland Memorial Hospital.

"One of my main passions is to reduce or eliminate health care disparities. Toward that end, I am very excited to teach trainees and treat patients at Clements University Hospital and the legendary Parkland Hospital," Dr. Capers said.

A native of Dayton, Ohio, Dr. Capers is a graduate of Howard University and Ohio State's College of Medicine. He completed an internal medicine residency and fellowships in vascular biology research, cardiovascular medicine, and interventional cardiology at Emory University.

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

Dr. Cryer holds the John C. Vanatta, III, Professorship.

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

Dr. Yin holds the Margaret Yin Chair for the Advancement of Women Faculty, and the Peter and Jean D. Dehlinger Professorship in Biomedical Science.

CLASS NOTES

IN MEMORIAM

Medical School

Robert L. Carr, M.D. ('51)
Barbara K. Spears, M.D. ('59)
Travis "Ward" Locklear, M.D. ('66)
Clement M. Talkington, M.D. ('69)

Housestaff

E. Ghent Graves Jr., M.D.
Drew P. Kelly, M.D.
Harlan Pollock, M.D.
Johannes "Peter" Thiele, M.D.

MEDICAL SCHOOL

Class of 1960: Richard L. Mabry, M.D., the bestselling author of 14 published novels and six published novellas, is currently writing a book with the working title *Medical Mystery* that is a story about a nurse who is writing a mystery novel while involved in a mystery herself. Dr. Mabry is well into a second career after retiring from practicing medicine. His novels have been referred to as "medical mystery with heart." Check out his blog at rmabry.blogspot.com.

Class of 1972: David J. Pillow Jr., M.D., retired in December after serving six years as an Instructor in UT Southwestern's Department of Emergency Medicine. Dr. Pillow is past President of the Texas College of Emergency Physicians, where he also served as Chairman of the Education Committee and President-elect of the Board of Directors. He is a member of several other professional organizations, including the American College of Emergency Physicians, the American Medical Association, and the Texas Medical Association. He was included among *D Magazine*'s Best Doctors for 2020.

GRADUATE SCHOOL

Class of 1972: John T. Watson, Ph.D., has been inducted into the National Academy of Engineering. He is the first and only individual from the National Institutes of Health to be inducted into the National Academy of Engineering and is the only medical doctor in the nation in the National Academy of Engineering. Dr. Watson is currently serving as Professor Emeritus in Bioengineering; Co-Director, MAS Medical Device Engineering; Director, BE Masters of Engineering Graduate Program; Director, Whitaker Center for Biomedical Engineering; former Executive Director, Cell Engineering Research Center; and founder, The William J. Von Liebig Center for Entrepreneurism and Technology Advancement, all at the University of California, San Diego.

SCHOOL OF HEALTH PROFESSIONS

Class of 1998: Shawna Ridley, MBA, RHICA, CPC, COC, CPMA, will speak at the College of Health Care Professions (CHCP) commencement in January 2021. Ms. Riley is also the 2020 recipient of the Legacy Award from the Texas Health Information Management Association.

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

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

IN MEMORIAM

Dr. David Minna: Pioneer in use of musculoskeletal ultrasound in rheumatology

By Patrick Wascovich

Dr. David A. Minna, Professor of Internal Medicine in the Rheumatic Diseases Division at UT Southwestern and a pioneer in incorporating musculoskeletal ultrasound into the specialty's clinical practice, passed away Nov. 5 after an extended battle with cancer. He was 73.

Dr. Minna was known as a devoted "clinician's clinician" and an outstanding educator who shared real-world knowledge drawn from more than 30 years of leading the largest private practice in rheumatology in Southern California. He came to UTSW in 2008, joining his older brother, Dr. John Minna, Director of the W.A. "Tex" and Deborah Moncrief Jr. Center for Cancer Genetics, Director of the Hamon Center for Therapeutic Oncology Research, and co-Director of the Experimental Therapeutics Program at the Harold C. Simmons Comprehensive Cancer Center, on the faculty. Dr. David Minna practiced at several locations, including UTSW's Medical Center at Park Cities.

"David was, like our father, a physician who took care of the 'whole patient.' While he specialized in rheumatology, he prided himself in being able to deal with all aspects of his patients' medical care," Dr. John Minna said. "David also loved both doing and teaching procedures and, finally, he was a 'treater' – he was always looking for a therapy program he could administer to each patient. Notably, he was working full time until the end and actually had a full load of outpatients 10 days before he passed away."

UTSW's clinical program in rheumatology was in a nascent stage when Dr. David Minna arrived. Under his stewardship, it quickly gained traction and became more patient-centered. He spearheaded the Division's musculoskeletal ultrasound training for the diagnosis and treatment of rheumatic diseases and for years served as co-Director of the James W. Aston Ambulatory Care Center's Infusion Clinic, using the knowledge he gained in practice to expedite the delivery of complex biological medications to patients.

"David was the epitome of what a physician should be – showing tireless devotion to his patients, his colleagues, and his trainees," said Dr. David Karp, Chief of Rheumatic Diseases. "We all could count on him to help with our most challenging cases, and he transmitted this knowledge to our medical students, residents, and fellows and made them much better doctors. He was most proud of the rigorous musculoskeletal ultrasound curriculum he developed here at UT Southwestern that has made our program highly desirable among applicants nationwide."

Dr. David Minna

Dr. David Minna was born in San Diego, the son of a general practitioner father and a nurse mother. He attended Stanford University as well as St. Louis University Medical School before completing his residency in internal medicine at Emory University in Atlanta followed by a fellowship in rheumatology at Los Angeles County/University of Southern California Medical Center. His private West Coast rheumatology practice was in Long Beach and Los Alamitos, where he served as Medical Director and his wife, Geraldine "Gerry" Minna, led daily business operations. Together, they raised three children.

Dr. David Minna's various passions were topped by family and included boats and fishing, tinkering with anything mechanical, world travel coupled with photography, as well as trains. Dr. Minna's model train collection included a large-scale train track elevated 2 feet above the ground that ran around the family's backyard, complete with a life-size real train crossing signal.

Dr. David Minna was preceded in death by his parents and an older sister, Judy Pike of San Diego. He is survived by wife Gerry, daughter Penny Minna, son Dr. David G. Minna, and daughter Joanna Minna, their spouses, and six grandchildren.

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Dr. Karp holds the Fredye Factor Chair in Rheumatoid Arthritis Research and the Harold C. Simmons Chair in Arthritis Research.

Dr. John Minna holds the Max L. Thomas Distinguished Chair in Molecular Pulmonary Oncology and the Sarah M. and Charles E. Seay Distinguished Chair in Cancer Research.

CenterTimes

Center Times is published by the Office of Communications, Marketing, and Public Affairs at UT Southwestern Medical Center. UT Southwestern is an Affirmative Action/Equal Opportunity Employer. Women, minorities, veterans, and individuals with disabilities are encouraged to apply.

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Topping out marks latest milestone in UT Southwestern expansion

By Patrick Wascovich

The next phase of development on North Campus reached a significant milestone with the completion of exterior framework on a new two-tower building dedicated to the growing research programs of the Peter O'Donnell Jr. Brain Institute and the outpatient care efforts of the Harold C. Simmons Comprehensive Cancer Center. A virtual topping out ceremony was held Nov. 30 to celebrate the occasion.

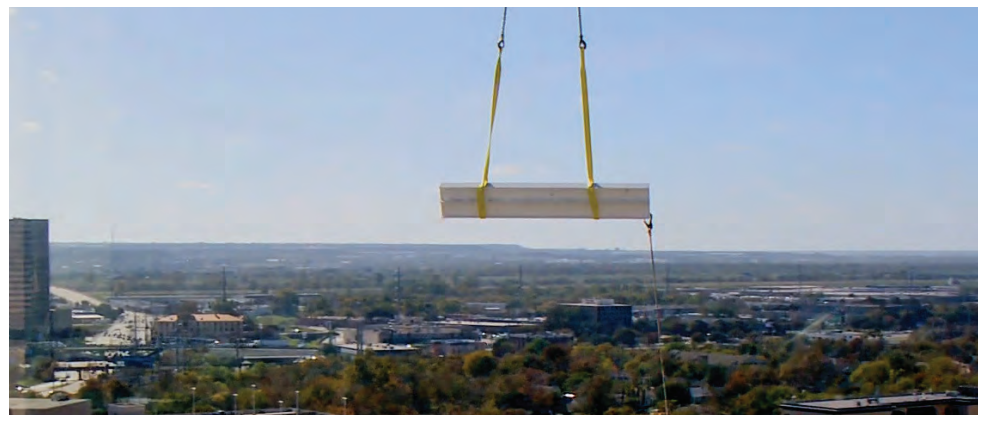
Dr. Daniel K. Podolsky, UT Southwestern President, watched as the last steel beam was ceremonially placed atop the building, marking a tangible commitment to patient-centered growth.

"This project epitomizes the close interrelationship between our commitment to heal, discover, and educate," Dr. Podolsky said. "It marks a milestone in writing the next chapter of UT Southwestern's journey and is creating a place and an opportunity for us to care for our patients and their families, juxtaposed to dynamic research programs in an environment that provides opportunities for training the next generation of physicians, medical scientists, and other health care providers."

The new structure, which broke ground in 2019, shares a four-story footprint topped off by two distinctive five-story towers. Rising above Harry Hines Boulevard just north of the C. Kern Wildenthal Research Building, the $328.5 million facility will add more than 600,000 square feet of space to North Campus when it opens in mid-2022.

It's part of a wave of construction underway on campus. Across Harry Hines, a 654,000-square-foot third tower has been added to William P. Clements Jr. University Hospital that is expected to be fully open by mid-January. Other major projects include a second Radiation Oncology Building adjacent to the existing building off Inwood Road, scheduled for completion in June, and renovations at both the former Red Bird Mall in South Dallas, where UT Southwestern will establish a clinic next year, and the James W. Aston Ambulatory Care Center, where upgrades began in August.

Also speaking at the topping out event were Dr. Carlos L. Arteaga, Director of the Simmons Cancer Center, and Dr. William T. Dauer, Director of the O'Donnell Brain Institute. The towers will offer opportunities to further expand



A construction crane lifts a beam as part of the development project for the new North Campus Outpatient Cancer Care and Brain Research Towers. A wave of construction is underway across UT Southwestern.

President Dr. Daniel K. Podolsky writes a message on a steel beam used in construction.

Dr. Nneka Ifejika, Associate Professor of Physical Medicine and Rehabilitation, adds her message to the steel beam.

cross-collaborative clinical and research initiatives, they said.

"This building will double our current cancer care capabilities on campus," Dr. Arteaga said. "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."

"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 Dr. Dauer.

Although virtual because of the COVID-19 pandemic, the event included well wishes campuswide from scores of UTSW faculty and employees who were invited to offer their messages electronically so that they could be written on the final structural steel beam before installation.

"The building in particular really allows us to go one step further both in patient care and in research," said Dr. Dwain Thiele, Vice Provost and Senior Associate Dean of Faculty Affairs and Initiatives, who championed the project before subsequently serving on its planning committees.

UT Southwestern's campus currently consists of about 14 million square feet of building space. More than 4.5 million square feet of new construction or renovation projects are either underway or in planning stages, including 1.75 million square feet of new buildings and garage space for 3,200 vehicles. This unprecedented growth at the institution reflects burgeoning opportunities to serve patients while also addressing the need for additional research laboratories.

"The new building has put patient care at the forefront," said Alexandra Huffman, Manager of Support Services at the Simmons Cancer Center. "It is a game changer, not just for clinical care but also supportive care. We can really ensure patients have access to everything they need."

Stroke expert Dr. Nneka Ifejika, Associate Professor of Physical Medicine and Rehabilitation, noted, "This means the world to us when it comes to translational science. It's our goal to integrate all aspects of clinical and basic research in this building. It's wonderful having a place where science comes together, and we're excited about what this means for brain recovery."

The expansion of Clements University Hospital, which began in 2017, will also contribute to expanded care for UTSW neurology patients. With the addition of more operating rooms, an expanded emergency department, and an increase in the number of patient rooms to about 750, CUH will also serve as the new home of relocated neurology services from Zale Lipshy Pavilion.

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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. Thiele holds the Jan and Henri Bromberg Chair in Internal Medicine.

More online: Read the full story and view a video on *Center Times Plus* at **utsouthwestern.edu/ctplus**.

UT Southwestern collaborations bring research discoveries to the marketplace

By Carol Marie Cropper

2020 was a difficult year in so many ways. But one bright spot has been UT Southwestern's continued effort to translate promising research findings into new or improved patient treatments.

In a nod to the growing importance of biotechnology in medicine, UT Southwestern worked with Lyda Hill Philanthropies and real estate developer J. Small Investments to plan a space to incubate fledgling biotech companies in Dallas.

UTSW's new Biotech+ Hub will be part of a renovation development called Pegasus Park – homage to the old Exxon Mobil regional headquarters with the iconic red-winged Pegasus symbol at its top.

Work is underway on the project, located across Interstate 35 from UT Southwestern's Dallas campus, with the first openings expected in 2021. The Biotech+ Hub will take up almost 40,000 square feet in the mixed-use development spread over 23 acres. It will share the space with offices for nonprofits and commercial innovators, along with a conference center, entertainment, and dining outlets.

BioLabs, a Cambridge, Massachusetts-based firm that manages shared laboratory facilities around the country, will develop and manage the laboratory space at Pegasus Park. Wet labs will be available for lease by UT Southwestern and area researchers and scientists, including those with venture capital firms, on an as-needed basis as they work to commercialize discoveries, said Dr. Claire Aldridge, Associate Vice President of Commercialization and Business Development at UT Southwestern.

Having such a space will help North Texas capitalize on its biotech strengths, including the innovations coming out of UT Southwestern laboratories and a community of biotech investors, said Dr. Aldridge, who holds a Ph.D. in immunology and genetics and is a scientific adviser to LH Capital, a private investment firm chaired by Lyda Hill, who also leads Lyda Hill Philanthropies. This will be BioLabs' first foray into the heart of the country, as all of its other labs are located on the East and West coasts.

"Dallas has all the important factors to become one of the major biotech hubs in the U.S.," said BioLabs Founder and President Dr. Johannes Fruehauf. "There is access to great talent, access to capital, and, most importantly, access to innovative academic institutions such as UT Southwestern."

In 2020, Dallas-Fort Worth moved up from seventh to sixth place on the annual list of Top 10 Emerging Clusters for life science put together by the CBRE Group, one of the world's largest commercial real estate services companies. Its rankings are based on employment in the field, inventory of leasable laboratory space, and funding received from venture capitalists and the National Institutes of Health.

UT Southwestern has been a local leader in moving its research to the marketplace.

Taysha Gene Therapies, a company founded in partnership with UT Southwestern, is an example of that. Taysha is working to further develop and commercialize gene therapies created by UT Southwestern researchers to treat genetic diseases that affect the central nervous system. These include Rett syndrome, which leads to intellectual disability as well as seizures, and Tay-Sachs disease, which also causes seizures and leads to early death. Another disease, known only as SLC13A5, can lead to persistent daily seizures, said Dr. Aldridge.

UT Southwestern worked with Lyda Hill Philanthropies and real estate developer J. Small Investments to plan a space to incubate biotech companies at Pegasus Park, a former Exxon Mobil complex that is undergoing renovations.

At UT Southwestern, Dr. Steven Gray, Associate Professor of Pediatrics, Molecular Biology, and Neurology in the Eugene McDermott Center for Human Growth and Development, works with Dr. Berge Minassian, Chief of the Division of Child Neurology, to find better ways to deliver therapeutic genes in order to replace a mutated gene or perhaps heighten the expression of a gene that has been silenced. Drs. Gray and Minassian are scientific advisers to Taysha.

Taysha raised $181 million in an initial public stock offering in September. In October, it received both rare pediatric disease designation and orphan drug designation from the Food and Drug Administration for its TSHA-104 therapy to treat Leigh syndrome tied to SURF1 deficiency, a fatal disease that causes progressive loss of mental and movement abilities.

Other promising efforts include OncoNano Medicine, a biotechnology company co-founded in 2014 by UT Southwestern's Dr. Jinming Gao, Professor of Otolaryngology – Head and Neck Surgery and Pharmacology in the Harold C. Simmons Comprehensive Cancer Center, and Dr. Baran Sumer, Professor of Otolaryngology – Head and Neck Surgery. The company in August received a grant of nearly $10 million from the Cancer Prevention and Research Institute of Texas to continue developing an imaging agent that lights up cancer cells during surgery to allow for more precise tumor removal.

The company's ONM-100 is now in multicentered phase two clinical trials for use when treating multiple tumor types.

Meanwhile, ReCode Therapeutics, co-founded by UT Southwestern Associate Professor of Biochemistry Dr. Daniel Siegwart and Professor of Physiology Dr. Philip Thomas, is developing nanoparticles that can deliver genomic medicines to specific organs, including the lungs, liver, and spleen. Dr. Siegwart, who also has an appointment in the Simmons Cancer Center, and his fellow researchers found that adding what they termed a selective organ targeting molecule to the nanoparticles controlled where they went inside the body, allowing for more precise targeting of disease-modifying medicines to replace a faulty gene with a healthy version. ReCode raised $80 million in Series A financing in March 2020. The company now focuses on life-limiting lung diseases and anticipates beginning clinical trials in 2022 for cystic fibrosis and primary ciliary dyskinesia.

UT Southwestern's Office of Technology Development is also preparing to roll out a free program for its researchers, faculty, and staff who want to become biotech entrepreneurs, said Dr. Aldridge. This month, the department will introduce Blackstone LaunchPad Powered by Techstars, which will offer educational programs and mentors to help the campus's budding entrepreneurs succeed by teaching some of the practical considerations needed to take an idea to market.

The program is being funded through a grant from the Blackstone Charitable Foundation.

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Dr. Gao holds the Elaine Dewey Sammons Distinguished Chair in Cancer Research, in Honor of Eugene P. Frenkel, M.D.

Dr. Minassian holds the Jimmy Elizabeth Westcott Distinguished Chair in Pediatric Neurology.

Dr. Sumer holds the T.C. Lupton Family Professorship in Patient Care, in Honor of Dr. John Dowling McConnell and Dr. David Andrew Pistenmaa.

Dr. Thomas holds the Ruth S. Harrell Professorship in Medical Research.

DFW COVID-19 Prevalence Study addresses gaps in local data

By Andrew Marton

As COVID-19 cases have continued to surge, the DFW COVID-19 Prevalence Study is providing vital information to help policymakers, business and civic leaders, and the general public make smart, informed decisions to help contain the spread of the SARS-CoV-2 virus.

This research effort, led by UT Southwestern and Texas Health Resources, began as a targeted study of 45,000 select participants, with a goal to understand how many people actually are or have been infected in our local North Texas community and to help develop effective and fair public health strategies to reduce any further deaths related to this disease.

The Prevalence Study is now expanding to allow anyone living in Dallas or Tarrant counties to participate via a brief survey online or by phone. Based on responses to the survey questions, some individuals may be selected for further testing to determine if they have COVID-19 or have previously been infected.

Prevalence study participants may receive a free COVID-19 test such as the one given at this drive-up testing facility on the UT Southwestern campus.

"Understanding the prevalence of COVID-19 in our community is critical to addressing the most challenging public health crisis of our time," said Dr. Daniel K. Podolsky, President of UT Southwestern. "The DFW COVID-19 Prevalence Study is designed to answer key questions about how our North Texas communities are being affected to provide policymakers with information needed to most effectively deploy mitigation strategies. We are extremely grateful for the public and private support that is making this vital work possible."

Dr. Amit Singal, Professor of Internal Medicine and Population and Data Sciences at UT Southwestern and the project's Principal Investigator, has seen a groundswell of interest from community participants.

"The large dataset from an anticipated 30,000 community volunteers – in addition to a targeted set of 14,000 front-line workers representing essential organizations like schools and retail stores – will address current gaps in local data," said Dr. Singal, a 2013 graduate of the UT Southwestern Graduate School of Biomedical Sciences. "Our study seeks critical answers we still don't have, including how many in the community have been infected with COVID-19 and why some communities are being harder hit."

Dr. Andrew Masica, Chief Medical Officer of Reliable Health for Texas Health and the study's co-Principal Investigator, explained that while important strides are being made in modeling and predicting COVID-19 surges, this data is mostly based on acute, or symptomatic, infections. "We still need to understand how many people may have had mild or no symptoms and were never tested but still had the infection," said Dr. Masica. "We also need to understand why the disease spreads more in some communities than others. Participation in this study is one way that individuals can help influence the DFW-area response to COVID-19."

To this end, volunteer participants from diverse socioeconomic, ethnic, and racial backgrounds are needed in order to maximize the study's impact. Investigators are particularly interested in understanding how COVID-19 has impacted Black and Hispanic communities, which have been disproportionately affected by the coronavirus.

Dr. Jasmin Tiro, a study co-investigator and Associate Professor of Population and Data Sciences at UT Southwestern, echoed Dr. Masica's call for a greater cross-section of volunteers in order to grasp the full scope of the virus's spread.

"We have the questions," said Dr. Tiro, "but our community holds the key. And we need as many participants as possible to help us unlock those answers."

Anyone residing in Dallas or Tarrant counties can participate. To volunteer, go to utswmed.org/covidstudy.

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

Dr. Singal holds the David Bruton, Jr. Professorship in Clinical Cancer Research and is a Dedman Family Scholar in Clinical Care.

Awards Continued from page 1

Internal Medicine, after receiving the Patricia and William L. Watson Jr., M.D. Award for Excellence in Clinical Medicine, UT Southwestern's highest honor in clinical care. The award recognizes a physician who exhibits both excellence in patient care and leadership in advancing clinical innovation.

Dr. Drazner, a cardiologist with expertise in treating cardiomyopathy and advanced heart failure, has led Advanced Heart Failure/Transplant within the Division of Cardiology for the past 14 years. This year, as COVID-19 spread worldwide and data showed that nearly 20 percent of those stricken suffered cardiovascular effects, Dr. Drazner took charge of the Cardiology Division's response, Dr. Podolsky said.

Dr. Drazner first came to UT Southwestern for an internship and fellowship 31 years ago, then returned after completing a fellowship in cardiology at Duke University and another in heart failure/cardiac transplantation at Brigham and Women's Hospital in Boston.

At UTSW, he said, he truly fell in love with the profession. "When you have a patient with advanced heart failure, their life is so limited. It's a really hard lifestyle, and the opportunity to intervene and change that and improve that is so gratifying."

Other award recipients had similar stories about the personal rewards earned from caring for patients.

Dr. Maxwell, who was all smiles holding her infant son during videotaped remarks accepting her honor, said it is very satisfying to be able to help people when they are in pain. "Any time you roll in with an epidural cart, you're definitely the most popular person in the room," she said.

Dr. Joel E. Wells, an Assistant Professor of Orthopaedic Surgery who received one of the four Patient and Family Recognition Awards for exceptional patient care, said he had two career goals when he was in college – to be a professional baseball player and to be a doctor.

During his senior year, he was both drafted by the New York Mets and accepted at the Tulane University School of Medicine in New Orleans. The prior year, Hurricane Katrina had devastated New Orleans.

The college baseball star chose medicine. "I just wanted to go and help out New Orleans and follow my dream of becoming a surgeon," Dr. Wells said. He also wanted to make his family proud. "There's no greater gift than taking care of patients, and I truly believe that patient care is not shift work. I wake up every morning wanting to help patients restore their quality of life and I go to bed every night worrying about them to make sure that they get the best care and the best quality of life outcome they can."

Dr. Wells now practices orthopedic and sports medicine at UT Southwestern Medical Center at Richardson/Plano.

A UTSW committee selected award recipients from more than 150 nominations submitted by fellow physicians and staff.

Before presentation of the awards, Dr. Podolsky noted that UT Southwestern recently celebrated the opening of a third tower that expanded Clements University Hospital, but said, "Excellence in clinical care is not a building. It's the work that goes on in the building; it's the commitment of all of those involved in delivering on our promise to our patients and their families.

"Every day there are heroes coming to campus prepared to roll up their sleeves, put on their masks, wear their eye protection, and provide the care that is needed for our patients today."

In a video shown before the awards presentations, several of UT Southwestern's health care heroes spoke about their experiences working during the COVID-19 pandemic. All expressed dedication to their mission to save lives despite potential risks to their own health.

"I believe it's just a very great time to be a nurse, especially here in the COVID unit because at the end of the day, you get to care for someone's loved one," said Priscilla Rodriguez, a nurse at Clements University Hospital.

"The pandemic has definitely brought us together. It has made us work hard and come together more as a team," said Sharen Henry, a nurse and infection preventionist.

■

Dr. Drazner holds the James M. Wooten Chair in Cardiology.

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

See the endowed titles held by Dr. Podolsky above.

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.

Congratulations to this year's honorees

Patricia and William L. Watson Jr., M.D. Award for Excellence in Clinical Medicine

Mark Drazner, M.D., M.Sc.
Professor of Internal Medicine
Clinical Chief of Cardiology

Rising Star Award

Jaime Almandoz, M.D., MBA
Assistant Professor of Internal Medicine

Neil Desai, M.D.
Assistant Professor of Radiation Oncology
Harold C. Simmons Comprehensive Cancer Center

Brad Lega, M.D.
Associate Professor of Neurological Surgery, Neurology, and Psychiatry
Peter O'Donnell Jr. Brain Institute

Megan Maxwell, M.D.
Assistant Professor of Anesthesiology and Pain Management

Mentoring Award

Susan Hedayati, M.D., M.H.Sc.
Professor of Internal Medicine – Nephrology
Director, Nephrology Clinical and Population Health Research
Associate Vice Chair, Research and Faculty Development

Una Makris, M.D., M.Sc.
Associate Professor of Internal Medicine and Population and Data Sciences
Division of Rheumatic Diseases

Patient and Family Recognition Award

Kevin Courtney, M.D., Ph.D.
Associate Professor of Internal Medicine – Hematology and Oncology
Co-leader of the Genitourinary Oncology Disease-Oriented Team
Harold C. Simmons Comprehensive Cancer Center
Graduate of the UT Southwestern Graduate School of Biomedical Sciences (2016)

A. Thomas Hyslop, M.D.
Assistant Professor of Obstetrics and Gynecology
Graduate of UT Southwestern Medical School (1988)

Catherine Ikemba, M.D.
Associate Professor of Pediatrics
Division of Cardiology
Director, Fetal Heart Program

Joel Wells, M.D., M.P.H.
Assistant Professor of Orthopaedic Surgery
UT Southwestern Orthopaedic Surgery Clinic
Sports Medicine Clinic at Richardson/Plano

Program Development Award

Abdominal Transplant Program
Steven Hanish, M.D.
Associate Professor of Surgery and Surgical Director of Liver Transplantation

Jorge Marrero, M.D.
Professor of Internal Medicine and Medical Director of Liver Transplantation

Parsia A. Vagefi, M.D.
Associate Professor of Surgery and Chief, Division of Surgical Transplantation

David Wojciechowski, D.O.
Associate Professor of Internal Medicine and Surgery and Medical Director of Kidney Transplantation

Care of the Vulnerable Elderly (COVE) program
Namirah Jamshed, M.D.
Associate Professor of Internal Medicine and Family and Community Medicine

Institutional Service Award

Cecelia (Shiela) Brewington, M.D., FACR
Professor of Radiology
Vice Chair of Clinical Operations
Chief of Community Radiology

Carol Croft, M.D.
Professor of Internal Medicine

The President's Award for Diversity and Humanism in Clinical Care

Naomi Winick, M.D.
Professor of Pediatrics
Division of Pediatric Hematology and Oncology

Dr. Mark Drazner was awarded UT Southwestern's highest clinical honor, the Patricia and William L. Watson Jr., M.D. Award for Excellence in Clinical Medicine.

More online: Watch videos and learn more about the award winners on *Center Times Plus* at **utsouthwestern.edu/ctplus.**

UT Southwestern research teams win prizes at Big Idea Competition

By Carol Marie Cropper

A UT Southwestern scientist who developed a compound to treat a genetic defect that can cause blindness won a $50,000 prize at the Big Idea Competition, an annual event to promote entrepreneurship at The University of Texas at Dallas.

A second UT Southwestern project claimed $12,500 for an algorithm that uses artificial intelligence (AI) to improve cancer diagnosis. Both were entries in a new category called the UT Southwestern Biotech+ Track.

And in a different category, a UT Southwestern ophthalmologist was the faculty adviser to a group of UT Southwestern Medical School and UTD students who designed an implant to treat glaucoma. That team won a $25,000 prize.

The finalists who competed at the Nov. 19 virtual event, timed to coincide with Global Entrepreneurship Week, pitched their ideas like contestants on the popular TV show "Shark Tank" to panels of business leaders, entrepreneurs, and venture capitalists. In all, more than $200,000 in prize money and scholarships was awarded in four categories: Biotech+, Student Pitch, Alumni Pitch, and Research and Commercialization Track.

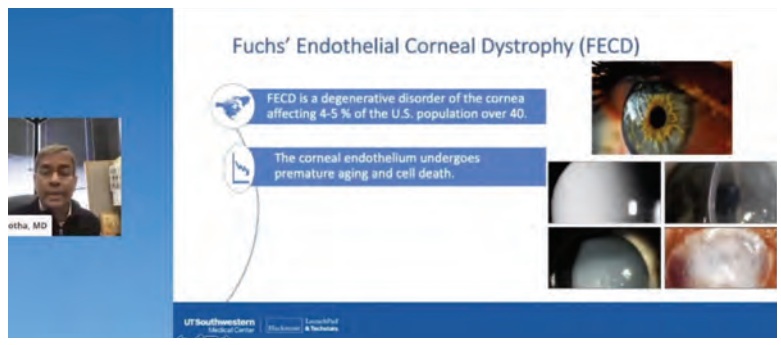
Mark Cuban, star of the popular ABC program as well as owner of the Dallas Mavericks basketball team, was the keynote speaker. He told an online audience of nearly 700 how he started his first business selling garbage bags door to door at age 12, then reentered the entrepreneurial world in his 20s after getting fired from a job selling software.

He said Dallas is ripe for creating biotechnology startups.

"North Texas is rapidly becoming a leader in AI," Cuban said after the event. "Combine this with the incredible base of knowledge we have at UTSW and throughout North Texas and I think we certainly will continue to have a position of leadership in all things science-driven."

UT Southwestern, along with UTD and Lyda Hill Philanthropies, presented this year's event.

Dr. V. Vinod Mootha, Professor of Ophthalmology and in the Eugene McDermott Center for Human Growth and Development, won the grand prize in the Biotech+ Track for his treatment for Fuchs' endothelial corneal dystrophy, an eye disease caused by a genetic defect.



Dr. V. Vinod Mootha won the grand prize in the Biotech+ Track for his project to treat a genetic defect that can cause blindness. All images courtesy of UT Dallas.

One in 20 Americans over the age of 40 suffer from the condition, he told the judges, and it requires a corneal transplant to prevent blindness. Even when done at specialized transplant centers, about 5 percent of grafts fail within five years and the surgery must be repeated, he added.

Dr. Mootha's lab has studied the genetics of Fuchs' dystrophy for eight years and, in conjunction with the Corey lab at UTSW, developed several promising compounds to neutralize the toxic effects of the overly long sequences of RNA encoded in Fuchs' dystrophy, he said. The solution is to create a so-called antisense oligonucleotide that will bind to the toxic RNA and neutralize it, he said.

Dr. Mootha said he was excited to win the $50,000 prize, which also comes with guidance on intellectual property law and a video marketing package from Zelaya Productions.

"The prize money will help grow our small but productive research team to further develop our project," he said. "We are probably five years away from clinical use." The next step, he said, will be to find a business partner to help.

A pitch from Dr. Yang Xie, Professor of Population and Data Sciences, led to a second-place prize for a project that developed an artificial intelligence algorithm to analyze pathological slides of tissue samples to check for signs and characteristics of cancer. Currently, an expert pathologist must manually read such tissue slides for disease diagnosis.

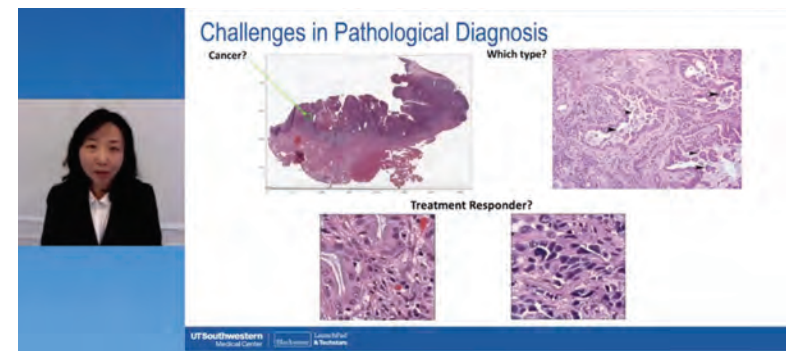
Mark Cuban, Dallas Mavericks owner and star of "Shark Tank," spoke at the Big Idea Competition about his early days as an entrepreneur.

Artificial intelligence can help pathologists make faster and more accurate diagnoses, Dr. Xie said. The AI model can also quantify and characterize spatial distributions of different types of cells, thereby improving treatment outcomes and providing new biological insights.

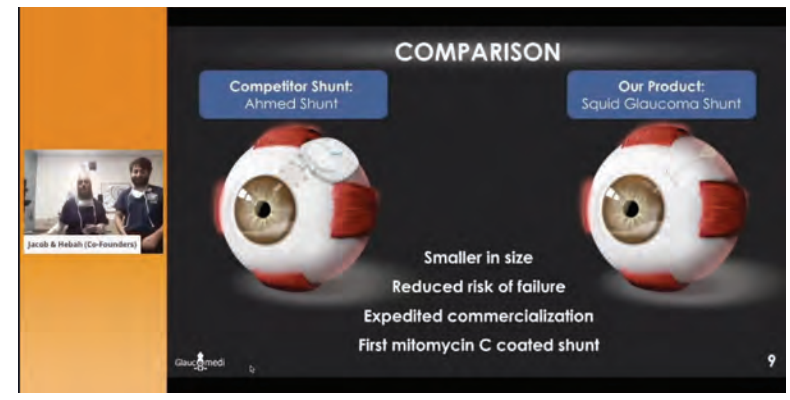
Money from the Big Idea prize will help her team develop the user-friendly software needed to take its product into a clinical setting, she told the judges. The event will also help the team connect with potential business partners, said Dr. Xie. In addition to the monetary award, she will receive intellectual property guidance and business service support.

Dr. Karanjit Kooner, Associate Professor of Ophthalmology, advised the team of students who won the Student Pitch Track for a device that is inserted into the eyes of glaucoma patients to drain excess fluid.

The group came up with the idea during UT Southwestern's hackathon in 2019 and is in the process of forming a company called Glaucomedi that has two patents pending for its Squid Glaucoma Shunt, Dr. Kooner said.



Dr. Yang Xie claimed second place in the Biotech+ Track for a project that uses special digital staining and artificial intelligence to read cancer tissue slides more quickly and accurately.



Students advised by Dr. Karanjit Kooner pitched their newly designed device to treat patients with glaucoma.

The novel device is smaller, more reliable, and less expensive than existing shunts, the group told judges. The U.S. market for such devices will top $2 billion in 2023, they said.

The prize money will allow them to produce prototypes and test their product in the laboratory, with hopes to take it to market in three years, Dr. Kooner said. They are currently looking for investors.

Winning the prize, which also comes with $10,000 in Amazon Web Services credits and a video marketing package from Zelaya Productions, boosted the team's spirits, he said. "We are invigorated and determined to keep on working toward our goals."

Finalists in the Biotech+ Track were selected after review of their proposals by UTSW faculty and staff. Two other finalists competed in the UT Southwestern Biotech+ Track: Dr. Kiyoshi Ariizumi, Professor of Dermatology, who presented an antibody to boost patient response in cancer immunotherapy; and Dr. Bo Li, Assistant Professor of Immunology and in the Lyda Hill Department of Bioinformatics, with a blood test for early cancer detection.

"The remarkable technologies represented in this competition are a testament to the rapidly growing, innovative ecosystem within North Texas," said Dr. Claire Aldridge, Associate Vice President of Commercialization and Business Development at UT Southwestern. "UT Southwestern is a global leader in advancing early stage research that is expanding the frontiers of health care."

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Dr. Mootha holds the Paul T. Stoffel/Centex Professorship in Clinical Care.

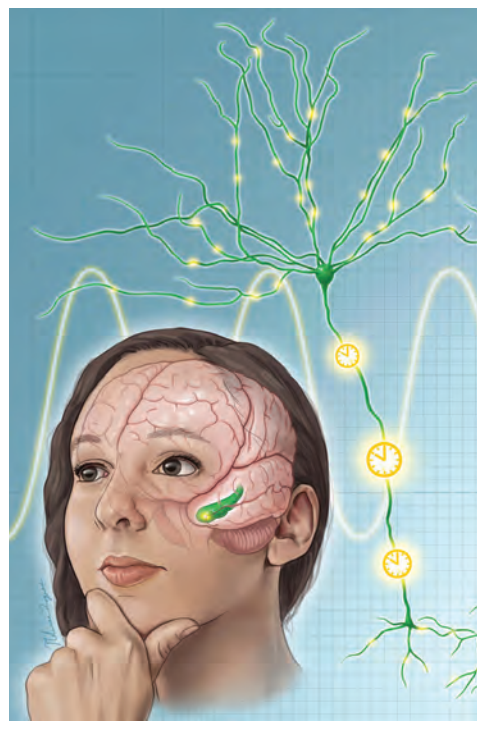
Dr. Xie holds the Raymond D. and Patsy R. Nasher Distinguished Chair in Cancer Research, in Honor of Eugene P. Frenkel, M.D.

Neurons Continued from page 1

Dr. Lega investigated whether humans also have time cells by using a memory task that makes strong demands on time-related information. Dr. Lega and his colleagues recruited volunteers from the Epilepsy Monitoring Unit at UT Southwestern's Peter O'Donnell Jr. Brain Institute, where epilepsy patients stay for several days before surgery to remove damaged parts of their brains that spark seizures. Electrodes implanted in these patients' brains help their surgeons precisely identify the seizure foci and also provide valuable information on the brain's inner workings, Dr. Lega said.

While recording electrical activity from the hippocampus in 27 volunteers' brains, the researchers had them do "free recall" tasks that involved reading a list of 12 words for 30 seconds, doing a short math problem to distract them from rehearsing the lists, and then recalling as many words from the list as possible for the next 30 seconds. This task required associating each word with a segment of time (the list it was on), which allowed Dr. Lega and his team to look for time cells. What the team found was exciting: Not only did they identify a robust population of time cells, but the firing of these cells predicted how well individuals were able to link words together in time. Finally, these cells appear to exhibit phase precession in humans, as predicted.

"For years scientists have proposed that time cells are like the glue that holds together memories of events in our lives," said Dr. Lega.



Hippocampal neurons create spatial and temporal "maps" of our world. A UTSW study determined how a group of neurons known as time cells allow the brain to correctly mark the order of events and assist in memory.
Illustration by Melissa Logies

Place memory

In the second study in *Science*, Dr. Brad Pfeiffer, Assistant Professor of Neuroscience, led a team investigating place cells – a population of hippocampal cells in both animals and humans that records where events occur. Researchers have long known that as animals travel a path they've been on before, neurons encoding different locations along the path will fire in sequence much like time cells fire in the order of temporal events, Dr. Pfeiffer explained. In addition, while rats are actively exploring an environment, place cells are further organized into "mini-sequences" that represent a virtual sweep of locations ahead of the rat. These radar-like sweeps happen roughly 8-10 times per second and are thought to be a brain mechanism for predicting immediately upcoming events or outcomes.

Prior to this study, it was known that when rats stopped running, place cells would often reactivate in long sequences that appeared to replay the rat's prior experience in reverse. While these "reverse replay" events were known to be important for memory formation, it was unclear how the hippocampus was able to produce such sequences. Indeed, considerable work had indicated that experience should strengthen forward, "look ahead" sequences but weaken reverse replay events.

To determine how these backward and forward memories work together, Dr. Pfeiffer and his colleagues placed electrodes in the hippocampi of rats, then allowed them to explore two different places: a square arena and a long, straight track. To encourage them to move through these spaces, they placed wells with chocolate milk at various places. They then analyzed the animals' place cell activity to see how it corresponded to their locations.

Particular neurons fired as the rats wandered through these spaces, encoding information on place. These same neurons fired in the same sequence as the rats retraced their paths, and periodically fired in reverse as they completed different legs of their journeys. However, taking a closer look at the data, the researchers found something new: As the rats moved through these spaces, their neurons not only exhibited forward, predictive mini-sequences, but also backward, retrospective mini-sequences. The forward and backward sequences alternated with each other, each taking only a few dozen milliseconds to complete.

"While these animals were moving forward, their brains were constantly switching between expecting what would happen next and recalling what just happened, all within fraction-of-a-second time frames," said Dr. Pfeiffer, who earned his Ph.D. from the UT Southwestern Graduate School of Biomedical Sciences in 2008.

Dr. Pfeiffer and his team are currently studying what inputs these cells are receiving from other parts of the brain that cause them to act in these forward or reverse patterns. In theory, he said, it might be possible to hijack this system to help the brain recall where an event happened with more fidelity. Similarly, added Dr. Lega, stimulation techniques might eventually be able to mimic the precise patterning of time cells to help people more accurately remember temporal sequences of events.

"In the past few decades, there's been an explosion in new findings about memory," he added. "The distance between fundamental discoveries in animals and how they can help people is becoming much shorter now."

Other UTSW researchers who participated in the *PNAS* study include Pranish Kantak, a research assistant in Neurological Surgery, Gray Umbach, a UTSW medical student, and Dr. Pfeiffer. A UTSW graduate student who participated in the *Science* study was Mengni Wang. Drs. Lega and Pfeiffer are both members of the O'Donnell Brain Institute.

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

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

All weight loss isn't equal for reducing heart failure risk

Study suggests that losing fat mass, but not lean mass, is key for heart health in obese patients with Type 2 diabetes

By Christen Brownlee

Reducing the level of body fat and waist size are linked to a lower risk of heart failure in patients with Type 2 diabetes, a study led by UT Southwestern researchers indicates. The findings, reported in *Circulation,* suggest that all weight loss isn't equal when it comes to mitigating the risk of heart disease.

The burden of diabetes is increasing, with an estimated 700 million adults worldwide predicted to have this disease by 2045. The vast majority of cases are Type 2 diabetes, characterized by insulin resistance, an inability for cells to respond to insulin. Type 2 diabetes doubles the risk of cardiovascular events such as heart failure and heart attacks.

Being overweight and obese are strong risk factors for both Type 2 diabetes and heart disease, and patients are often counseled to lose weight to reduce the likelihood of developing both conditions. However, not all weight loss is the same, explained Dr. Ambarish Pandey, senior author of the study and Assistant Professor of Internal Medicine.

"We have long counseled patients to lower their body-mass index into the 'healthy' range. But that doesn't tell us whether a patient has lost 'fat mass' or 'lean mass,' or where the weight came off," Dr. Pandey said. "We didn't know how each of these factors might affect patients' risk of heart disease."

Fat mass accounts for fat in different parts of the body while lean mass is mostly muscle.

Understanding the relationship between heart disease and body composition has proved especially challenging, Dr. Pandey explained, because there hasn't been an easy and inexpensive way to evaluate body composition. The gold standard of determining fat mass and lean mass is to measure it directly with tools like dual-energy X-ray absorptiometry (DXA), a scan that's cumbersome, expensive, and exposes patients to radiation.

To help answer how different types of weight loss can affect cardiovascular disease, Dr. Pandey and his colleagues used data from the Look AHEAD (Action for Health in Diabetes) Trial, which investigated the effects of either an intense lifestyle intervention focused on weight loss and physical activity or diabetes support and education in more than 5,000 overweight or obese adults with Type 2 diabetes. The study collected information on the volunteers' weight, body composition, and waist circumference at the baseline and again one and four years later. It also tracked the incidence of heart failure in this group over a 12-year period.

The Look AHEAD Trial determined body composition with DXA. But Dr. Pandey and his colleagues used a new equation that incorporates age, sex, race/ethnicity, height, body weight, and waist circumference to estimate fat and lean mass – producing results that closely matched those from DXA scans.

Among the 5,103 participants in the Look AHEAD Trial, 257 developed heart failure over the follow-up period. Dr. Pandey and his colleagues found that the more these volunteers lowered their fat mass and waist circumference, the lower were their chances of developing heart failure. Just a 10 percent reduction in fat mass led to a 22 percent lower risk of heart failure with preserved ejection fraction and a 24 percent lower risk of heart failure with reduced ejection fraction, two subtypes of this condition. A decline in waist circumference significantly lowered the risk of heart failure with preserved injection fraction but not heart failure with reduced ejection fraction.

Dr. Ambarish Pandey

More studies are needed to determine if reducing fat and retaining or increasing muscle may be more effective at decreasing the risk of heart failure, research that's facilitated with the new equation to estimate body composition, Dr. Pandey added. In the meantime, he said, patients may benefit from incorporating strategies toward this goal – such as resistance training – into their weight loss efforts.

"Our study suggests that simply losing weight is not enough," said Dr. Pandey, who earned his Ph.D. in 2017 from the UT Southwestern Graduate School of Biomedical Sciences. "We may need to prioritize fat loss to truly reduce the risk of heart failure."

The study was supported by the National Heart, Lung, and Blood Institute T32 postdoctoral training grant (5T32HL125247-03), the Texas Health Resources Clinical Scholars Program, and National Institutes of Health (NIH) grants R01AG18915, R01AG045551, and P30AG21331. The Look AHEAD Trial was not conducted at UT Southwestern, but data from that trial was used for the *Circulation* study.

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

Mutation could worsen heart function in Duchenne muscular dystrophy patients

Those carrying a cystic fibrosis gene mutation could benefit from aggressive and earlier cardiac interventions, study suggests

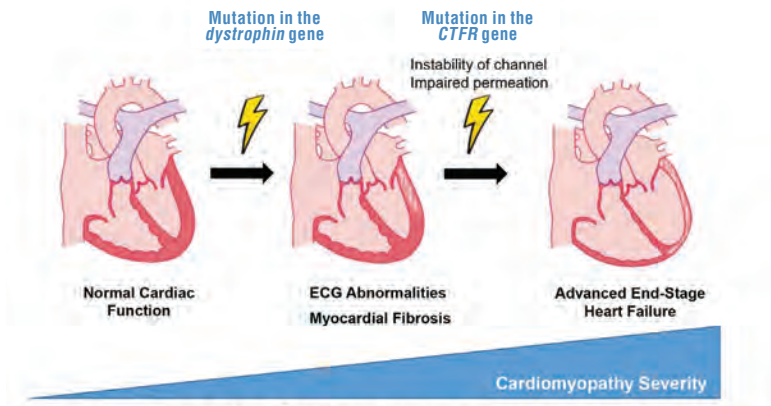
By Christen Brownlee

A mutation in the gene that causes cystic fibrosis may accelerate heart function decline in those with Duchenne muscular dystrophy (DMD), a UT Southwestern study suggests. The findings, published online recently in the *Journal of the American Heart Association*, could help doctors develop new strategies to preserve heart function in this population, potentially extending patients' lives.

DMD, caused by a mutation on the X chromosome, affects 1 of every 3,500 to 5,000 boys worldwide. This mutation results in the failure to produce dystrophin, a protein that protects muscle cells from damage, which in turn causes progressive muscle weakness. Although patients with DMD can suffer a variety of neuromuscular and lung complications, the cause of death – usually before age 35 – is typically cardiomyopathy, or weakness of the heart muscle.

All DMD patients eventually develop cardiomyopathy. But how early it develops and how progressive it manifests varies considerably, explained Dr. Pradeep Mammen, Associate Professor of Internal Medicine in the Division of Cardiology at UTSW, who runs a cardiology clinic specifically for patients with DMD and other neuromuscular disorders.

The reason for this variability has been unknown. However, Dr. Mammen and his colleagues suspected that it might result from an additional genetic variation, which may synergistically worsen heart function in DMD patients, accelerating the underlying cardiomyopathy.



Summary Figure: The *CFTR* gene may serve as a genetic modifier that accounts for more severe cardiomyopathy in DMD patients.

To search for genetic variants that might have this effect, Dr. Mammen and his team recruited 22 male patients with DMD from their clinic and 12 female carriers, mostly mothers of patients. (Carriers were included in the study since they often also develop cardiomyopathy.) Cardiac function was assessed in 32 of these volunteers using either cardiac magnetic resonance imaging (cMRI), echocardiography, or cardiac computed tomography. Each volunteer also submitted blood to check for additional markers of cardiac function and to perform whole exome sequencing, a genetic test that reads all protein-making genes in the body.

In DMD patients with the worst cardiac function, the researchers identified a few candidate genes that might exacerbate their cardiomyopathy. But one in particular, a switch in a single unit of the *cystic fibrosis transmembrane regular (CFTR)* gene known as a "missense" mutation, stood out due to its role in heart cells. This gene, which causes cystic fibrosis when both the body's copies carry a different characteristic mutation, is responsible for creating channels in heart cells that let bicarbonate in and regulate cell electrolyte levels.

Dr. Pradeep Mammen

DMD patients with the missense mutation in a single copy of this gene had a variety of markers of worse heart function compared with those who didn't, including lower left ventricular ejection fraction, larger end-diastolic volume, and higher levels of a blood protein called N-terminal pro-B-type natriuretic peptide.

Although it is unknown how this *CFTR* mutation exerts its effects, Dr. Mammen said doctors who treat these patients might eventually test for this mutation to identify DMD patients who need more aggressive cardiac care at a younger age. Currently, DMD patients receive a range of interventions as cardiomyopathy develops and worsens, ranging from drugs (including ACE inhibitors, beta blockers, and mineralocorticoid receptor agonists) to left ventricular assist devices. Although patients typically begin receiving cardiac care in their teens to early 20s, patients carrying the *CFTR* mutation may benefit from starting aggressive care earlier to prevent heart damage.

"Even with new strategies to treat these patients on the horizon, such as genome editing that could convert DMD to a less severe form known as Becker's muscular dystrophy, cardiomyopathy will continue to be a patient's most serious and life-ending consequence," said Dr. Mammen. "Finding ways to help preserve heart function over time could offer new hope for patients with DMD."

This study was supported by a National Institutes of Health Research Project Grant (NIH R01HL102478) and the National Institutes of Health-funded UT Southwestern Sen. Paul D. Wellstone Muscular Dystrophy Cooperative Research Center (NIH U54HD087351).

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Dr. Mammen holds the Alfred W. Harris, M.D. Professorship in Cardiology.

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

MiRNAs

Continued from page 1

Howard Hughes Medical Institute (HHMI) Investigator and member of the Harold C. Simmons Comprehensive Cancer Center. "So understanding how cells get rid of miRNAs when they are no longer needed is pivotal for fully appreciating how and when they do their jobs."

To answer this question, Drs. Mendell, Han, and their colleagues harnessed CRISPR-Cas9, a gene-editing tool that recently won the 2020 Nobel Prize in Chemistry for two scientists who developed the tool eight years ago. By serving as "molecular scissors," Dr. Mendell said, this system can cut out individual genes, allowing researchers to explore their functions.

In a human cancer cell line known as K562, the researchers used CRISPR-Cas9 to target most of the 20,000 protein-coding genes in the human genome, looking for any that caused a normally short-lived miRNA known as miR-7 to linger in cells. Their search turned up at least 10 genes that are needed to degrade this miRNA.

The researchers learned that the proteins encoded by these genes come together in cells to form a larger assembly known as a ubiquitin ligase, which functions to tag other proteins for destruction. This particular ubiquitin ligase had never been described before, Dr. Mendell said, but like other ubiquitin ligase complexes, it appears to mark proteins destined for degradation. However, rather than tag miR-7 itself, further investigation showed that this complex instead tags a protein called Argonaute, which ferries miRNAs through cells.

Once the Argonaute protein attached to miR-7 is targeted for degradation, this miRNA is left naked in the cell – a state that triggers cells to destroy the miRNA using RNA-degrading enzymes.

The research team found that this ubiquitin ligase complex is key for degrading not only miR-7 in K562 cells, but also a variety of other miRNAs in other cell types and species. These results suggest that this mechanism for miRNA decay acts broadly to control the levels of miRNAs during animal development and across tissues. Because other studies have shown that abnormal levels of various miRNAs are associated with a variety of diseases and infections, finding ways to control miRNA degradation – either to eradicate problematic miRNAs in cells or hold on to beneficial ones – could represent a new way to treat these conditions.

"For over a decade, researchers have been searching for mechanisms through which cells degrade miRNAs," said Dr. Han. "Now that we've discovered new cellular machinery that can accomplish this, we will be able to apply this discovery to better understand how miRNAs are regulated and, we hope, eventually develop new therapies."

This study was funded by grants from the National Institutes of Health (R35CA197311, P30CA142543, and P50CA196516), The Welch Foundation (I-1961-20180324), American Heart Association (19POST34380222), the Cancer Prevention and Research Institute of Texas (RP150596), and the HHMI.

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

Telemedicine class gives students unique COVID-19 insight

By Nyshicka Jordan

For months last spring, UT Southwestern medical students were left in limbo regarding their clinical training when the COVID-19 pandemic forced Dallas residents to shelter in place. To preserve personal protective equipment and minimize exposure to the virus, clinical rotations were suspended.

But with the health crisis arose an opportunity to solve two critical problems – how to keep students engaged in clinical training and how to track the health of COVID-19 patients discharged from William P. Clements Jr. University Hospital.

As a solution, Dr. Gary Reed, Associate Dean of Quality, Safety and Outcomes Education, and Dr. Carol Croft, Professor of Internal Medicine, created COVID-19 Follow-up Telemedicine, an elective course in which medical students initiated follow-up calls with those patients. Medical students had not been taught telemedicine previously, but the current climate highlights its value in an evolving patient care landscape.

"Because of COVID-19, many clinics are doing some form of telemedicine. Now it's something that medical students need to learn how to do because telemedicine is going to be with us from now on," said Dr. Reed, also Professor of Internal Medicine and Surgery.

The telemedicine elective launched in May with students enrolled in the M.D. with Distinction in Quality Improvement and Patient Safety program, who helped design the pilot course over a two-week period. It was then opened up to other medical students seeking elective hours.

"Before, I hadn't known a lot about telemedicine. I thought it might be something patients struggled to use or be problematic for patients without access to the internet, computers, or tablets," said Isabel Wees, a third-year medical student who took the pilot course. "But since we were using the phone in our course, it was incredibly convenient. And with this resource, we can tell patients things they might not have known if we did not reach out to them."

In the course, students were assigned patients to call two days after discharge from Clements University Hospital. Students made up to five calls daily and always identified themselves as medical students to patients. They used the same script to assess warning signs, as well as an algorithm and daily briefings with Internal Medicine physicians to determine if patients needed to return to the hospital. A physician was on call while students made the contacts to jump in and respond if needed. Patients who were advised to continue recovering at home were counseled on proper self-isolation procedures.

Dr. Reed said since students initiated calls, the elective took a proactive approach to engaging with patients. Many patients were appreciative of the follow-ups, students said.

"This is a way to bridge the gap between when patients are treated in the hospital to when they see their primary care doctor. Some patients don't initially appear to be sick when they first come to the hospital, but over the first week or so, patients can deteriorate. We didn't want that to happen while they were at home and not have anyone to tell them to come back to the emergency room," Dr. Reed said.

Third-year medical student Imran Murtuza takes notes during his clerkship. Mr. Murtuza helped design the telemedicine elective pilot.

Third-year medical student Isabel Wees helped design the pilot course for the telemedicine elective.

The course included a multidisciplinary clinic involving COVID-19 patient telemedicine visits. One day per week students assisted in the clinic.

"In our daily debrief calls with attending physicians, we discussed how to talk about patient care and we also discussed the COVID-19 pandemic, staying up to date with all the studies, and what's going on in the hospitals around the nation. So it's a really valuable educational tool for students," said Imran Murtuza, a third-year medical student who also collaborated on the pilot course.

As quarantine restrictions eased in Dallas and at UT Southwestern, clinical rotations resumed in June for third- and fourth-year medical students. Ms. Wees said she has already experienced the benefit from the telemedicine course since returning to clinics.

"Now that I am back in clinics, there is still a lot of telemedicine being incorporated. So I am really glad that I had this exposure to it through helping create the elective," she said.

Once students returned to clinical rotations, the elective was ended in August. However, Dr. Reed said if students are removed from the clinic for a second time due to deteriorating COVID-19 conditions, then the course could be used again in medical education.

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Dr. Croft holds the Baldridge Family Professorship in Internal Medicine and Preventive Care.

Dr. Reed holds the S.T. Harris Family Distinguished Chair in Internal Medicine, in Honor of Gary Reed, M.D. and the Eva A. Rosenthal Professorship in Internal Medicine, in Honor of Gary Reed, M.D.

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

Medical School Class of 2024 includes record level of underrepresented minority students

By Lori Sundeen Soderbergh

Growing up outside of Pittsburgh, Dr. Shawna Nesbitt was well aware that minorities were greatly underrepresented among health care professionals.

"In those days, being a minority in America usually meant you were Black or Hispanic, and their numbers in medicine were really low," recalled Dr. Nesbitt, Associate Dean, Student Diversity and Inclusion at UT Southwestern. "It didn't improve much until recently. The percentage of minority applicants to medical schools was consistently around 7 percent until around 2013."

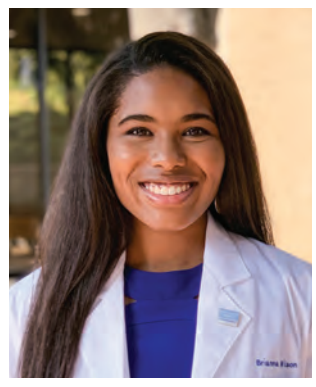
That's why it's a remarkable achievement that underrepresented minority (URM) students make up a record 27 percent of the UT Southwestern Medical School Class of 2024 – significantly higher than the nationwide average of 14 percent cited by the Association of American Medical Colleges (AAMC). At UT Southwestern, URM groups include African American, Hispanic, Native American, Pacific Islander, and multiracial students.

Dr. Nesbitt, who joined UTSW in 2001 as a Professor of Internal Medicine, has led efforts within the Office of Student Diversity and Inclusion to increase representation on campus for underrepresented minorities since 2011, when UTSW's URM levels hovered around the national average.

The Office of Student Diversity and Inclusion uses speakers, webinars, mentors, and cultural celebrations to honor diverse backgrounds and help students develop empathy and greater understanding. Students of all three UTSW schools (Medical School, Graduate School of Biomedical Sciences, and School of Health Professions) are welcome at the events.

Speakers are recruited to discuss topics that are often recommended by the students themselves, such as microaggressions (indirect, subtle, or unintentional discrimination against members of a marginalized group) and imposter syndrome (a psychological pattern in which a person doubts their accomplishments or talents and has a persistent fear of being exposed as a fraud).

First-year medical student Hector Chaires



Second-year medical student Brianna Wilson

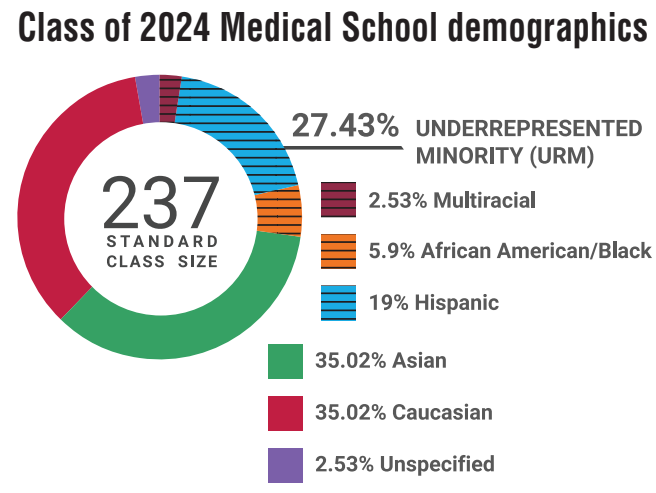
Celebratory events such as Dia de los Muertos (Day of the Dead), Juneteenth, and Eid al-Fitr (an Islamic holiday that marks the end of Ramadan) are well attended. They often include foods and traditions representing different cultures. Some focus on one school while others bring all three schools together.

Today, the positive trend toward inclusiveness is apparent not only in the Medical School but also at the School of Health Professions, where 25 percent of students are classified as URM, and the Graduate School of Biomedical Sciences, where 21 percent are URM.

"Our URM program is about celebrating your individuality and sharing it with your class. Inclusion really matters. It's inclusion that begins the conversation that we need so desperately in our culture, in both medicine and education," Dr. Nesbitt said.

For some learners, minority representation can be a deciding factor in choosing their school. "During my interview, there were others here who looked like me. That's one reason I chose to come here," said second-year medical student Brianna Wilson, who is Black and of Caribbean descent.

First-year medical student Hector Chaires, a native of Juarez, Mexico, did his homework. He applied to 28 medical schools and interviewed at many of them. Ultimately, UT Southwestern won his vote of confidence.



Dr. Shawna Nesbitt

"Many other schools have a much lower percentage of underrepresented minority students. Here, I can be surrounded by people that I can identify with," he said. "We can bring a different perspective to medicine. The URM program helps us to envision ourselves in leadership positions in health care."

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

Pregnancy

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develop severe or critical illness. Five percent is a major concern when a pandemic is making its way through a population; however, it's lower than previous reports from the Centers for Disease Control and Prevention (CDC)," said Dr. Emily Adhikari, Assistant Professor of Obstetrics and Gynecology at UT Southwestern and first author of the study. "Most women with asymptomatic or mild infection will be relieved to know that their babies are unlikely to be affected by the virus."

The researchers set out to measure how COVID-19 infection impacts pregnancy outcomes, how severely ill a pregnant woman gets, placental pathology, and neonatal infections by studying women at Parkland Health and Hospital System. The team followed 3,374 mothers, 252 of whom tested positive for the virus during pregnancy, from March through August. The group was predominantly Hispanic (75 percent), followed by Black (18 percent) and white (4 percent). There were no significant differences between the expectant mothers in age, number of previous births, BMI, or diabetes.

The pandemic has hit the Hispanic population in Dallas particularly hard. "While they make up 75 percent of the population of over 12,000 women delivering annually at our institution, women of Hispanic ethnicity made up over 90 percent of COVID-19-positive women. The higher frequency among Hispanic women in our study is consistent with data on racial and ethnic disparities in COVID-19 cases and deaths reported nationwide," said Dr. Adhikari, also Medical Director of Perinatal Infectious Diseases at Parkland Memorial Hospital.

Among the 252 women who tested positive, 239, or 95 percent, were asymptomatic or had mild symptoms at first. Six of those women subsequently developed severe or critical COVID-19 pneumonia. Comparing mothers with and without COVID-19 diagnosed any time during pregnancy, the COVID-19 virus did not increase the risk of adverse outcomes, including preterm birth, preeclampsia with severe features, or cesarean delivery for abnormal fetal heart rate. However, preterm birth was higher among mothers who developed severe or critical illness before reaching 37 weeks in their pregnancy. The study found that diabetes may be one factor that increases the risk for severe or critical maternal illness.

Pathologists who examined placentas – the organ that functions as the source of oxygen and nourishment for unborn babies – found that the majority were unaffected by the virus.

COVID-19 mothers who were outpatients were followed using telemedicine with a scripted evaluation of symptoms and protocol-based management, including instructions for referral to the emergency department for worsening respiratory symptoms or obstetric concerns. Telemedicine has been a vital tool used by many UT Southwestern and Parkland physicians during the pandemic.

Further study is needed to understand whether maternal infection with COVID-19 impacts long-term maternal or infant health.

"Our goal is to develop evidence-based guidelines for the majority of pregnant women who are recovering at home," said Dr. Adhikari, a 2011 graduate of UT Southwestern Medical School. "It's difficult to predict who will become severely ill, which is why prevention strategies such as handwashing, masking, and social distancing are still extremely important."

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

Immunotherapy side effect could be a positive sign for kidney cancer patients

Patients who developed acute interstitial nephritis, an autoimmune reaction, respond to immune checkpoint inhibitor drugs

By Christen Brownlee

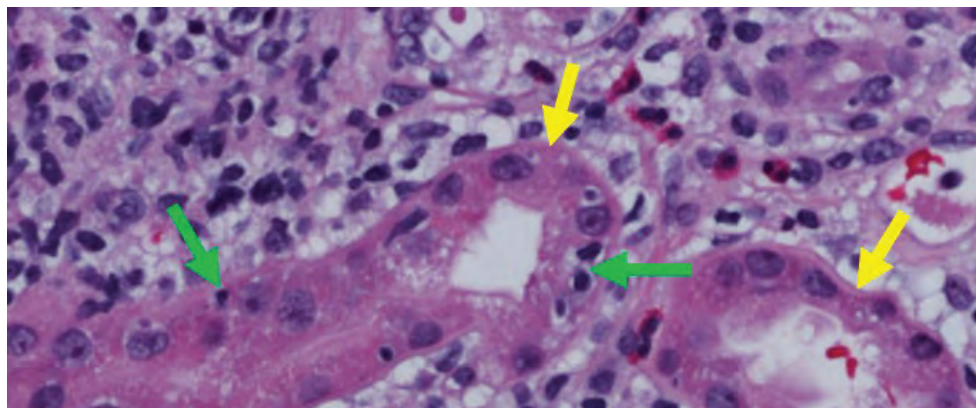
An autoimmune side effect of immune checkpoint inhibitor (ICI) drugs could signal improved control of kidney cancer, according to a new study by researchers in UT Southwestern's Kidney Cancer Program (KCP).

The study, published in the *Journal for Immuno-Therapy of Cancer*, may have broad implications for patients being treated with ICIs, a type of immunotherapy that is used against a large number of cancers, including lung, breast, liver, and head and neck tumors.

Renal cell carcinoma, the most common type of kidney cancer, is the ninth leading cause of cancer in the U.S. Once the cancer has spread to other organs, or metastasized, the survival rate averages 12 percent at five years.

With the advent of ICIs, kidney cancer survival rates are improving. However, only a fraction of patients respond to ICIs – and who will respond is unpredictable. ICIs disable cloaking mechanisms put in place by tumors to evade killing by immune cells. But disabling these cloaking mechanisms also increases the chances that the immune system will turn against the body, causing autoimmune side effects.

KCP investigators hypothesize that kidney cancer patients whose immune system attacked their kidneys may be more likely to benefit from ICIs. Using Kidney Cancer Explorer (KCE), a proprietary tool that extracts information from electronic health records, investigators identified metastatic kidney cancer patients treated with ICIs between 2014 and 2018. They analyzed thousands of laboratory test results provided by KCE to identify patients whose kidney functions became impaired. Out of 177 patients, they found 36 such patients.



Microscopic image of a kidney biopsy from a kidney cancer patient showing acute interstitial nephritis (AIN). Kidney tubules (yellow arrows) are under an immune attack (green arrows). The cancer became controlled with immunotherapy.

In three of the 36 patients, the impairment was due to an immune-mediated attack. A fourth more recent patient was also identified. All four patients developed acute interstitial nephritis (AIN), an autoimmune condition in which immune cells attack kidney cells, causing inflammation and swelling. While ICIs induce responses in the cancer in up to 40 percent of patients, in this case all four patients with AIN had a response.

"For 100 percent of patients to respond is quite significant," said Dr. Roy Elias, Assistant Instructor of Internal Medicine and co-first author of the study. "If a patient develops AIN, it is a sign that the treatment may be working."

This is not the first time that a particular autoimmune effect has been linked to increased response rates to ICIs, said Dr. James Brugarolas, Professor of Internal Medicine and Director of the Kidney Cancer Program. In fact, patients with melanoma who developed vitiligo, a condition in which skin pigment cells are killed by immune cells, also had higher chances of response.

Upon identifying a second example of an immune attack to the tissue of origin associated with a favorable cancer response, KCP investigators propose that this finding may be generalizable to other tumor types.

Dr. Roy Elias

Dr. James Brugarolas

"All cancer cells start out as normal cells," said Dr. Brugarolas. "Even after turning malignant, they retain some of their original traits. Thus, an attack against the tissue of origin may signal a higher chance that the immune system will also recognize and attack the cancer."

Further study will be needed to determine whether positive outcomes could be generalizable to patients with other cancers who are experiencing similar immune attacks against the cell of origin of the cancer.

■

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 on *Center Times Plus* at **utsouthwestern.edu/ctplus**.

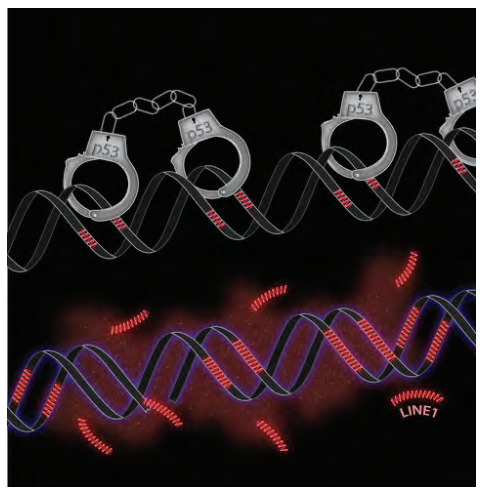
Cancer-fighting gene restrains 'jumping genes'

By Sarah Williams

About half of all tumors have mutations of the gene *p53*, normally responsible for warding off cancer. Now, UT Southwestern scientists have discovered a new role for *p53* in its fight against tumors: preventing retrotransposons, or "jumping genes," from hopping around the human genome. In cells with missing or mutated *p53*, the team found, retrotransposons move and multiply more than usual. The finding could lead to new ways of detecting or treating cancers with *p53* mutations.

"There's been long-standing literature associating retrotransposons with cancer," said Dr. John Abrams, Professor of Cell Biology at UTSW and senior author of the study published recently in *Genes & Development*. "What this work does is deliver the first empirical link between *p53* and retrotransposons in humans."

As a tumor suppressor gene, *p53* works by blocking cell growth, or inducing cellular suicide, when cells are under stress or dividing abnormally, as is the case in tumors. But researchers have long wondered whether the gene has another function. Even when the previously known targets of *p53* – genes involved in cell growth and death – are removed or mutated, *p53* still protects cells from cancer, suggesting additional, unknown targets. Moreover, the gene is found throughout evolution, including in ancient single-celled organisms.



This illustration depicts how retrotransposons are "handcuffed" by the tumor suppressor gene *p53*. But when *p53* is lost, these mobile elements can erupt. Credit: Study authors Drs. Amanda Jones and Bhavana Tiwari. Artwork by Angela Diehl.

"These genes existed long before the need for blocking cancer," Dr. Abrams said. "My lab has wondered what originally drove the evolution of *p53* genes and whether that knowledge can help us target cancer."

Retrotransposons are stretches of DNA that, after being transcribed into RNA, can insert themselves into new spots in the genome. These mobile genetic elements are considered beneficial to some degree – they can help genes evolve with new functions. However, they also have the potential to shuffle genomes and insert themselves into genes that are critical for cell health and growth, potentially contributing to cancer.

Dr. John Abrams

In 2016, Dr. Abrams and his colleagues discovered that retrotransposons were especially mobile when *p53* was inactivated in cells of flies and fish. In the new work, they set out to study whether the same was true in human cells.

When the researchers used CRISPR-Cas9 gene editing technology to remove *p53* from human cells, they found that the abundance of retrotransposons quickly increased. Cells derived from both cancers and normal lung tissue that were engineered to lack *p53* had roughly four times the rate of retrotransposon movement than cells still containing *p53*.

Dr. Abrams' team also introduced a synthetic, fluorescent-tagged retrotransposon to cells that let them follow the movement of the retrotransposon throughout the genome in real time. The results were similar to their first experiment; the retrotransposon was about four times more mobile, and therefore became more prevalent over time when cells lacked *p53*. The finding hints that one way in which *p53* works to prevent cancer is by blocking retrotransposons from leading to other cancer-causing mutations.

"In the clinic, one could use this information to possibly detect or mitigate *p53*-driven cancers by quantifying or blocking retrotransposon activity," said Dr. Abrams. A liquid biopsy, for instance, could be developed to detect an overabundance of retrotransposons that, theoretically, may precede cancers or be easier to detect than other cancer mutations.

The research team further solidified the link between *p53* and retrotransposons by showing that the p53 protein binds directly to one region of human retrotransposons. And they showed that a drug blocking the ability of retrotransposons to copy themselves prevented inflammation otherwise seen in cells with high levels of retrotransposon movement. More work is needed to determine whether a drug targeting retrotransposons could slow or stop the growth of existing cancers.

Co-first authors of the study in the Abrams lab are Dr. Bhavana Tiwari, a postdoctoral fellow, and Dr. Amanda Jones, Assistant Instructor of Cell Biology.

This research was supported by funds from the Cancer Prevention and Research Institute of Texas (RP170086), the American Cancer Society (128847-PF-15-160-01-DDC), and the National Institutes of Health (R01GM115682 and R01CA222579).

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O'Donnell

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where she later served on the Board of Trustees. In 1948, she graduated with a Bachelor of Arts in psychology from UT Austin, and later received the Distinguished Alumnus Award. That same year, she met her future husband, and the two were married in 1952, raising three daughters, Carol, Ann, and Ruth.

The couple established the O'Donnell Foundation in 1957 and worked together to oversee its substantial endeavors, which began with an initiative to improve passing rates for Advanced Placement test-takers and blossomed over decades to recognize outstanding teaching efforts, research efforts, arts education, and support that was instrumental in establishing Dallas' arts community.

At UT Southwestern, the O'Donnell Foundation provided funds for the Center for Human Nutrition and to support the research of Nobel Laureates Dr. Michael Brown and Dr. Joseph Goldstein. The Foundation continues to support their work, as well as fellow Nobel Laureate Dr. Bruce Beutler, and the many members of the National Academy of Sciences and the National Academy of Medicine with roots at UT Southwestern. To help ensure financial support for UTSW to train and mentor the next generation of medical scientists, the O'Donnell Foundation created the Endowed Scholars Program in Medical Science and provided a lead gift to help launch UT Southwestern's Clinical Services Initiative. In addition, the couple supported the establishment of the Peter O'Donnell Jr. Brain Institute, a comprehensive center dedicated to better understanding the basic molecular workings of the brain and applying those discoveries to the prevention and treatment of brain, spine, nerve, and muscle disorders.

Beyond her commitment to UT Southwestern, Mrs. O'Donnell spent much of her effort cultivating the Dallas Museum of Art, where she began as a docent, served as a member and Chair of its Education Committee, and served as a DMA Trustee since 1989. Recently, her passion and support for arts education led to an endowment allowing free general admission to the museum, the posting of its collection online, and the creation of an arts institute at UT Dallas bearing her name, which collaborates with UT Southwestern Medical School to foster research, teaching, and programs.

Mrs. O'Donnell was appointed to the Texas Commission on the Arts, the original board of the Friends of the Governor's Mansion of Texas, and the advisory board of The University of Texas College of Fine Arts. She also co-founded Young Audiences of Greater Dallas in 1989 (now Big Thought).

The O'Donnells developed the plan to endow the Dallas Symphony Orchestra Principal Musician Chairs, provided significant support to the Dallas Opera, and launched Met: Live at the Booker T. Washington High School for the Performing and Visual Arts.

In 2008, Edith and Peter O'Donnell together received honorary Doctor of Humane Letters degrees from Southern Methodist University for their pivotal roles in advancing the arts and education, and they were presented the College Board's Lifetime Achievement Award for excellence in education.

"Edith's efforts to cultivate arts, education, and health for Dallas is difficult to fully appreciate, and will be sorely missed. But it certainly carries forward in so many lives that her caring efforts were able to touch," said Dr. Podolsky.

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Dr. Beutler, a Regental Professor, is Director of the Center for the Genetics of Host Defense and a Professor of Immunology. He holds the Raymond and Ellen Willie Distinguished Chair in Cancer Research, in Honor of Laverne and Raymond Willie, Sr.

Dr. Brown, a Regental Professor, is Director of the Erik Jonsson Center for Research in Molecular Genetics and Human Disease, as well as a Professor of Molecular Genetics and Internal Medicine. He 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, is Chair of Molecular Genetics and a Professor of Molecular Genetics and Internal Medicine. He holds the Julie and Louis A. Beecherl, Jr. Distinguished Chair in Biomedical Research and the Paul J. Thomas Chair in Medicine.

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