CenterTimes

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NCI renews Simmons Cancer Center's comprehensive designation

The Simmons Cancer Center is one of the world's premier institutions for cancer research, diagnosis, and treatment. A 71,000-square-foot Radiation Oncology expansion opened this summer, and a new nine-story, 300,000-square-foot Outpatient Care Tower will open in 2022.

From Staff Reports

The National Cancer Institute has renewed the Harold C. Simmons Comprehensive Cancer Center's comprehensive designation, reaffirming its place among the country's elite cancer institutes.

There are 71 NCI-designated cancer centers in the U.S. Fifty-one of them are designated as Comprehensive Cancer Centers. This designation recognizes the centers' leadership in fighting cancer and includes them in a nationwide infrastructure that advances cancer discovery and patient care by integrating laboratory, clinical, and population-based research, as well as community outreach, education, and training.

Renewal of the NCI comprehensive designation came soon after the Simmons Cancer Center was ranked in the top 25 among hundreds of cancer centers in the nation by *U.S. News & World Report*.

The Simmons Cancer Center added a 71,000-square-foot Radiation Oncology expansion that opened this summer and will open a new nine-story, 300,000-square-foot Outpatient Care Tower in 2022.

"The Simmons Cancer Center is reaching new heights in translational cancer research and care. This latest recognition renews our commitment to fighting cancer using the latest laboratory and translational discoveries, clinical trials, and multidisciplinary patient care. It is an honor to lead an institution of some of the world's best clinicians and researchers in cancer," said Carlos L. Arteaga, M.D., Director of the Simmons Cancer Center.

With an interdisciplinary approach to investigating and treating cancer, the Simmons Cancer Center draws its members from 34 departments at UTSW and has 252 members, including Nobel Laureate Bruce Beutler, M.D., 13 members of the

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Tu, Tagliabracci selected as HHMI Investigators

Benjamin Tu, Ph.D.

Vincent Tagliabracci, Ph.D.

By Deborah Wormser

Two UT Southwestern researchers – a biochemist and a molecular biologist – are among 33 distinguished scientists nationwide recently named Howard Hughes Medical Institute (HHMI) Investigators.

Benjamin Tu, Ph.D., Professor of Biochemistry, and Vincent Tagliabracci, Ph.D., Associate Professor of Molecular Biology, bring to 14 the number of HHMI Investigators at UT Southwestern, the most of any Texas institution and the fourth largest in the nation. Both are members of UT Southwestern's Harold C. Simmons Comprehensive Cancer Center.

"We are delighted that Drs. Tagliabracci and Tu have been selected for this high honor on the basis of both their past work and especially their promise for important discoveries in the future," said Daniel K. Podolsky, M.D., President of UT Southwestern.

"Dr. Tagliabracci has uncovered an unexpected and novel family of pseudokinases that alter protein form and function in a way that's categorically distinct from canonical

Please see HHMI on page 2

UT Southwestern nurses celebrate earning renewed Magnet recognition, nursing's highest honor

John Warner, M.D., celebrates with Susan Hernandez, D.N.P., after learning UT Southwestern had once again earned nursing's highest honor, Magnet designation.

By Carol Marie Cropper

UT Southwestern's nurses were once again honored for excellence Sept. 15 as the Medical Center earned redesignation as a Magnet organization from the American Nurses Credentialing Center (ANCC).

Fewer than 9% of U.S. hospitals have earned Magnet designation, according to the ANCC's Commission on Magnet. It is considered the ANCC's highest honor, given to health care organizations that design nursing goals to improve patient outcomes. Although UT Southwestern first achieved Magnet status in 2016, programs must reapply and be reevaluated every four years. UTSW's appraisal, delayed by the pandemic, was in July.

Nurses and UTSW leaders across the campus watched and listened via Zoom videoconference that Wednesday morning as the hoped-for call arrived with the Chair of the ANCC's Commission on Magnet, Jeanette Ives Erickson, D.N.P., RN, NEA-BC, FAAN.

"The Commission has reviewed all of your submitted documentation and the findings from your site visit," Dr. Erickson said on the call broadcast to listeners. "… It's my absolute honor to tell you and your colleagues that we are officially notifying you that the Commission on Magnet has unanimously voted to credential UT Southwestern Medical Center as a Magnet organization."

UTSW's Associate Chief Nursing Officer for Nursing Excellence, Victoria England, D.N.P., RN, NE-BC, immediately called for a celebration.

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Peterson aims to transform UTSW into a clinical research powerhouse

Eric Peterson, M.D., M.P.H.

By Carol Marie Cropper

An extensive national search was conducted by UT Southwestern leadership for the right candidate to become its inaugural Vice Provost and Senior Associate Dean for Clinical Research, ultimately recruiting a prolific researcher who had run a major clinical research institute at Duke University.

Eric Peterson, M.D., M.P.H, joined the University last fall, charged with building UT Southwestern's clinical research program – which aims to translate lab findings into the clinic and test potentially lifesaving drugs and treatments in patients – into a powerhouse equal to its long-respected basic science program. His position was created to stimulate and

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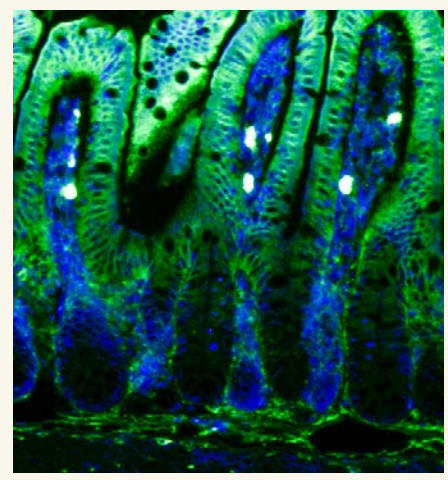

A microscope image of LRP1-expressing cells (green) in the intestine (cell nuclei are blue).

Scientists reveal how vitamin A enters immune cells in the gut

Study offers potential insights to treat digestive diseases, aid vaccine efficacy

By Christen Brownlee

Immunologists and geneticists at UT Southwestern have discovered how vitamin A enters immune cells in the intestines – findings that could offer insight to treat digestive diseases and perhaps help improve the efficacy of some vaccines.

"Now that we know more about this important aspect of immune function, we may eventually be able to manipulate how vitamin A is delivered to the immune system for disease treatment or prevention," said Lora Hooper, Ph.D., Chair of Immunology, a Howard Hughes Medical Institute Investigator, and

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Spong named Chair of Obstetrics and Gynecology

By Carol Marie Cropper

Catherine Spong, M.D., has been named Chair of the Department of Obstetrics and Gynecology, where she has served as Vice Chair since 2018. Dr. Spong is a tenured Professor of Obstetrics and Gynecology and a renowned expert in maternal-fetal medicine, a field in which she has led research to better understand fetal development, created an evidence base for obstetrical management, and been an advocate for including pregnant and lactating women in clinical studies.

In announcing the appointment, W. P. Andrew Lee, M.D., Executive Vice President for Academic Affairs, Provost, and Dean of UT Southwestern Medical School, noted that Dr. Spong is the author of many landmark clinical trials in obstetrics, gynecology, pediatrics, and fetal surgery that have defined the standard of care. Under her watch as Vice Chair, Dr. Lee said, William P. Clements Jr. University Hospital and Parkland Memorial Hospital achieved the highest level of maternal care, Level 4, from the state of Texas.

Before joining UTSW, Dr. Spong served as Deputy Director of the National Institute of Child Health and Human Development (NICHD), a division of the National Institutes of Health (NIH), where she spent 23 years in numerous capacities, including Acting Director, Director of Extramural Research, and Chief of the Pregnancy and Perinatology Research Branch.

Catherine Spong, M.D.

UT Southwestern drew Dr. Spong's interest because it has one of the largest obstetrics and gynecology departments in the country and combines excellence in research, education, and clinical care, she said.

"My passion has always been obstetrics, and I wanted to find a place that had great clinical volume, great research infrastructure, and a great name for education. Clearly, UT Southwestern fit the bill," Dr. Spong explained, adding that the department, which includes Clements University Hospital and Parkland Memorial Hospital, together deliver about 14,000 babies annually.

A focus of her research has been to provide evidence for the care of pregnant women and their babies by better understanding the developing fetus and placenta, said Dr. Spong. In order to better understand in real time the role of the placenta in fetal development, she launched the Human Placenta Project to critically study the placenta during pregnancy and how it changes throughout development rather than focusing only on the organ after delivery, which had been the common practice.

Dr. Spong is also a leader in advocating for inclusion of pregnant and lactating women in clinical trials, as well as for the inclusion of other underrepresented groups, such as children and older adults. She chaired the Task Force on Research Specific to Pregnant Women and Lactating Women established by Congress in 2017, which provided recommendations to Congress and the Secretary of Health and Human Services.

Other research she has led includes investigations into the optimal timing to deliver a preterm baby and the benefit of surgery to treat spina bifida, or myelomeningocele, on fetuses in the mother's womb before birth.

At UT Southwestern, Dr. Spong has continued her research calling for greater inclusion of pregnant and lactating women in studies. An opinion article she co-authored in *JAMA* earlier this year pointed out that while pregnant women hospitalized with COVID-19 are at greater risk of delivering their babies early, they were not included in the development and clinical evaluation of vaccines and treatments, leaving them and their doctors with limited information to make decisions.

"Oftentimes, pregnant and lactating women are excluded from research, as well as children and the elderly, and that then limits the ability to determine whether interventions can improve outcomes for them," she said.

As Chair, Dr. Spong said she plans to expand research, grow the Division of Gynecology, and develop specialty clinics to enhance the institution's local, national, and international reputation.

"We have an excellent foundation and we're going to build on that foundation – we have the ability to do more," she said.

Dr. Spong completed a six-year combined B.A./M.D. program at the University of Missouri-Kansas City School of Medicine. She then completed her internship and residency at Harbor-UCLA Medical Center and a fellowship in maternal-fetal medicine at the NIH and Georgetown University.

Among honors in her field, she has received the Society for Maternal-Fetal Medicine Lifetime Achievement Award and the American College of Obstetricians and Gynecologists' Distinguished Service Award.

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

Dr. Spong holds the Paul C. MacDonald Distinguished Chair in Obstetrics and Gynecology.

Acute care cardiologist joins UTSW as Chief of Pediatric Cardiology

By Carol Marie Cropper

Nicolas Madsen, M.D., M.P.H., a specialist in acute care cardiology, has been named Chief of Pediatric Cardiology at UT Southwestern and Chief of Cardiology and co-Director of The Heart Center at Children's Health.

Dr. Madsen, Associate Professor of Pediatrics and Population and Data Sciences, joined UT Southwestern in September from Cincinnati Children's, where he served as Medical Director of the Heart Institute and the Acute Care Cardiology Unit and as an Associate Professor at the University of Cincinnati's Department of Pediatrics.

His expertise is in acute care cardiology, caring for children hospitalized with congenital and acquired heart conditions and adults with congenital heart disease. He is co-founder and co-Director of the Pediatric Acute Care Cardiology Collaborative, an international learning network with over 40 hospital member centers that aims to drive better outcomes and experiences for children hospitalized with heart conditions.

"I'm thrilled to join the team at UT Southwestern, given the tremendous opportunities for discovery, innovation, and multidisciplinary collaboration," Dr. Madsen said. "I am excited to lead the Division as we explore new horizons and develop new programs that optimize outcomes for our patients, including traditional cardiac measures, as well as those specific to neurodevelopment, mental health, and quality of life."

The cooperation between UT Southwestern and Children's Health attracted him to the role.

"The advancement of knowledge and the symbiotic relationship between academic research and hospital implementation is a passion," Dr. Madsen said. "With the close affiliation between Children's Health and UT Southwestern, I see profound opportunities for discovery and learning."

Dr. Madsen received his medical degree from the University of Washington School of Medicine, as well as a Master of Public Health degree from the University of Washington School of Public Health. He completed his residency in pediatrics and a cardiology fellowship at Seattle Children's Hospital.

"Dr. Madsen is highly regarded on the national stage, and he brings important leadership and vision that will bring much honor to the Division of Cardiology and the Department of Pediatrics," said Stephen Skapek, M.D., Professor and Interim Chair of Pediatrics.

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Dr. Skapek holds the Distinguished Chair in Pediatric Oncology Research.

Nicolas Madsen, M.D., M.P.H.

HHMI Continued from page 1

kinases. His work shines a new light on a diverse array of physiological processes that rely on these enzymes," said Dr. Podolsky. "Dr. Tu's work linking cellular metabolism to critical cell functions is leading to a better understanding of a variety of diseases, including cancer."

Each Investigator will receive roughly $9 million over a seven-year term, which is renewable pending a scientific review by HHMI, a philanthropic organization created to advance basic biomedical research and science education for the benefit of humanity.

Dr. Benjamin Tu

Dr. Tu's lab studies how fundamental cellular processes, such as cell growth and division, transcription, translation, mitochondrial homeostasis, and autophagy, are coordinated with the metabolic state of the cell. For many of their studies, Dr. Tu and his colleagues use the budding yeast *Saccharomyces cerevisiae* as a model organism to discover fundamental regulatory principles; they have also expanded some of their findings to mammalian systems.

"I am grateful to my past and present trainees for their dedication and perseverance in the process of scientific discovery. Seeing their excitement when the HHMI announcement came out was one of the nicest feelings," said Dr. Tu. "For our approach and work to be recognized by the HHMI is reassuring and truly an honor. And now, to have the freedom and resources to venture in new research directions, it's exhilarating to think of the possibilities."

Dr. Tu's research has shown that metabolites play underappreciated roles in the regulation of cell growth and homeostasis. For example, in a 2011 study published in *Molecular Cell*, Dr. Tu and his colleagues defined a key role for the metabolite acetyl-CoA in turning on the genes necessary for cell growth. This new understanding of the importance of acetyl-CoA led to a 2014 *Cell* paper in which the team reported how the metabolite might also be important for the survival and growth of liver cancer cells. Dr. Tu's current research in mice is investigating if chemicals that inhibit acetyl-CoA synthesis may slow the growth of pancreatic cancer.

Dr. Tu came to UT Southwestern in 2004 after receiving master's and bachelor's degrees in chemistry from Harvard University and a Ph.D. in biochemistry and biophysics from the University of California, San Francisco. He worked as a postdoctoral fellow with Steven McKnight, Ph.D., Professor and former Chair of Biochemistry, before joining the UTSW faculty in 2007. His previous honors include selection as a finalist for the Blavatnik National Award for Young Scientists.

Dr. Vincent Tagliabracci

Dr. Tagliabracci's lab studies how extracellular proteins are modified by phosphorylation – the addition of a phosphate group that can change the proteins' activity – by a novel family of enzymes called pseudokinases that are secreted from cells. This branch of the kinase family is so different from canonical kinases that it was originally not included on the human kinome tree.

The pseudokinases were long considered to be nonfunctional; however, Dr. Tagliabracci's work has shown that these enzymes perform completely different kinds of chemical reactions than classical kinases. These reactions include a process called AMPylation, in which some pseudokinases transfer adenosine monophosphate, one of the nucleotides that makes up DNA, to proteins, and glutamylation, in which pseudokinases transfer the amino acid glutamate to proteins.

"I am honored to join the ranks of HHMI Investigators and thankful for my lab members, collaborators, departmental colleagues, and Chair, Eric Olson, Ph.D., for helping to push this research in new directions," said Dr. Tagliabracci. "This support will allow us to continue to unravel the mysteries of pseudokinases and their relevance to human health."

Pseudokinases appear to play key roles in a broad array of physiological processes important to human health, including lipid metabolism, wound healing, cell migration, biomineralization, inflammation, and nervous system development, he said.

Dr. Tagliabracci received his B.S. in chemistry and biology from the University of Indianapolis and his Ph.D. in biochemistry and molecular biology from Indiana University. In 2010, he joined the laboratory of Jack Dixon, Ph.D., as a postdoctoral fellow at the University of California, San Diego, where he identified the pseudokinase Fam20C as the long-sought kinase that phosphorylates a milk protein. In 2015, he joined the faculty at UT Southwestern as an Assistant Professor in the Department of Molecular Biology.

Among previous honors are the Pathway to Independence Award from the National Institutes of Health, the Norman Hackerman Award in Chemical Research from The Welch Foundation (2020), an NIH Director's New Innovator Award (2019-2024), and a Cancer Prevention and Research Institute of Texas (CPRIT) recruitment of first-time, tenure-track faculty member award.

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

Dr. Olson holds the Pogue Distinguished Chair in Research on Cardiac Birth Defects, The Robert A. Welch Distinguished Chair in Science, and the Annie and Willie Nelson Professorship in Stem Cell 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. Tagliabracci is a Michael L. Rosenberg Scholar in Medical Research.

Dr. Tu, a UT Southwestern Presidential Scholar, holds the Martha Steiner Professorship in Medical Research and is a W.W. Caruth, Jr. Scholar in Biomedical Research.

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

CenterTimes

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President: Dr. Daniel K. Podolsky

Executive Vice President for Institutional Advancement: Dr. Marc Nivet

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Director, Institutional Communications: Debbie Bolles

Editor: Debbie Bolles

Writers: Courtney Borchert, Christen Brownlee, Carol Marie Cropper, Jan Jarvis, Rachel Stowe Master, Patrick McGee, Patrick Wascovich, Deborah Wormser

Copy Editors: Denita Nash, Rachel Stowe Master

Town Hall highlights UTSW successes, advancements during pandemic

By Patrick Wascovich

In a virtual Town Hall held on Sept. 21, UT Southwestern President Daniel K. Podolsky, M.D., shared an update on priorities and progress the institution has made over the past year in the midst of fighting a pandemic. In his address, held online due to continuing COVID-19 protocols, Dr. Podolsky also informed the UTSW community about upcoming growth opportunities, planned initiatives, and the institution's identified strategic priorities for the next year.

"Great things have been accomplished throughout the past year by the dedicated people who come to UT Southwestern each day," Dr. Podolsky said. "A foremost priority of FY22 will necessarily be to prepare for and respond to the various challenges that the pandemic presents, including the health and well-being of each of you, along with the patients and families we serve."

Dr. Podolsky outlined other priorities of the new fiscal year, including planning for a School of Public Health; recruiting leadership for several academic departments; expanding equity, diversity, and inclusion efforts; enacting a plan to transform, enhance, and grow clinical efforts; investing in future campus growth; and promoting the well-being of faculty, staff, and learners.

The President discussed how UT Southwestern has successfully addressed the multifaceted challenges of COVID-19 in new ways, focused on improved patient outcomes and greater patient satisfaction. In addition to acknowledging UT Southwestern's success in pivoting thousands of faculty, employees, and students to work and learn remotely, Dr. Podolsky also highlighted UT Southwestern's return to exceptional in-person clinical care and expansion of telemedicine as an option when appropriate.

In 2021, record numbers of patients turned to UT Southwestern seeking help from our physicians, working along with our nursing colleagues and staff as well as our learners, Dr. Podolsky said. There was an increase of more than 10% – fully 4,400,000 patient visits – in the number of patients cared for in our University Hospital and clinics, as well as our partners. The way in which UTSW is delivering that care has continued to evolve, he added, with nearly 20% of patients' visits provided in a virtual format.

Other significant achievements highlighted from the 2021 fiscal year included:

- William P. Clements Jr. University Hospital ranked by *U.S. News & World Report* as the No. 1 Best Hospital in Dallas-Fort Worth for the fifth year in a row
- Planning for the first state psychiatric hospital in the Dallas-Fort Worth region, in partnership with the Texas Health and Human Services Commission
- Growing UTSW's clinical presence in North Texas, including construction of a new regional medical center at the redeveloped RedBird Mall in southern Dallas
- Redesignation of the Harold C. Simmons Comprehensive Cancer Center as a Comprehensive Cancer Center by the National Cancer Institute

President Daniel K. Podolsky, M.D.

- Magnet redesignation by the American Nurses Credentialing Center
- Continued growth of Southwestern Health Resources as a vital network that provides care for nearly 100,000 Medicare beneficiaries in North Texas – more than any other accountable care organization in the region

In Academic Affairs, Dr. Podolsky said the top priority for the new fiscal year will be to implement plans for a School of Public Health, UTSW's first new school in more than 50 years and the institution's fourth overall. Dr. Podolsky also shared that he was eager to see UTSW's vision to advance the science of public health through research innovation, while preparing a robust public health workforce, to come to life for the benefit of those who live in North Texas and beyond. Celette Sugg Skinner, Ph.D., Chair of Population and Data Sciences, has been named Interim Dean of the new school, which will enroll Master of Public Health students in the fall of 2023 and Ph.D. students in the fall of 2024.

Dr. Podolsky also mentioned another important priority for the institution – one that will positively shape and impact the region: a joint project with the Texas Health and Human Services Commission to plan and build DFW's first state-funded psychiatric hospital. UT Southwestern will oversee the construction of the new hospital and will operate it to provide much needed expanded access to this dimension of the continuum of mental health services, said Dr. Podolsky.

Another key initiative is expansion of the Biomedical Engineering program – in collaboration with UT Dallas – into a full-fledged department that will be led by the inaugural Chair, Samuel Achilefu, Ph.D., and located in a new building to open in 2023 on the East Campus. Other key departmental leadership appointments announced recently include Catherine Spong, M.D., Chair of Obstetrics and Gynecology, and J. William Harbour, M.D., Chair of Ophthalmology.

Dr. Podolsky also cited the continued efforts by researchers, saying, "Our research community has remained focused on the important unanswered questions, particularly those that can eventually lead to better means of treatment, cure, and prevention of disease."

Of note, major accomplishments or key leadership appointments in the research area include:

- Election to the National Academy of Sciences of Margaret Phillips, Ph.D., Chair of Biochemistry and Professor of Pharmacology; and Donald Hilgemann, Ph.D., Professor of Physiology, Internal Medicine, and in the Charles and Jane Pak Center for Mineral Metabolism and Clinical Research
- Election to the National Academy of Medicine of Ralph DeBerardinis, M.D., Ph.D., Professor of Pediatrics and Chief of the Division of Pediatric Genetics and Metabolism, whose primary appointment is Professor at the Children's Medical Center Research Institute at UT Southwestern (CRI)
- Selection by the Howard Hughes Medical Institute (HHMI) of Vincent Tagliabracci, Ph.D., Associate Professor of Molecular Biology, and Benjamin Tu, Ph.D., Professor of Biochemistry, as new Investigators
- The recruitment of Eric Peterson, M.D., M.P.H., to the newly created role of Vice Provost and Senior Associate Dean for Clinical Research; the recruitment of Joan Conaway, Ph.D., as the new Vice Provost and Dean of Basic Research; and the appointment of Elliott Ross, Ph.D., to the new position of Associate Dean for Basic Research

Dr. Podolsky again emphasized that UT Southwestern is unequivocally committed to promoting diversity, providing equal opportunity, and prohibiting racial discrimination – and to sustaining a safe and secure environment for learning and working for all students, trainees, faculty, and staff.

"We must lean in and assure that our commitment to these values and obligations permeates all aspects of what we do as an institution," he said. "Promoting diversity is a moral imperative for our institution. In addition to being the right thing to do, it is a catalyst for innovation in fulfilling our mission, and it is essential for achieving UT Southwestern's full potential as a leading academic medical center."

To that end, UTSW is launching a national search for a Chief Diversity Officer. This new executive will focus exclusively on diversity, inclusion, equity, and community engagement, with responsibility for identifying barriers that limit opportunity for any historically underrepresented groups on campus and proposing actions to help ensure that each community member develops the cultural awareness and competency needed to advance the Medical Center's mission.

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

Dr. DeBerardinis holds the Joel B. Steinberg, M.D. Distinguished Chair in Pediatrics, and is a Sowell Family Scholar in Medical Research.

Dr. Hilgemann holds the Roy and Christine Sturgis Chair in Biomedical Research, and the Floyd C. Rector, Jr., M.D. Professorship in Acid-Base Regulation.

Dr. Peterson holds the Adelyn and Edmund M. Hoffman Distinguished Chair in Medical Science.

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

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. Ross holds the Greer Garson and E.E. Fogelson Distinguished Chair in Medical Research.

Dr. Skinner holds the Parkland Community Medicine Professorship.

Dr. Spong holds the Paul C. MacDonald Distinguished Chair in Obstetrics and Gynecology.

Dr. Tagliabracci is a Michael L. Rosenberg Scholar in Medical Research.

Dr. Tu, a UT Southwestern Presidential Scholar, holds the Martha Steiner Professorship in Medical Research and is a W.W. Caruth, Jr. Scholar in Biomedical Research.

NCI Continued from page 1

National Academy of Sciences, five members of the National Academy of Medicine, and 14 Howard Hughes Medical Institute Investigators.

Simmons Cancer Center members continue to publish in the most prestigious journals, including *Science*, *Cell*, *Nature*, *JAMA*, *The New England Journal of Medicine*, and *The Journal of Clinical Oncology*. They published more than 700 pieces in medical and scientific journals in 2020. Twenty-three patents have been issued to Simmons Cancer Center members.

Clinical teams in the Center treat more than 8,000 new cancer patients a year, and the Center has 376 active clinical trials. The Simmons Cancer Center has two of the NCI's highly competitive Specialized Programs Of Research Excellence (SPORE) grants, in kidney cancer and in lung cancer.

The Simmons Cancer Center supports five research programs: Cellular Networks in Cancer, Chemistry and Cancer, Development and Cancer, Experimental Therapeutics, and Population Science and Cancer Control, as well as an Office of Community Outreach, Engagement, and Equity; and an Office of Education and Training. Cancer screening and prevention efforts extend beyond North Texas, and patients from all parts of the U.S. come to the Simmons Cancer Center for its high-quality care.

Currently, Simmons Cancer Center members have over $90 million in extramural cancer-focused research funding. For the last 10 years, the Center has received more than $493 million for cancer research, training, and prevention from the Cancer Prevention and Research Institute of Texas (CPRIT).

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

Dr. Beutler, a Regental Professor, holds the Raymond and Ellen Willie Distinguished Chair in Cancer Research, in Honor of Laverne and Raymond Willie, Sr.

Simmons Cancer Center Director Carlos L. Arteaga, M.D., left, examines samples in the lab with Instructor Dhivya Sudhan, Ph.D.

Sending out an SOS to protect the heart

Distress signal from fat cells prompts heart to shore up defenses against consequences of obesity

By Christen Brownlee

A stress signal received by the heart from fat could help protect against cardiac damage induced by obesity, a UT Southwestern-led study suggests. The finding, published in *Cell Metabolism*, could help explain the "obesity paradox," a phenomenon in which obese individuals have better short- and medium-term cardiovascular disease prognoses compared with those who are lean, but with ultimately worse long-term outcomes.

"The mechanism we have identified here could be one of many that protects the heart in obesity," said study leader Philipp E. Scherer, Ph.D., a UTSW Professor of Internal Medicine and Cell Biology who has long studied fat metabolism.

Study co-leader Clair Crewe, Ph.D., former Assistant Instructor of Internal Medicine, explained that the metabolic stress of obesity gradually makes fat tissue dysfunctional, causing its mitochondria – the cellular organelles that generate energy – to shrink and die. Eventually, this unhealthy fat loses the ability to store lipids generated by excess calories in food, poisoning other organs through an effect called lipotoxicity. Some organs, including the heart, appear to mount a preemptive defense to protect against lipotoxicity. To date, how the heart senses the dysfunctional state of fat has been unknown.

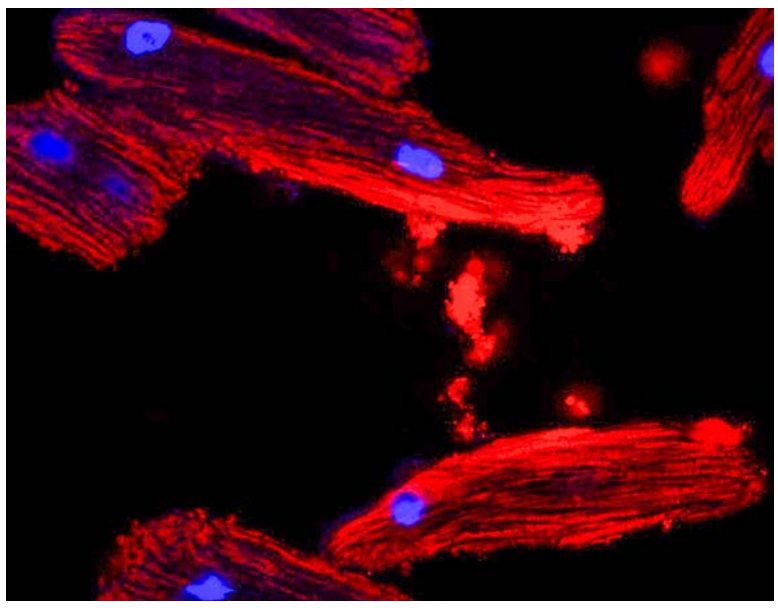
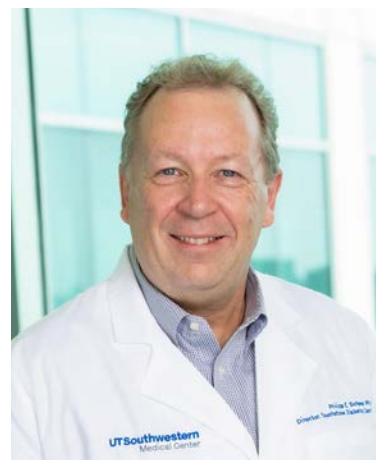


Image shows heart cells that have taken up red-colored fat cell-derived extracellular vesicles.

UTSW researchers used a genetic technique to speed the loss of mitochondrial mass and function in mice. When these animals ate a high-fat diet and became obese, their fat cells began sending out extracellular vesicles filled with small pieces of dying mitochondria. Some of these mitochondrial snippets traveled through the bloodstream to the heart, triggering oxidative stress, a state in which cells generate harmful free radicals.



Philipp E. Scherer, Ph.D.

To counteract this stress, heart cells produce a flood of antioxidant molecules. This protective backlash was so strong that when the scientists injected mice with extracellular vesicles filled with mitochondrial snippets and then induced a heart attack, the animals had significantly less heart damage compared with mice that didn't receive an injection.

Further research using fat tissue sampled from obese patients showed that these cells also release mitochondria-filled extracellular vesicles, Dr. Crewe said, suggesting that the effects observed in mice also take place in humans.

Eventually, she explained, the heart and other organs in obese individuals become overwhelmed by lipotoxic effects, leading to many of obesity's comorbidities. Learning how to artificially generate the protective mechanism identified in this study could lead to new ways to buffer obesity's negative consequences, Dr. Crewe said. This knowledge could even suggest strategies to protect the heart against damage in lean individuals as well.

"By better understanding the distress signal from fat," Dr. Crewe said, "we may be able to harness the mechanism to improve heart health in obese and nonobese individuals alike."

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Dr. Scherer holds the Gifford O. Touchstone, Jr. and Randolph G. Touchstone Distinguished Chair in Diabetes Research and the Touchstone /West Distinguished Chair in Diabetes Research.

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

NEJM: Anticoagulants help moderately ill COVID-19 patients

By Patrick McGee

Moderately ill patients hospitalized with COVID-19 have better chances of survival if treated with therapeutic-dose anticoagulation, according to an international study involving 121 sites including UT Southwestern.

Moderately ill COVID-19 patients treated with therapeutic-dose anticoagulation with unfractionated or low molecular-weight heparin were 27% less likely to need cardiovascular respiratory organ support, such as intubation, said Ambarish Pandey, M.D., Assistant Professor of Internal Medicine, who served as site investigator and co-author of the study in *The New England Journal of Medicine*. Moderately ill patients had a 4% increased chance of survival until discharge without requiring organ support with anticoagulants, according to the study involving 2,200 patients.

Heparin is an anticoagulant, or blood thinner, that prevents the formation of blood clots. The injectable medication is typically used to treat and prevent blood clots.

Ambarish Pandey, M.D.

In patients hospitalized with moderate COVID-19, the study found those treated with therapeutic-dose heparin were 27% less likely to need respiratory support such as intubation.

"The 4% increase in survival to discharge without needing organ support represents a very meaningful clinical improvement in these patients," said Dr. Pandey, a Texas Health Resources Clinical Scholar who specializes in preventive cardiology and heart failure with preserved ejection fraction. "If we treat 1,000 patients who are hospitalized with COVID-19 with moderate illness, an additional 40 patients would have meaningful improvement in clinical status."

Participating platforms for the study, which defined moderately ill patients as those who did not need intensive care unit-level support, included Antithrombotic Therapy to Ameliorate Complications of COVID-19 (ATTACC); A Multicenter, Adaptive, Randomized Controlled Platform Trial of the Safety and Efficacy of Antithrombotic Strategies in Hospitalized Adults with COVID-19 (ACTIV-4a); and Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP). Comparisons among the three platforms are provided in the supplementary appendix, available with the full text of the article at nejm.org.

A parallel study in *The New England Journal of Medicine* found that therapeutic-dose anticoagulation did not help severely ill patients.

Vitamin A Continued from page 1

Lora Hooper, Ph.D.

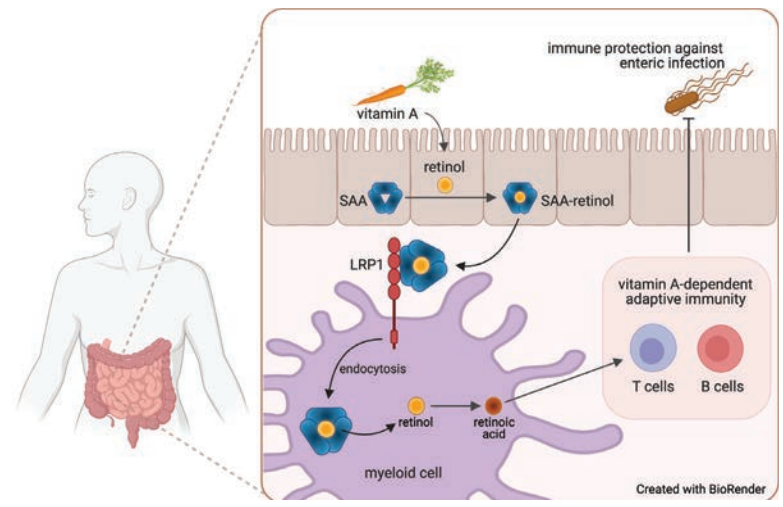
senior author of the study published in *Science*.

Vitamin A – a fat-soluble nutrient that the body converts to a molecule called retinol and then to retinoic acid before it can be used – is important for every tissue in the body, said Dr. Hooper, also Professor of Immunology, Microbiology, and in the Center for the Genetics of Host Defense. The vitamin is particularly crucial for the adaptive immune system, a subset of the broader immune system that reacts to specific pathogens based on immunological memory, the type formed by exposure to disease or vaccines.

Although researchers knew that some intestinal immune cells called myeloid cells can convert retinol to retinoic acid, how they acquire retinol to perform this task was a mystery, said Dr. Hooper, whose lab investigates how resident intestinal bacteria influence the biology of humans and other mammalian hosts.

Lead author Ye-Ji Bang, Ph.D., a postdoctoral fellow in the Hooper lab, and colleagues focused on serum amyloid A proteins, a family of retinol-binding proteins that some organs produce during infections. They used biochemical techniques to determine which cell surface proteins they attached to, and identified LDL receptor-related protein 1 (LRP1).

LRP1 was discovered more than 30 years ago by fellow UT Southwestern researcher Joachim Herz, M.D., Director of the Center for Translational Neurodegeneration Research and Professor of Molecular Genetics, Neurology, and Neuroscience. The Herz lab focuses on the molecular mechanisms by which the members of the LDL receptor gene family function as signaling and endocytic receptors in the brain and vascular wall. The discovery of the LDL receptor, made at UT Southwestern, helped earn Michael Brown, M.D., and Joseph Goldstein, M.D., the 1985 Nobel Prize in Physiology or Medicine. Dr. Brown is Professor of Molecular Genetics and Internal Medicine, while Dr. Goldstein is Chair of Molecular Genetics and Professor of Internal Medicine.



Dietary vitamin A becomes retinol, which is internalized into cells by LRP1 and promotes adaptive immunity in the intestine. Credit: Courtesy of the Hooper lab using biorender.com

Drs. Bang, Hooper, Herz, and colleagues showed that LRP1 was present on intestinal myeloid cells, where it appeared to shuttle retinol inside. When the researchers used genetic techniques to delete the gene for this receptor in mice – preventing their myeloid cells from taking up the vitamin A derivative – the adaptive immune system in their gut virtually disappeared, said Dr. Hooper. T and B cells and the molecule immunoglobulin A, critical components of adaptive immunity, were significantly reduced. Researchers then compared the response to *Salmonella* infection between mice with LRP1 and those without. Those missing the receptor were quickly overcome by the infection.

The findings suggest that LRP1 is the vehicle by which retinol enters myeloid cells. If researchers can develop a way to inhibit this process, said Dr. Hooper, it could tamp down the immune response in inflammatory diseases that affect the intestines, such as inflammatory bowel and Crohn's diseases. Alternatively, finding a way to enhance LRP1 activity could boost immune activity, making oral vaccines more effective.

Other UTSW researchers who contributed to this study include Zehan Hu, Yun Li, Sureka Gattu, Kelly A. Ruhn, and Prithvi Raj.

This work was supported by grants from the National Institutes of Health (R01 DK070855), The Welch Foundation (I-1874), the Walter M. and Helen D. Bader Center for Research on Arthritis and Autoimmune Diseases, and the Howard Hughes Medical Institute.

■

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

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

Dr. Herz holds the Presbyterian Village North Foundation Distinguished Chair in Alzheimer's Disease Therapeutic Research, and the Thomas O. and Cinda Hicks Family Distinguished Chair in Alzheimer's Disease Research.

Dr. Hooper holds the Jonathan W. Uhr, M.D. Distinguished Chair in Immunology and is a Nancy Cain and Jeffrey A. Marcus Scholar in Medical Research, in Honor of Dr. Bill S. Vowell.

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

Enzyme could be major driver of preeclampsia

Finding could lead to new treatments for life-threatening pregnancy complication

By Christen Brownlee

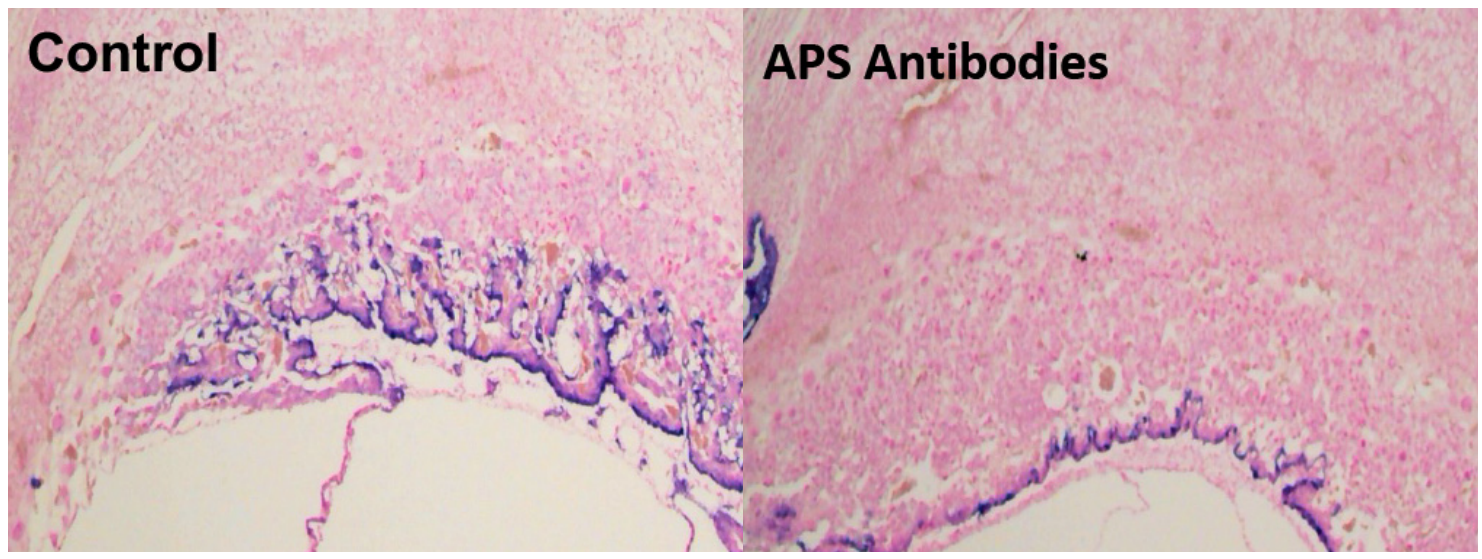
A study by UT Southwestern scientists indicates that the enzyme protein phosphatase 2 (PP2A) appears to be a major driver of preeclampsia, a dangerous pregnancy complication characterized by the development of high blood pressure and excess protein in the urine. The finding, published in *Circulation Research*, could lead to new treatments for preeclampsia other than premature delivery, which is often the only option.

"Preeclampsia is a regrettably common cause of premature birth, which can be life-threatening for babies and lead to lifelong consequences. Through identifying PP2A's role in this condition, we may be able to develop treatments for preeclampsia that are far better for both mothers and babies," said study leader Philip W. Shaul, M.D., Professor and Vice Chair for Research in the Department of Pediatrics and Director of the Center for Pulmonary and Vascular Biology. Dr. Shaul co-led the study with Chieko Mineo, Ph.D., Professor of Pediatrics and Cell Biology.

Preeclampsia, which affects 5% to 7% of pregnant women worldwide, can be deadly for gestating mothers and their babies and require premature delivery.

Although the causes of preeclampsia are not well understood, researchers have linked the condition to a variety of risk factors. One is the autoimmune disease antiphospholipid syndrome (APS), in which antibodies react to proteins on the surface of some cells. Although APS is relatively rare – affecting only about 5 in every 100,000 people – studies have identified APS antibodies in about 29% of pregnant women with preeclampsia.

To understand how APS leads to preeclampsia, researchers created an animal model by injecting pregnant mice with APS antibodies. These animals developed high blood pressure and a rise in urine protein, both characteristics of preeclampsia.



Images show how APS antibodies inhibit trophoblast migration in the mouse placenta.

Based on previous work, the researchers knew that the protein ApoER2 may be related to the harmful actions of APS antibodies on placental cells called trophoblasts. These cells, which normally journey from the fetal side of the placenta to the maternal side to provide the fetus with nutrients, do not successfully make that connection in preeclampsia. In mice, the APS antibodies prevented trophoblast migration and growth of the fetus was restricted. When the researchers genetically engineered mice without ApoER2 in trophoblasts, the fetuses developed normally despite APS antibody treatment and the mothers were protected from developing preeclampsia.


Philip W. Shaul, M.D.

But the scientists knew ApoER2 didn't tell the whole story. They found that in the presence of the APS antibodies, ApoER2 triggered the activity of PP2A, an enzyme that regulates protein functions. Further experiments showed that in the pregnant mice with APS antibodies, heightened activity in PP2A increased trophoblast production of proteins involved in preeclampsia.

When the researchers gave the pregnant mice a drug inhibiting PP2A, the rodents were protected from preeclampsia – and the treatment had no apparent harmful effects on the mice or their gestating babies.

Hoping to translate these findings to humans, the scientists examined placentas from women with APS, finding that the placentas, too, had increased PP2A activity. However, compared with placentas from normal pregnancies, those from preeclamptic patients without APS also had increased PP2A activity, suggesting that this mechanism could be operative in a variety of forms of preeclampsia. With further research, Dr. Shaul said, treatments targeting PP2A or its related machinery in the trophoblast may eventually be viable treatments for preeclampsia in pregnant women.

■

Dr. Shaul holds the Associates First Capital Corporation Distinguished Chair in Pediatrics.

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

Magnet Continued from page 1

"I think we deserve a great big cheer. Everybody unmute," she said, followed by a chorus of "Woohoo!" and "Congratulations everybody!"

"I'm so proud of this team. They're fantastic," said UTSW's Associate Vice President and Chief Nurse Executive Susan Hernandez, D.N.P., M.B.A., BSN, RN, adding that the designation is a reflection of true multidisciplinary teamwork.

"Yes, Magnet is a nursing designation, and yes, I'm a proud nurse," Dr. Hernandez said. "But we don't do this by ourselves, and we know that. So thank you to all the teammates who dove in and helped us along in this five-year journey."

UT Southwestern President Daniel K. Podolsky, M.D., as well as Executive Vice President for Health System Affairs John Warner, M.D., also took part in the Zoom video meeting.

"I am thrilled by this recognition of the outstanding work that our nursing colleagues here at UT Southwestern carry out day in and day out," Dr. Podolsky said.

Dr. Warner spoke of how he worked with nursing leaders over almost a decade to arrive at this moment of recognition.

"You really have come together to produce an amazing nursing program across UT Southwestern and something I am personally really proud of," he said.

To earn initial Magnet recognition, a medical center must submit a comprehensive application that is reviewed by the Commission on Magnet. Commission reviewers then visit the campus to evaluate the level of nursing care provided and the respect that nurses are given within the institution, as well as opportunities for them to advance their practice through research and professional development.

In announcing the Commission's decision, Dr. Erickson cited four areas of UTSW excellence, referred to as Exemplars:

- The nursing staff's mobilization in response to COVID-19, setting up four community sites and providing 80,000 tests over two months and more than 4,000 vaccinations during the height of the pandemic
- Creation of a culture and organizational support network that encourages focus on patients and their families
- Support for research and evidence-based practices by nurses
- Nurse involvement in leadership and activities to find ways to improve patient care and safety

Such efforts are part of a plan for excellence, Dr. Hernandez said.

"We want to be mentioned in the first sentence of the best nursing programs in the United States," she said.

■

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

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

More online: To watch videos related to the Magnet announcement, go to *Center Times Plus* at **utsouthwestern.edu/ctplus**.

Clinical Research Continued from page 1

enhance UT Southwestern's growing clinical research enterprise, according to W. P. Andrew Lee, M.D., UTSW's Executive Vice President for Academic Affairs, Provost, and Dean of the Medical School.

"I want UTSW to be a national leader in clinical research," said Dr. Peterson, a cardiologist and Professor of Internal Medicine.

On his agenda: increasing the number of top-notch clinical researchers, as well as transforming UTSW research operations into a model for supporting efficient and high-quality clinical research. Dr. Peterson comes well prepared for the task. For six years, he was Executive Director of the Duke Clinical Research Institute, one of the nation's largest clinical research institutes.

"We want to increase our capacity of high-quality researchers," Dr. Peterson said. "This recruitment will be broad-based and done in conjunction with departmental and center Chairs across the campus."

Dr. Peterson's past as a researcher himself gives him an understanding of what the institution can do to make a clinical researcher's life easier – or more difficult. As such, he also wants to make the operations for clinical research stronger.

He added, "We need to make UT Southwestern a place that clinical researchers want to be. They're not going to come or stay unless we have a solid infrastructure for clinical research."

That means adding faster computers, cloud computing, and other digital and mobile technologies, Dr. Peterson said. It also will mean helping researchers use existing data, such as that contained in the Health System's electronic medical records, to identify and more easily recruit patients into their studies. William P. Clements Jr. University Hospital and Parkland Memorial Hospital, as well as the entire Texas Health Resources system, should all become places where clinical care and research are merged, he said.

Dr. Peterson is also committed to improving the processes supporting research. He said this will include hiring individuals to support grant writing, creating standardized templates for study budgets, and streamlining the ethical review process required for a research project.

Additionally, Dr. Peterson is a strong believer in the need for clinical research training. Through a collaboration with the UTSW School of Health Professions, a Master of Science in Clinical Science program has been relaunched that will give physicians the tools to conduct clinical research. The first class began this fall. He also is committed to creating a series of training modules for study coordinators to support their skills and qualifications.

When asked why he came to UTSW, Dr. Peterson answered emphatically that he saw an institution fully committed to science and primed to soar.

"Here is a place where science is revered. That really isn't as apparent these days at a lot of places in this country," he said.

Dr. Peterson added that he also likes that the institution is not mired down in bureaucracy.

"You can get things done here. Change can happen here," he said.

UT Southwestern's research got a boost this June when it won a $46 million, five-year Clinical and Translational Science Award from the National Institutes of Health under the leadership of Dr. Robert Toto, Associate Dean for Clinical and Translational Research.

"UT Southwestern is going to soar over the next few years," Dr. Peterson said. "My goal is to make it rise even faster and higher."

■

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

Dr. Peterson holds the Adelyn and Edmund M. Hoffman Distinguished Chair in Medical Science.

Dr. Toto, a Professor of Internal Medicine, Population and Data Sciences, and in the Charles and Jane Pak Center for Mineral Metabolism and Clinical Research, holds the Mary M. Conroy Professorship in Kidney Disease.

A background built on clinical research excellence

For the past six years, Thomson Reuters and now Clarivate Analytics have named Dr. Eric Peterson to its list of the world's most highly cited researchers.

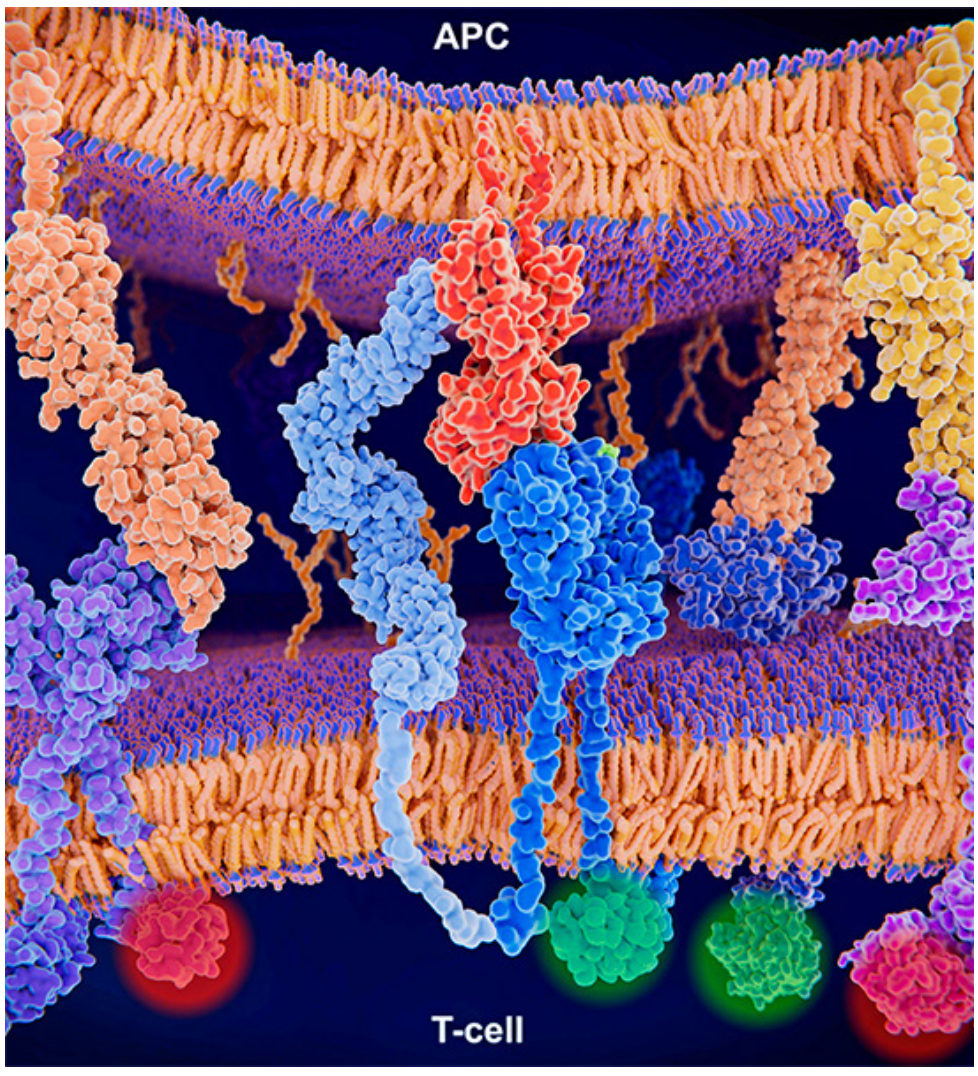
He was one of the first researchers to report on the disparity in medical treatment given to Black individuals versus white people in this country, which he described in a 1994 paper based on thousands of Veterans Affairs hospital discharge records and published in *JAMA*. His study three years later in *The New England Journal of Medicine* showed that these disparities can increase deaths.

Such studies honed his ability to analyze data, the focus of the rising field of data science. He helped create large national clinical registries with data from millions of cardiology patients, making it easier and less costly to do large clinical trials to evaluate the efficacy of drugs and treatments. As an example, Dr. Peterson was co-Principal Investigator of the data coordinating centers for the Society of Thoracic Surgeons' National Adult Cardiac Surgery Database, the American College of Cardiology's National Cardiovascular Data Registry, and the American Heart Association's Get With the Guidelines registries. He also was a co-founder of the CRUSADE Registry, which helped transform the treatment of patients with myocardial infarction in this country.

Dr. Peterson completed medical school at the University of Pittsburgh, an internship and residency at Brigham and Women's Hospital, and a Master of Public Health degree at the Harvard School of Public Health. He did a fellowship in cardiovascular disease at Duke University Medical Center. He has now gone on to author or co-author more than 1,400 peer-reviewed papers.

Scientists develop artificial intelligence method to predict anti-cancer immunity

Machine learning algorithms are shedding light on neoantigen T cell-receptor pairs



Activation of T cell immune response with the interaction of MHC-II (red) with the T cell receptor (TCR, blue) and also CD4 (light blue). CD4 and MHC-II are proteins expressed by T cells and antigen-presenting cells (APCs), respectively, to aid in the recognition of antigens by TCRs.

By Christen Brownlee

Researchers and data scientists at UT Southwestern and MD Anderson Cancer Center have developed an artificial intelligence technique that can identify which cell surface peptides produced by cancer cells called neoantigens are recognized by the immune system.

The pMTnet technique, detailed online in *Nature Machine Intelligence*, could lead to new ways to predict cancer prognosis and potential responsiveness to immunotherapies.

"Determining which neoantigens bind to T cell receptors and which don't has seemed like an impossible feat. But with machine learning, we're making progress," said senior author Tao Wang, Ph.D., Assistant Professor of Population and Data Sciences, and with the Harold C. Simmons Comprehensive Cancer Center and the Center for the Genetics of Host Defense.

Mutations in the genome of cancer cells cause them to display different neoantigens on their surfaces. Some of these neoantigens are recognized by immune T cells that hunt for signs of cancer and foreign invaders, allowing cancer cells to be destroyed by the immune system. However, others seem invisible to T cells, allowing cancers to grow unchecked.

"For the immune system, the presence of neoantigens is one of the biggest differences between normal and tumor cells," said Tianshi Lu, first co-author with Ze Zhang, both doctoral students in the Tao Wang lab, which uses state-of-the-art bioinformatics and biostatistics approaches to study the implications of tumor immunology for tumorigenesis, metastasis, prognosis, and treatment response in a variety of cancers. "If we can figure out which neoantigens stimulate an immune response, then we may be able to use this knowledge in a variety of different ways to fight cancer."

Being able to predict which neoantigens are recognized by T cells could help researchers develop personalized cancer vaccines, engineer better T cell-based therapies, or predict how well patients might respond to other types of immunotherapies. But there are tens of thousands of different neoantigens, and methods to predict which ones trigger a T cell response have proved to be time-consuming, technically challenging, and costly.

Searching for a better technique with support of grants from the National Institutes of Health and the Cancer Prevention and Research Institute of Texas, the research team looked to machine learning. They trained a deep learning-based algorithm that they named pMTnet using data from known binding or nonbinding combinations of three different components: neoantigens; proteins called major histocompatibility complexes (MHCs) that present neoantigens on cancer cell surfaces; and the T cell receptors (TCRs) responsible for recognizing the neoantigen-MHC complexes. They then tested the algorithm against a dataset developed from 30 different studies that had experimentally identified binding or nonbinding neoantigen T cell-receptor pairs. This experiment showed that the new algorithms had a high level of accuracy.

The researchers used this new tool to gather insights on neoantigens cataloged in The Cancer Genome Atlas, a public database that holds information from more than 11,000 primary tumors. pMTnet showed that neoantigens generally trigger a stronger immune response compared with tumor-associated antigens. It also predicted which patients had better responses to immune checkpoint blockade therapies and had better overall survival rates.

Tao Wang, Ph.D., explains the algorithm his lab developed that predicts the pairing between T cell receptors and T cell epitopes.

Tianshi Lu

Ze Zhang

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

Gene for sex hormone synthesis could play key role in eczema

By Christen Brownlee

A study led by UT Southwestern dermatologists suggests that a common inflammatory skin condition may stem from poorly regulated sex hormones. The finding, published in *PNAS*, could offer an unexpected new target to fight this condition.

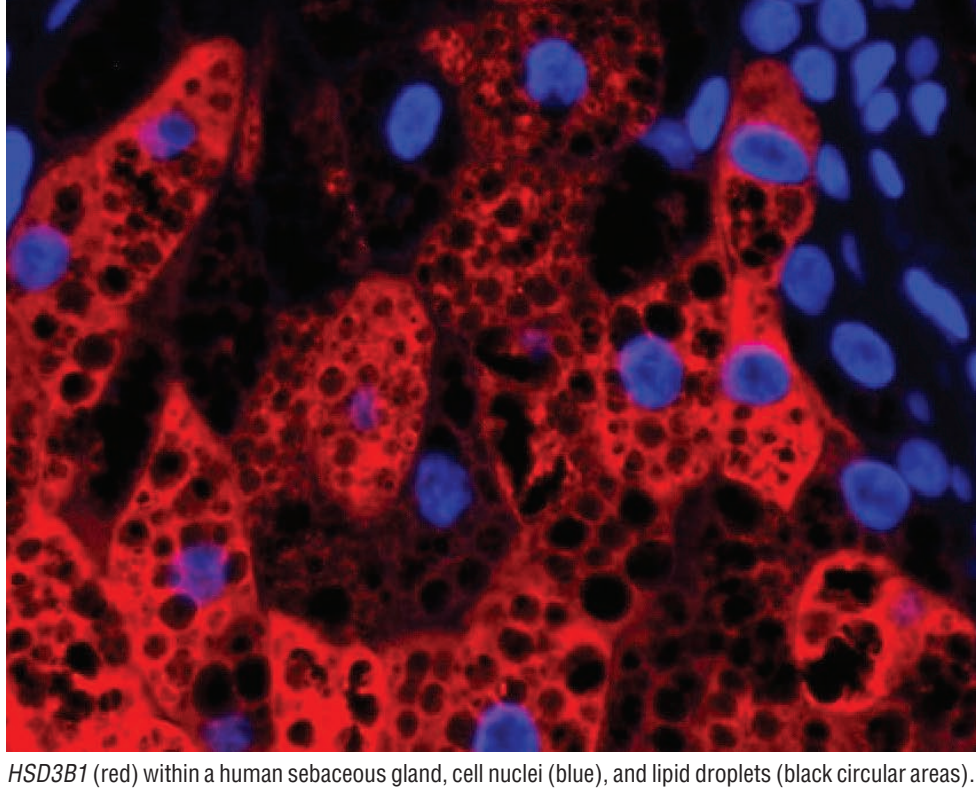
Atopic dermatitis (AD) is a form of eczema that affects up to 13% of children and 10% of adults, with an annual treatment cost of $5.3 billion in the U.S. alone.

"We often think of eczema as a dry-skin condition and treat mild cases with moisturizers," said corresponding author Tamia Harris-Tryon, M.D., Ph.D., Assistant Professor of Dermatology and Immunology. "Here, we're showing that a gene that's important for making sex hormones seems to play a role in the skin making its own moisturizers. If we could alter this gene's activity, we could potentially provide relief to eczema patients by helping the skin make more oils and lipids to moisturize itself."

Previous research has linked AD to overactivity in genes responsible for the production of two inflammatory immune molecules, interleukins 4 and 13 (IL-4 and IL-13). The drug dupilumab – a monoclonal antibody that reduces inflammatory molecules – has been extremely effective in many patients with moderate-to-severe AD. However, the molecular mechanisms behind how IL-4 and IL-13 contribute to this form of eczema was unknown.

To investigate, Dr. Harris-Tryon and her colleagues focused on sebocytes, the cells that make up sebaceous glands. These glands produce an oily, waxy barrier that coats the skin, helping it retain moisture.

The researchers dosed human sebocytes growing in petri dishes with IL-4 and IL-13, then used RNA sequencing to get a readout on gene activity and compared it with gene activity in sebocytes that were not treated with these immune molecules. They found that the gene *HSD3B1*, which makes the enzyme 3ß-hydroxysteroid dehydrogenase 1, became up to 60 times more active when exposed to the two interleukins.



HSD3B1 (red) within a human sebaceous gland, cell nuclei (blue), and lipid droplets (black circular areas).

The finding was a surprise, Dr. Harris-Tryon said, because this enzyme is known for playing a key role in the production of sex hormones testosterone and progesterone. But it had never been linked to atopic dermatitis and skin lipid production. Databases of human gene activity showed that *HSD3B1* tends to be overactive in patients with eczema. In addition, a study of patients on dupilumab showed that this drug appears to lower *HSD3B1*'s activity. Both pieces of evidence suggest that IL-4 and IL-13 drive up the activity of this gene.

To determine how this gene affects sebum output, the researchers manipulated *HSD3B1*'s activity in sebocytes growing in petri dishes. When they made this gene less active, the levels of sex hormones decreased and skin sebum production increased. The reverse also proved true – with more gene activity leading to higher levels of sex hormones and less sebum. The researchers made similar findings in a mouse model of AD.

Tamia Harris-Tryon, M.D., Ph.D.

Together, Dr. Harris-Tryon said, these findings suggest that *HSD3B1* could be a new target for fighting AD and other forms of eczema.

"Changing the output of this gene could eventually offer a way to treat AD that's completely different from any treatment that currently exists," she said.

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

Ross appointed Associate Dean for Basic Research

By Jan Jarvis

Elliott M. Ross, Ph.D., a faculty member in the Department of Pharmacology for 40 years, has been promoted to Associate Dean for Basic Research. In this new role, Dr. Ross will oversee research support cores and the Scientific Integrity program, which guarantees that research is carried out with the highest standards of scientific rigor and ethical standards. He will also provide guidance and coordination of business service functions that directly impact research activities.

"My goal in this new position is to provide administrative support and encouragement for outstanding basic science research at UT Southwestern," Dr. Ross said.

While he will spend most of his time on administrative activities, he will continue to perform duties in research and education, reporting to Joan Conaway, Ph.D., Vice Provost and Dean of Basic Research.

"Dr. Ross is an accomplished scientist with much experience and a deep knowledge of UT Southwestern. I am grateful to have the opportunity to partner with him to maintain and enhance UT Southwestern's position at the forefront of biomedical research," said Dr. Conaway, also Professor of Molecular Biology.

Dr. Ross' research focuses on how cells use signaling proteins to integrate and amplify information from hormones, neurotransmitters, and drugs that mimic these molecules. He conducts quantitative biochemical and biophysical studies of how G proteins – key nodes in cellular signaling circuits – convey information from diverse receptors to an array of intracellular regulatory networks. He designed and executed the research that resulted in the discovery of the first known G protein.

His recent research has examined how signal timing and signal intensity are independently regulated and how information is faithfully processed in cellular networks of multiple receptors, G proteins, and associated proteins.

Among his long history of contributions at UTSW, Dr. Ross led the Pharmacology Graduate Program and founded the Summer Undergraduate Research Fellowship (SURF) program, which he directed for 10 years.

Dr. Ross also served on the UTSW Promotions and Tenure Committee for 15 years and currently chairs the Post-Tenure Review Committee. In 2016, he became the Research Integrity Officer and Assistant Dean of Scientific Integrity. Since 1999, he has chaired the institution-supported Core Laboratories Oversight Committee and directed the Biochemical Kinetics Core. Additionally, he is Associate Director for Shared Resources of the Harold C. Simmons Comprehensive Cancer Center.

■

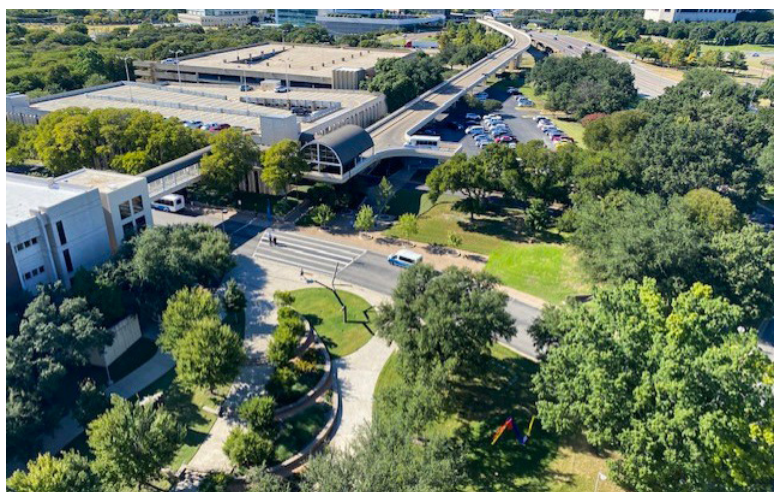
Dr. Conaway holds the Cecil H. Green Distinguished Chair in Cellular and Molecular Biology.

Dr. Ross holds the Greer Garson and E.E. Fogelson Distinguished Chair in Medical Research.

Elliott M. Ross, Ph.D.

UT Southwestern enhances environmentally conscious initiatives

Wide-ranging sustainability efforts across campus include energy and water conservation programs, solid waste reduction, and environmentally conscious landscaping with heat-tolerant plants and trees.



By Jan Jarvis

UT Southwestern's efforts to reduce its carbon footprint can be seen in the variety of campus sustainability measures, including energy and water conservation programs and solid waste reduction initiatives, along with the expanded use of native plants, a lush tree canopy, and monarch butterfly-friendly landscaping.

"When you look at the big picture, it's a green island surrounded by concrete," said Juan Guerra Jr., Vice President of Facilities Management.

A closer look reveals even more ways in which UT Southwestern endeavors to be environmentally focused, said Daniel K. Podolsky, M.D., President of UT Southwestern.

"Our campus Sustainability Committee actively monitors and initiates a variety of sustainability measures, including energy and water conservation and solid waste reduction initiatives," Dr. Podolsky shared in a recent campus briefing. "In Facilities Management, we have many processes and programs aimed at reducing greenhouse gas emissions. We also have robust recycling and reuse programs to reduce our solid waste stream."

UT Southwestern actively looks for opportunities to conserve energy, Mr. Guerra said.

"Over the past 10 years, energy consumption has been reduced about 12% per square foot," he said.

Boilers are tested monthly to ensure all emissions are within federal and state regulatory guidelines. In addition, old steam boilers were recently replaced at the North and South Thermal Energy Plants with higher efficiency units that have low greenhouse gas emissions potential.

"We do everything we can to minimize air emissions," Mr. Guerra said.

UT Southwestern also applies LEED (Leadership in Energy and Environmental Design) green building standards when designing and constructing all new facilities.

Recycling also plays a role in reducing the carbon footprint. In fiscal year 2020, UT Southwestern recycled an estimated 750 tons of mixed recycling, which equates to an 11% reduction in waste from 2016 to 2020.

The Blue Bin Recycling Program has grown over the years to accommodate mixed recycling for paper, cardboard, envelopes, newspapers, magazines, file folders, plastic materials, cartons, and aluminum cans. Efforts to recycle plastic foam products are underway.

In hospital and clinical areas, the hospital's "Green Team" focuses on areas to improve the overall sustainability impact, said Donald McLaughlin, Associate Vice President of Hospital Clinical Operations. The team focuses annually to improve overall sustainability impact and align with the overarching UT Southwestern Sustainability Steering Committee.

"We implemented a program at William P. Clements Jr. University Hospital in which we no longer place sheets on an empty bed until a patient is admitted," Mr. McLaughlin said.

This led to a reduction of 498,016 pounds of linen used annually at Clements and Zale Lipshy Pavilion.

Clements University Hospital also increased usage of a shredding recycling program (the shredded material is recycled by a company providing this service). The reduction of waste equated to 1,810 trees saved for the last fiscal year, Mr. McLaughlin said.

Environmentally friendly landscaping efforts include planting native and adaptive plants that tolerate Texas weather and require less watering. To maintain soil moisture and reduce disposal of landscaping trash, all mulch is made from recycled plant materials. Also, an arborist manages the landscaping to protect the trees during extreme weather, Mr. Guerra said. These efforts have earned UT Southwestern recognition as a 2020 Tree Campus Healthcare Facility from the Arbor Day Foundation.

Old steam boilers were recently replaced at the North and South Thermal Energy Plants with higher efficiency units that have low greenhouse gas emissions potential.

In addition, monarch butterfly-friendly plants have been added to the landscaping to support the butterflies and provide migration waystations.

To further reduce the carbon footprint, carpooling and use of mass transit are highly encouraged on campus, and subsidized DART passes are available.

"Collectively, we can make a huge difference by all the little things we do when we're on campus, from turning off lights in empty rooms to reporting leaking faucets or using the stairs instead of elevators," Mr. Guerra said.

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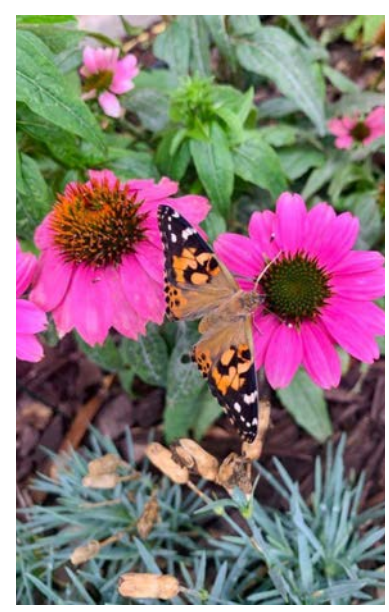
Dr. Podolsky holds the Philip O'Bryan Montgomery, Jr., M.D. Distinguished Presidential Chair in Academic Administration, and the Doris and Bryan Wildenthal Distinguished Chair in Medical Science.



Monarch butterfly-friendly plants have been added to the landscaping to support the butterflies and provide migration waystations.

Aston renovation enhances space for clinical research

An extensive renovation project on the ninth floor of the James W. Aston Ambulatory Care Center is optimizing clinical research space for faculty, staff, and study participants.

The 14-month project involves refreshing and redesigning research space, work areas, and the patient lobby on the ninth floor into the new 12,684-square-foot Aston U-9 Clinical Research Unit.

The first phase began in October 2020 and was completed in June, enabling the relocation of the Clinical Research Unit (CRU) and the Neuroscience Translational Research Center (NTRC) to the ninth floor of the Aston Center in July. The second phase – expected to be completed in December – will open 38 new exam, procedure, and consult rooms dedicated to clinical research.

The expanded research facility will support the Dallas Heart Study as well as clinical studies from the Departments of Internal Medicine, Physical Medicine and Rehabilitation, Obstetrics and Gynecology, Urology, Surgery, and others.

The improvements optimize clinical research facilities for faculty and staff as well as make the research experience more comfortable for participants, said John D. Beaver, M.P.A., M.Ed., CCRP, Assistant Director of Clinical Research Operations in the Office of Clinical Research. For example, state-of-the-art medical equipment and a new specimen prep room will help ensure positive results for UTSW community members conducting clinical research. In addition, dual-energy X-ray absorptiometry (DEXA) imaging services – which are used to measure bone density – will also be available to clinical researchers.

"The UTSW research community is committed to providing innovative solutions through the everyday practice of clinical trials," Mr. Beaver added. "The new Aston U-9 Clinical Research Unit provides a positive environment for our patients, Principal Investigators, and study teams to conduct clinical research to advance tomorrow's medicine today."

– Rachel Stowe Master

The James W. Aston Ambulatory Care Center has been undergoing renovation to optimize and add space for clinical research.

Bringing the UTSW community together for a cause

Heart Walk, Steps Challenge events on same day raise awareness of cardiovascular disease impact

By Courtney Borchert

Members of the UT Southwestern community gathered virtually for the second year in a row to show their commitment to raising awareness in the fight against cardiovascular disease.

On Sept. 11, UTSW had 720 registered walkers participate in the 2021 American Heart Association's Dallas Heart Walk. UTSW's 53 teams raised $21,054 to help train thousands in lifesaving CPR and fund groundbreaking brain and heart research. This year, participants were encouraged to walk 1 to 3 miles in the comfort of their homes or anywhere in their community to avoid large gatherings during the pandemic.

To up the ante, more than 100 employees also took up the UTSW Steps Challenge on the same day for some friendly competition. Those participants collectively walked 1,579,888 steps – an average of about 15,000 steps per person.

Thelma Morgan, a Medical Transcriptionist for Clinical Laboratory Services pictured directly below, took home a three-peat victory after racking up an astonishing 133,673 steps in 24 hours, her new personal best. Others who finished at the top of UTSW's Steps Challenge leaderboard with more than 45,000 steps were: Alvaro Noriega Ramirez, Clinical Laboratory Assistant in Transfusion Services; Jaymol Mathew, Registered Nurse II at William P. Clements Jr. University Hospital; and May Dela Cruz, B.S.M.T., H(ASCP), Quality Assurance Coordinator for Clinical Laboratory Services.

In the 2020 Steps Challenge, Ms. Morgan amassed 105,745 steps and, in the Heart Month Step Challenge seven months before that, she walked 85,637 steps in a single day. Each year she has paced with more fervor, driven by her motivation and love for her late father, who passed away from a heart attack five years ago.

"I could hear his voice telling me, 'You can do this,' throughout the challenge," she said.

More online: To read the full story and see more photos, go to *Center Times Plus* at **utsouthwestern.edu/ctplus**.


On Sept. 11, members of the UTSW community gathered virtually for the American Heart Association's Dallas Heart Walk. Registered walkers numbered 720, with teams raising more than $21,000. In conjunction, more than 100 employees also took up the UTSW Steps Challenge that day, collectively walking 1,579,888 steps.