CenterTimes

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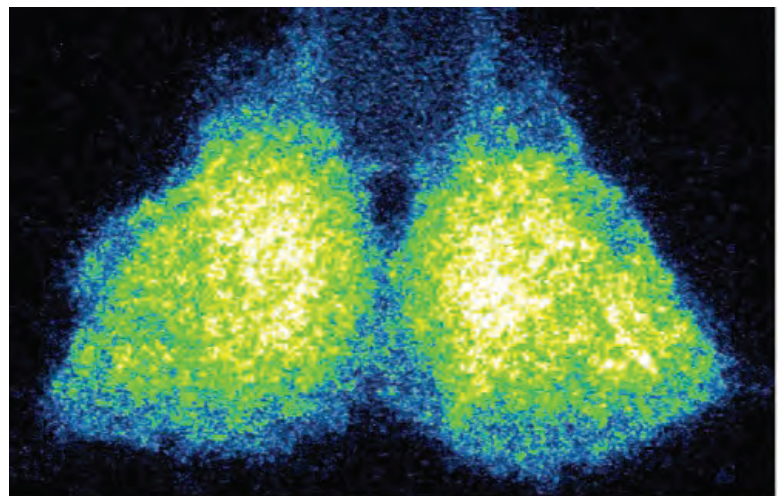
Takahashi receives global award for pioneering work on circadian rhythms

By James Beltran



The discovery and cloning of the *Clock* gene (right) by Dr. Joseph Takahashi (left) in the 1990s elevated circadian rhythms research beyond fruit flies and put scientists in a position to unlock many of the mysteries of human health and behavior.

Dr. Joseph S. Takahashi, Chairman of Neuroscience at UT Southwestern, has received an international award for his pioneering work on the molecular and genetic bases of circadian rhythms in mammals.

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

"Dr. Takahashi has made groundbreaking discoveries in the neurobiology of circadian rhythms," the Gruber Foundation stated in its news release announcing the award. "His use of innovative approaches to observe clock oscillations throughout the body in real time has revealed the broader impact of the circadian system in regulating the timing of cellular events in health and disease."

The prize, which includes a $500,000 award, will be presented to Dr. Takahashi on Oct. 20 at the annual meeting of the Society for Neuroscience in Chicago.

The recognition comes 25 years after *Science* published a breakthrough study by Dr. Takahashi that led to the discovery of *Clock*. A cascade of other findings has stemmed from his lab's work over the years, helping scientists understand the important role biological clocks have in some of the most crucial functions in the human body – from sleep and mental health to metabolism and defending against deadly diseases such as cancer.

"I am extremely honored and humbled to have received the Gruber Prize in Neuroscience," said Dr. Takahashi, an Investigator with the Howard Hughes Medical Institute. "It is gratifying to be recognized for my lab's discoveries

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

By Carol Marie Cropper

Two new buildings to serve UT Southwestern's ongoing growth in the high-priority areas of brain research and cancer patient care were celebrated at a groundbreaking June 4 on North Campus.

The Outpatient Cancer Care Tower of the Harold C. Simmons Comprehensive Cancer Center and the Research Tower of the Peter O'Donnell Jr. Brain Institute are expected to open in the fall of 2022.

The two nine-story buildings – approximately 300,000 square feet each – will stand adjacent to the C. Kern Wildenthal Research Building (NL Building), which is located on the North Campus at 6000 Harry Hines Blvd. They will be physically connected on some floors, with the O'Donnell Research Tower also adjoined to NL, allowing staff to easily move among the three buildings.

Architectural renderings of two buildings planned for North Campus

At the groundbreaking ceremony, UT Southwestern President Dr. Daniel K. Podolsky spoke to donors, administrators, clinicians, researchers, and supporters gathered under a canopy outside the NL Building. "We're here to begin the next great project on the UT Southwestern campus – buildings that will expand our ability to respond to those in need of cancer

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Drs. Christine Ochoa and John Brooks

UT Southwestern ranked top institution globally for published research in Nature Index health care category

From staff reports

For a second consecutive year, UT Southwestern is the top institution internationally within the health care category for publishing high-quality scientific research, according to the recently released Nature Index 2019 Annual Tables.

Ongoing support from federal agencies such as the National Institutes of Health, along with the state of Texas, foundations, individuals, and corporations, provides nearly $470 million annually to fund research at UT Southwestern, which also ranked globally among the top 25 biomedical institutions and among the top 25 academic institutions,

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Nominata goes to Mingjian Du for advances in innate immunity

By Deborah Wormser

Growing up in a small village in northwest China, Mingjian Du became fascinated with life science while helping on his parents' farm and later while studying biology in high school.

"My parents have the best scientific spirits, which they showed in improving crop yields and quality. My mom told me that science is all around us," said the recipient of the 2019 Nominata Award, the highest honor that UT Southwestern bestows on a student in the Graduate School of Biomedical Sciences.

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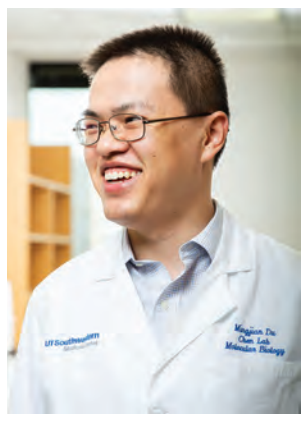

Mingjian Du

Scientists now on cusp of solving genetic diseases by snipping defective DNA

By James Beltran

Ben Dupree peered through the microscope at the beating heart cells, awestruck by the implications.

These were his cells, edited in the lab to correct a genetic flaw that had caused his muscles to deteriorate since childhood, forced him into a wheelchair, and perpetuated the prospects of an early death from Duchenne muscular dystrophy (DMD).

Here he witnessed a breakthrough that changed the narrative, a realization that after years of despair and depression, a lifesaving treatment for his condition was no longer a far-fetched dream.

"It's unbelievable," Mr. Dupree, 26, said as he

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Ben Dupree looks through a microscope during a visit to the lab of Dr. Eric Olson, left.

Cobb elected to American Academy of Arts and Sciences

By Patrick McGee

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

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

The election of more than 200 new members for 2019 was announced by the AAAS in mid-April.

Dr. Cobb leads UT Southwestern's Cancer Cell Networks Program and headed a team that discovered one class of protein kinase enzymes that play critical roles in cancer development.

"Melanie is a pioneer in protein kinase research who started multiple fields of study that are now pursued by hundreds of other scientists," said Dr. Elizabeth Goldsmith, Professor of Biophysics and Biochemistry at UT Southwestern. "Many of the proteins that she discovered are now drug targets for major diseases."

Dr. Cobb came to UT Southwestern after finishing her postdoctoral work in 1983. She stayed in large part because her Chairman at the time, the late Dr. Alfred G. Gilman, a 1994 Nobel Laureate, was so supportive of her work.


Dr. Melanie Cobb

"He opened doors for me that led to important collaborations with leaders in the kinase field, including the Nobel Prize winner Ed Krebs. As you might imagine, collaborations such as these would have been extremely difficult to establish on my own, given my early career stage," Dr. Cobb said.

Dr. Cobb identified the first mammalian mitogen-activated protein kinases in the early 1990s. She purified them, isolated cDNAs encoding these proteins, and named them ERK1, ERK2, and ERK3, or ERKs. It was a meaningful breakthrough because Ras, an important protein involved in cell growth and differentiation, has a critical relationship with these kinases.

"ERK1 and ERK2 are downstream of Ras, one of the most commonly mutated oncogenic proteins in human cancers," Dr. Cobb said. "The Ras/ERK pathway is also essential in embryonic development – mutations upstream in the pathway account for a large number of human birth defects. It's a crucial crossroad in intracellular signaling."

Dr. Cobb went on to identify more than a dozen other protein kinases, but downplays this innovative work as something that has become almost routine, as scientists can now pluck nearly any molecule they need from a database. She said those advances have enabled scientists to use systems approaches not possible earlier. Dr. Cobb said she still maintains a sharp focus on a mechanistic understanding of protein kinases themselves.

"We're still missing a lot of what might be described as details, but those details are basic fundamental mechanisms that will provide new insight once we identify them," she said. "For example, we're still trying to learn how ERK recognizes only a handful of protein substrates among the hundreds of possible proteins in a cell to carry out specific physiological responses."

Dr. Cobb is the 23rd UT Southwestern faculty member elected to the AAAS. Others include Nobel Laureates Drs. Bruce Beutler, Michael Brown, and Joseph Goldstein.

"Melanie is the exemplar of a UT Southwestern faculty member," said Dr. David Mangelsdorf, Chair of Pharmacology. "She puts her heart and soul into everything she does, from her science to her mentoring, teaching, and institutional service. This is a most deserving honor."

What she really hopes the laurel will bring is what Dr. Gilman made possible for her: more collaboration with the nation's best scientists.

"Whenever your name is raised within the scientific community, the possibility of new collaborations and novel scientific directions can also emerge. Collaboration is what moves so much of this work forward," Dr. Cobb said.

■

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

Dr. Brown, a Regental Professor and Director of the Erik Jonsson Center for Research in Molecular Genetics and Human Disease, holds The W.A. (Monty) Moncrief Distinguished Chair in Cholesterol and Arteriosclerosis Research, and the Paul J. Thomas Chair in Medicine.

Dr. Cobb holds the Jane and Bill Browning, Jr. Chair in Medical Science.

Dr. Goldsmith holds the Patti Bell Brown Professorship in Biochemistry.

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

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

NEWS

MAKER

Wax receives highest honor in toxicology from American College of Medical Toxicology

Dr. Paul Wax, Professor of Emergency Medicine, has received the Matthew J. Ellenhorn Award from the American College of Medical Toxicology (ACMT) in honor of lifetime contributions to the specialty of toxicology.

The annual award from ACMT, the largest physician toxicology group in the world, honors individuals who have made extraordinary contributions to the field in teaching, clinical practice, research, and/or service. Dr. Wax is the 23nd recipient of the award.


Dr. Paul Wax

A UT Southwestern faculty member since 2006, Dr. Wax followed his Presidency of the College by serving as the Executive Director of ACMT in 2008. In that role, he led the College through significant growth, including helping it obtain the National Grant for Pediatric Environmental Health Specialty Units, the largest grant the ACMT had ever obtained. He co-created the Toxicology Investigators Consortium (ToxIC) Registry, a patient registry within the ACMT to broaden research in the field. He founded the Chemical Agents of Opportunity Course, which has trained over 15,000 people in chemical terrorism education in the last 15 years. He developed the Agency for Toxic Substances and Disease Registry Subject Matter Expert network to provide expert consultation for the Department of Homeland Security's Chemical Terrorism Risk Assessment.

Dr. Wax also led the charge to start the College's *Journal of Medical Toxicology* and has been instrumental in ACMT's expanded relationship with the National Institute on Drug Abuse and the growth of toxicology within addiction medicine and forensic medicine.

"The Awards Committee could not have chosen a more deserving Ellenhorn recipient than Paul Wax," said Dr. Kurt Kleinschmidt, Chief of the Emergency Medicine Department's Division of Medical Toxicology. "Paul has done more for the advancement of medical toxicology than many other specialty leaders combined. He brings an immense amount of expertise and knowledge to our Division and we are honored to work with and learn from him. This is a remarkable achievement not only for Paul but also for our Division, our Department, and UT Southwestern."

In April, Dr. Wax received the award at the ACMT's 2019 Annual Scientific Meeting in San Francisco, where he presented the Ellenhorn Address.

CenterTimes

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President: Dr. Daniel K. Podolsky

Executive Vice President for Institutional Advancement: Dr. Marc Nivet

Interim Assistant Vice President for Communications: Jennifer Doren

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Design Editor: Mark Hoffer

Q&A with Janelle Browne, new VP of Human Resources at UTSW

By Heather Svokos

In March, Janelle Browne, a leader in the field of health care human resources in North Texas, joined UT Southwestern as Vice President for Human Resources and Chief Human Resources Officer.

Ms. Browne, formerly Vice President for Human Resources at Texas Health Resources, joined Texas Health in 2008 and had oversight of human resources for the company's 13 wholly owned hospitals and Texas Health Physicians Group. She helped launch Texas Health's first externally benchmarked employee engagement survey and developed practices that helped it become nationally recognized as one of the Great Places To Work. Before that, she had extensive experience in academia with executive roles at the University of Washington Health Sciences Center and the University of New Mexico Health Sciences Center.

In her new position, she succeeds Ivan Thompson, who retired in 2018. *Center Times* recently sat down to talk with Ms. Browne about what drew her to the top Human Resources post at UT Southwestern.

What attracted you to UT Southwestern?

I think about my career decisions and where I want to work; I pick wisely. And then I just invest every bit of my blood, sweat, and tears into making a difference. I love what I do. What most attracted me to UT Southwestern were the outstanding people. Over the last few years I have had the opportunity to work with UT Southwestern leaders and employees in the partnership with Texas Health. I am now happy to fully support this outstanding organization and the entire campus.

How do you wrap your arms around all the moving parts of an academic medical center like UT Southwestern?

As I learn more about the institution's three-part mission – research, education, and patient care – I learn more about the needs of each area. I'm learning what the day-to-day challenges are, about the pipelines for the people they need, and what engages people to stay.

What excites you about your job?

I love to build on the success of this organization with the new growth. I'm


Janelle Browne

drawn toward learning and understanding the operations and workforce needs. My role and work is: How do I ensure a great work environment and the right people in that environment to do that job? I want the HR team to be there absolutely supporting every bit of talent management that we need to make this organization successful.

What does a good organizational culture look like to you?

Culture is really ensuring that people are acting in each other's best interests and also the best for the organization and the people we serve. My role is to support the alignment of the organizational mission and goals with each team member's passion – then you really have the magic for things to happen. That is reinforced by our institutional values – excellence, innovation, compassion, and teamwork.

We understand there will be a new employee engagement survey this year.

Yes, and it is one very important way employees and UTSW colleagues can provide their voice – by taking these surveys. We take the surveys seriously, and we learn from them and use them. I'd really like to see more than 90 percent of the organization participating in the survey. Feedback is important. That's part of your contribution – to close that loop and give feedback.

How did you get into the HR field?

I kind of fell into it. I had applied for a new position as a budget analyst in the New Mexico state government, and they said: "We actually have a newly formed Department of Public Safety, and we think you'd be great as the Human Resources Director." So my first job was as an HR Director for Public Safety in Santa Fe. From then on, I've been in and around HR.

Not many candidates for this job would have already been as up close and personal with Southwestern Health Resources, the clinically integrated partnership between UTSW and Texas Health. Tell us about that.

What a journey that has been; it's such a unique situation. It takes a lot of creativity to keep parallel organizations going. I always felt like I was a steward for Southwestern Health Resources. I was looking after UT Southwestern's investment in people as much as I was for Texas Health. It's been an interesting learning experience, and I'm very much invested in the next phase of that organization and ensuring that the employees and managers get the support they need. I appreciate places that take bold moves to create new partnerships – I think it's necessary.

Last year, we celebrated a milestone with our 75th anniversary. How do you bridge the gaps between the past, present, and future?

I respect and understand the history of UT Southwestern. I really appreciate and will learn from those individuals who have been here for 20 and 30 years. And I'm also going to work toward our innovation value to meet the workforce needs of the future.

What do you do for fun?

My husband, Mark, and I enjoy traveling – with an emphasis on historical locations and art, and some beach time. I like to read fiction when I get a chance, including thrillers and mystery novels – I love Douglas Preston and Lincoln Child. I really like to container garden – I've got some flowers and some vegetables around the backyard.

We hear you're a dog person.

Yes, we have always had dogs: Bailey is a golden retriever who thinks she's Esther Williams. She's a good swimmer; she taught herself to swim when she was a puppy. And we have a brand new addition! We now have an 11-week-old golden retriever puppy named Brodie and he has not declared a specialty yet other than chewing everything in sight.

Mihalic receives prestigious Piper Professor Award for educators

By Patrick Wascovich

Dr. Angela Mihalic, Dean of Medical Students and Associate Dean of Student Affairs, has received the 2019 Minnie Stevens Piper Foundation's Piper Professor Award, a prestigious honor that recognizes outstanding college professors across Texas.

Dr. Mihalic, a Distinguished Teaching Professor in the Department of Pediatrics, is the 15th UT Southwestern faculty member to receive the elite award, established in 1958 to honor dedication to teaching and outstanding academic achievement.

"Dr. Mihalic is universally regarded as an exceptional educator by students and peers. Her passion for engaging medical students to become lifelong learners is matched with a compassion to guide them to success that exemplifies the best of UT Southwestern's educational mission," said Dr. Daniel K. Podolsky, President of UT Southwestern, who bestowed the honor on Dr. Mihalic May 9 at a Faculty Assembly meeting. "Her contributions to reshaping our curriculum and robust mentoring reflect the spirit that the Piper Award was designed to acknowledge."

In accepting the award, Dr. Mihalic said she was overwhelmed by the wonderful honor. The UT Southwestern Medical School graduate of 1995 noted her appreciation for teaching evolved during her medical education.

Dr. Angela Mihalic receives her award from President Dr. Daniel K. Podolsky.

"My best friend was a classmate and her mother became very ill," Dr. Mihalic recalled. "As she became the primary caretaker, I assumed the role of teacher and tutor to ensure that she kept up. I learned that I loved teaching and was so proud when my friend continued to do well despite the burden she faced."

A member of Alpha Omega Alpha Honor Medical Society as a student, she completed her pediatric internship and residency at Children's Medical Center Dallas before being invited to join the UTSW faculty in 1998. Her tenure includes serving as one of the first mentors for the Academic Colleges program and as pediatric clerkship director, along with multiple outstanding teacher honors that include twice receiving the Socrates Award for clinical teaching and being selected by students as Commencement Marshall 12 times.

"This love of teaching grew as I chose my specialty. Pediatricians are teachers at the core – helping parents learn how to care for their infants, how to support their development, and how to prevent illness and injury. And I quickly confirmed my passion for teaching as a faculty member. Nothing was as fulfilling as seeing learners' excitement, understanding, and desire to learn more," Dr. Mihalic said. "But I also soon began a career-long passion for finding the gap through needs assessments, developing curriculum, delivering it, and evaluating its success. My passion for advising and mentorship grew as an Academic Colleges mentor, and the opportunity presented as Associate Dean broadened the impact I could have to all medical students by developing initiatives that would have a lasting impact."

Dr. Charles Ginsburg, Vice Provost and Senior Associate Dean for Education and former Chair of Pediatrics, recruited her in 1998 to the Pediatrics faculty.

"Angela Mihalic is clearly one of the two or three most outstanding physician-educators that I have had the good fortune to encounter during my 42 years in academic medicine," said Dr. Ginsburg, Professor of Pediatrics. "She has integrity, grit, passion for learning and teaching, superb clinical skills and judgment, a strong work ethic, a cheerful and upbeat demeanor, and she has the protective maternal instincts of a grizzly bear when it comes to medical students. Dr. Mihalic epitomizes, in all respects, the term 'physician-educator.'"

■

Dr. Ginsburg holds the Marilyn R. Corrigan Distinguished Chair in Pediatric 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.

About the Piper Professor Award

The Piper Foundation was created in 1950 by Randall Gordon Piper and Minnie Stevens Piper. The next year the Foundation launched a loan program that allowed economically disadvantaged students in Texas to attend college.

After the Pipers' deaths in 1955, their Foundation initiated the Piper Scholars Program for undergraduates, the Pipers Fellows Program for graduate students, and the Piper Professors Program to recognize inspiring educators.

More online: To read the full story, go to **ct.utsouthwestern.edu/ctplus/stories/2019/piper-award-mihalic.html**.

Congratulations UTSW graduates of 2019!

Commencement ceremonies in May celebrated the graduations of 211 students from UT Southwestern Medical School and 93 students from the UT Southwestern Graduate School of Biomedical Sciences. Dr. Victor J. Dzau, President of the National Academy of Medicine, gave the May 7 commencement address for the Medical School at the Morton H. Meyerson Symphony Center. Dr. Margaret Phillips, UTSW Chair of Biochemistry, delivered the May 23 keynote for the Graduate School ceremony at the Tom and Lula Gooch Auditorium on South Campus. Both schools held hooding ceremonies on campus. To see more photos from both Commencement ceremonies, go to *Center Times Plus* at ct.utsouthwestern.edu.

Dr. Yu-San Yang is hooded by Dr. Benjamin Tu at the Commencement ceremony of the Graduate School of Biomedical Sciences.

Dr. Victor J. Dzau of the National Academy of Medicine delivers the Medical School Commencement address.

Medical School graduate Dr. Evan Wright gets help with regalia from Adrienne Walker, a third-year medical student.

At the Medical School Commencement, Dr. Marvin J. Stone congratulates Dr. Bethany Werner, recipient of the school's most prestigious honor, the Ho Din Award.

Olusoji Adeyemi Afuwape, M.D., Ph.D, walks across the stage at the Tom and Lula Gooch Auditorium upon receiving his doctorate degree at the Graduate School Commencement.

Outgoing Internal Medicine Chair honored as a Giant of Cancer Care

By Patrick McGee

When Dr. David Johnson talks about his part in cancer drug development, he says, "I played a small role." Others would disagree, however, describing his contributions as giant.

On May 30, Dr. Johnson was honored as one of 15 Giants of Cancer Care at the American Society of Clinical Oncology conference in Chicago. The award was given by OncLive.com, the website for the Oncology Specialty Group. Past inductees have included leading cancer experts from Harvard Medical School, Stanford, Yale, and the National Cancer Institute. Dr. John Minna, Professor and Director of the Hamon Center for Therapeutic Oncology Research at UT Southwestern, was among oncologists honored as a Giant of Cancer Care in 2015.

The honor comes as Dr. Johnson prepares to step down after nine years of service as UT Southwestern's Chair of Internal Medicine. He is an oncologist who has been on all sides of cancer; he's an attending physician, a leading expert in clinical trials, an enthusiastic supporter of cancer research, and a former cancer patient himself.

Dr. Johnson was in his early 40s, treating cancer patients in Tennessee, when he was diagnosed with lymphoma.

"It came as somewhat of a shock, to say the least," he said. Dr. Johnson soon had the chemotherapy he had prescribed for hundreds of patients in the past. He lost his hair and was hit with every side effect: neuropathy, neutropenia, fever, infections, and more. He would get his chemotherapy through an IV and then roll the IV pole into his office to write grants and papers. He made a conscious decision to take a break from seeing patients. When he returned to caring for patients, he found that many of them knew that he had chemotherapy.

Photography courtesy of OncLive

Dr. David Johnson, center, receives his award as one of 15 Giants of Cancer Care. Pictured with him are Michael J. Hennessey Jr., left, President of MJH Associates Inc., the parent company of OncLive, which bestowed the award, along with Dr. David Gandara, a former winner in the Lung Cancer category.

"I decided I wasn't going to talk about my experience because, once again, I felt it would be unfair to the patient to focus on me when the issue was their illness. But what I found out was that the chemotherapy nurses were telling my patients, 'Dr. Johnson has been through chemotherapy, and you should talk to him about it,'" he said, explaining that patients felt a sense of comfort knowing that a doctor had been through it.

Eventually he found there were times he could mention his own fight with cancer as a way to help others. While connecting with patients on a level that few other doctors could match, Dr. Johnson also pushed forward with clinical trials for several new drugs that would later become staples in lung cancer treatment.

"Through a very methodical, systematic testing of drugs in clinical trials, I played a small role along with dozens of other investigators around the world in pushing the ball down the field so that patients are better off today than they were when I started in this field more than 40 years ago," he said.

While he describes it as a small part, it was a significant contribution that led UT Southwestern to appoint him as the institution's fourth Chair of Internal Medicine. During Dr. Johnson's time as Chairman, he developed cancer again, this time on his tongue, and the cancer was surgically removed by a colleague. He was able to return to work quickly. He hired tremendous talent, producing a net gain of 150 new faculty members, and he played a role in opening the 460-bed William P. Clements Jr. University Hospital.

These were useful steps to advance UT Southwestern's excellence in research and patient care, fundamentals Dr. Johnson promoted when he became President of the American Society of Clinical Oncology in 2004. He was the first President of the organization to have had cancer, and he led the development of guidelines for the formation of cancer survivorship groups throughout the nation.

Survivorship groups, now common throughout the country, focus on steps cancer survivors can take to improve physical and mental health.

Dr. Johnson said he remembers working as a young resident, seeing patients with a much older doctor he respected. The doctor stopped abruptly in the hall once and said to him, "You just can't believe how much medicine has changed in the last 40 or 50 years."

He drove home that night thinking, "That's what an old person would say." Now he smiles broadly when he retells the story.

"I thought to myself, 'I'm never going to do that,'" Dr. Johnson said. "Now I find myself saying, 'You just can't believe the changes that have taken place over the last 40 or 50 years."

■

Dr. Johnson holds the Donald W. Seldin Distinguished Chair in Internal Medicine.

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

More online: To read the full story and watch a video, go to ct.utsouthwestern.edu.

Gene editing Continued from page 1

looked at his cells during a recent visit to a UT Southwestern gene-editing lab. "This could save so many lives one day."

Advancements in gene editing, buoyed by the discovery of CRISPR technology that enables precise editing of the human genome, have put scientists on the cusp of solving some of mankind's most devastating and baffling disorders. Among them is DMD, a muscle-withering disease that UT Southwestern geneticists have halted in animals and human cells through a single-cut gene-editing technique.

The next major step: a clinical trial that could change the prognosis for the most common fatal genetic disease in children and perhaps set the stage to treat other deadly diseases.

"Duchenne muscular dystrophy is a holy grail of genetic diseases, and we're so close now to helping people like Ben," said Dr. Eric Olson, Chair of Molecular Biology and an expert in genetic engineering at UT Southwestern. "Once we make headway with this condition, CRISPR in principle could be used for almost any disease in which we know the error in the DNA."

A rare mutation

Diagnosed at age 9, Mr. Dupree has spent most of his life dealing with the demoralizing effects of DMD. He recalls, even before diagnosis, the daunting task of keeping up with other children during soccer games or school exercise.

"Other kids would be running around, and I would be sitting with my hands on my knees trying to catch my breath," he said. "It was hard to go through that."

His family later learned this was far more serious than a lack of athleticism. Soon he was struggling to get up the stairs. Standing became a strenuous effort.

At the urging of an occupational therapist, Mr. Dupree's mother sought neuromuscular testing and a biopsy that returned disturbing results: He had a rare genetic mutation that prevents his body from producing dystrophin, a protein that acts like a shock absorber for heart and muscle fibers when they expand and contract. Without dystrophin, the boy's muscle fibers were falling apart – a condition that leads to muscle and heart failure and death by the early 30s, often much earlier.

Debbie Dupree did her best to hide the prognosis from her son as she began researching what could be done. She read about the latest findings on DMD, traveled to conferences, and met with doctors and other families dealing with the disease. Meanwhile, the boy's muscles continued to deteriorate, and by middle school he was using a wheelchair full time.

"When a doctor tells you your child will most likely be gone within a decade because there is no treatment, you go into shock," Mrs. Dupree said.

'Patient Zero'

Mrs. Dupree, who had not heard of Duchenne before her son showed signs of the disease, was dismayed to learn of the lack of immediate options for DMD patients. Yet hope remained. Scientists had known for decades that DMD is caused by a defect in any of the 79 exons that comprise the *dystrophin* gene, and medical technology had recently reached a point where these defects could potentially be corrected through gene editing.

Coincidentally, one of the world's leading experts on muscle disease lived in Mr. Dupree's neighborhood and was researching this very strategy. Dr. Olson invited Mr. Dupree to UT Southwestern in 2015 to give a blood sample to test whether a new CRISPR method his lab developed could work on human cells.

Dr. Olson's team followed a series of biochemical steps to convert the sample into heart cells and used CRISPR to correct the exon defect and restore *dystrophin*. The team then invited Mr. Dupree to see the results through the microscope.

"That was one of the most inspiring moments of the work, to see Ben's face when he saw his cells beating in a dish, producing the *dystrophin* that his body cannot make," Dr. Olson said. "He was our Patient Zero. Now the challenge is to adapt the technique to safely deliver the gene-editing components into the human body."

Dr. Pradeep Mammen (left) and Dr. Eric Olson with Duchenne muscular dystrophy patient Ben Dupree.

Dr. Olson's work is a notable part of a series of programs at UT Southwestern aimed at developing genetic treatments for muscle diseases and a number of ultra-rare neurological conditions largely overlooked by the medical field.

UT Southwestern is trailblazing a series of clinical trials for the latter in which a single healthy gene missing from the patient's DNA can be packaged into a harmless virus and delivered into cells. But scientists had to devise a different approach for DMD because the *dystrophin* gene – one of the largest in the human body – cannot fit inside the virus.

Dr. Olson's team developed a CRISPR-Cas9 technique to fix the gene instead of adding a healthy copy into the cells. The technique requires two components: an enzyme called Cas9 that cuts DNA and a guide RNA that functions like a molecular GPS device to direct Cas9 to the specific exon to be edited.

Cas9 and the RNA are each loaded into an adeno-associated virus (AAV), with the RNA directing the Cas-9 to the mutated exon where it snips the DNA. The editing process bypasses the mutation and enables muscle fibers to produce *dystrophin*, with positive results documented in studies by Dr. Olson in dogs, mice, and human cells.

Success with these treatments could lay the foundation for the more intricate gene therapies of common conditions – from epilepsy to autism – involving multiple genes that are either mutated or missing. But for now Dr. Olson's team is focused on saving patients like Mr. Dupree, one of about 300,000 people in the world with DMD.

"We've come a long way," said Dr. Olson, whose lab has since edited cells taken from other patients with different exon mutations.

Mental strife

Mr. Dupree has come a long way as well. He overcame early mental strife to become a vocal advocate for DMD research and takes pride in helping younger patients deal with the complexities that lie ahead.

"I was able to come out of that dark place through the community of support," Mr. Dupree said. "The people I came to know fostered a feeling that we're all in this together and that brought me back to where I am today."

He still keeps in touch with Dr. Olson, discussing the latest in science and sharing personal stories as well. It's a relationship built on mutual respect and admiration, two people who are overcoming challenges to reach their ultimate goals.

"From the first time I met Ben, I felt we had a real connection," Dr. Olson said. "It is probably surprising to people who realize many scientists will work their entire lives on a disease and not know someone personally who has that disease."

Mr. Dupree continues to devote much of his time to helping others. He earned a bachelor's degree in biochemistry – with the initial aim of researching DMD – and is now seeking a master's in social work to counsel those with disabilities.

Regarding the prospects of overcoming DMD, Mr. Dupree takes nothing for granted.

"I'm not necessarily hoping for a cure, but for anything that could slow the progression of the disease," he said. "Even if I'm not here to see the lifesaving treatment, my hope is that people being born now with the disease can still benefit."

■

Dr. Olson, also Director at the Hamon Center for Regenerative Science and Medicine, 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.

More online: To read the full story and watch a video, go to ct.utsouthwestern.edu.

Striking art installations change the face of South Campus

By Amy Stumbris

Denizens of UT Southwestern's Dr. Donald Seldin Plaza are now greeted by two stunning new sculptures that have effectively changed the face of South Campus. The pieces – *Dumna* by Ursula von Rydingsvard and an untitled work by Joel Shapiro – were recently gifted to UT Southwestern by Nobel Laureate Dr. Joseph L. Goldstein, Chairman of the Department of Molecular Genetics.

These two works are the latest additions to UTSW's expansive art collection, which enhances the entire campus.

"These significant donations elevate UT Southwestern's already impressive art collection, and all who enter this campus benefit from the generosity of donors who understand the value of art in inspiring and comforting those who work and visit our campus," said UT Southwestern President Dr. Daniel K. Podolsky. "We are extremely grateful for the generosity of Dr. Goldstein for making these additions possible and to the teams who saw the installation through."

At just under 11 feet tall, Ms. von Rydingsvard's *Dumna* is situated atop the berm on Seldin Plaza, nestled among trees and layered flower beds.

"*Dumna* appears to be a natural formation, such as wood or stone, and the effect of its colorful patina changes with the light," said UTSW Art Curator Courtney Crothers. "It seems to belong where it is, as if it's always been there."

Ms. von Rydingsvard was born in Germany in 1942 and came to the United States in 1959. Based in Brooklyn, she began her career in the mid-1970s. Her work is acclaimed for its rich, earthy texture and is found in important museum collections around the world. Ms. von Rydingsvard sculpted *Dumna* in 2014 from cedar beams and cast the work in bronze the following year. UTSW's piece is the last in an edition of three.

At the entrance to Seldin Plaza just off Sen. Kay Bailey Hutchison Drive stands the untitled bronze piece by Mr. Shapiro. At approximately 21 feet tall and nearly as wide, the piece branches up and out from a single point in the ground.

Mr. Shapiro is an American sculptor who lives and works in New York City and is renowned for his dynamic work composed of simple rectangular shapes, often resembling the human form. Commissioned especially for UT Southwestern, the piece is compelling in both scale and geometry.

"Shapiro's work has a lyrical quality to it, and this massive piece is animated by its leaning form and cantilevered appendages," Ms. Crothers said. "The form changes with the viewer's perspective and imbues UT Southwestern's 'front door' with energy and elegance."

Installation required cooperation among Ms. Crothers, employees from Facilities Management and the Office of Safety and Business Continuity, and representatives from the Talley Dunn Gallery in Dallas, who oversaw placement and facing of the pieces. A large crane was positioned on Sen. Kay Bailey Hutchison Drive for two days as each piece was carefully lifted and assembled in its new home.

Talley Dunn Gallery helped Dr. Goldstein identify the sculptures to be donated and then handled all the logistics of getting the pieces from the artists' studios to Dallas.

"The desire was to look at artists who have national and international followings as well as representation in museums – and to also identify artists who are making work that is appropriate for the site and that Dr. Goldstein and curators were excited about," said Talley Dunn, owner of the gallery.

Untitled work ©2018 Joel Shapiro/Artists Rights Society (ARS), New York

Dumna by Ursula von Rydingsvard

Workers use a crane to lift *Dumna* and place it on Seldin Plaza.

More online: To watch a video on this story and to view more photos on *Center Times Plus*, go to **ct.utsouthwestern.edu/ctplus/stories/2019/seldin-plaza-sculptures.html**.

"It's very exciting because we took a model that was in Mr. Shapiro's study and envisioned it at 21 feet tall," Ms. Dunn said. "His work is in museum collections around the world, and this piece was made just for UT Southwestern. Both Joel and Ursula are at the peaks of their careers, and these pieces are of international significance."

Ms. Dunn has had a long-standing relationship with UT Southwestern and with Dr. Goldstein, but previously has primarily helped facilitate indoor work.

"With outdoor work, I need to be here to make sure that the pieces are placed properly, since they have both a front and a back," Ms. Dunn said. "It's very exciting to be here today as this is the culmination of several months of work and a lot of moving parts."

Faculty, employees, students, and visitors watched with curiosity, some stopping along the Campus Connector bridge to watch; others asked for details as they walked along the Plaza during the installations that took place the week of May 20.

Dr. Alisa Winkler, Associate Professor of Cell Biology, was one of the observers. "It's a special moment to see these pieces being installed. I walk down Seldin Plaza every day, and having beautiful things on campus makes UT Southwestern a wonderful working environment and is an inspiration for me. I think a lot of people in the scientific community value art, as it comforts and welcomes us."

■

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. 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.

Arnoldo honored as first recipient of Purdue Chair in Burn Care

By Nyshicka Jordan

Professor of Surgery Dr. Brett Arnoldo chose to pursue a medical career later than most physicians. Initially, he earned a master's degree in fine arts – his media were painting and drawing – with a goal to become the next Picasso.

"But, I fell in love and recognized I needed to make a living," Dr. Arnoldo said.

After a few years of soul searching following graduate school, he decided to attend medical school in his early 30s. An ambitious person, Dr. Arnoldo was seeking both a challenge and a fulfilling career that would serve a greater good. Once he established medicine as his focus, he quickly gravitated to surgery. As he trained, burn surgery excited him the most.

Dr. Brett Arnoldo

"For me, there are a lot of similarities between artwork and the surgical career," Dr. Arnoldo said. "Everyone thinks being a surgeon is all in your hands, but no – it's in your eyes. It's looking at something and knowing what to do with it. The art really comes in handy with that. You train your hands to do what they need to do, but I think it's more visual than it is in your hands."

In 2003, Dr. Arnoldo was recruited to UT Southwestern by Dr. Gary Purdue, a surgical faculty member who died in a motorcycle accident in 2010. Dr. Arnoldo had previously trained as a fellow under Dr. Purdue. The doctors, who were both from New York, made a quick connection.

"He was more than just a surgeon – he was just a great human being," Dr. Arnoldo said about Dr. Purdue.

Now Dr. Arnoldo will help carry on Dr. Purdue's legacy. This year Dr. Arnoldo was appointed the Laurel and Gary F. Purdue, M.D. Chair in Burn Care. The endowment is also named for Dr. Purdue's widow.

"I know Gary would be ecstatic that Brett has been awarded our endowment. His compassion, commitment, and skills as a burn doctor exemplify everything Gary believed in," Laurel Purdue said. "Gary spent his career at Parkland Memorial Hospital doing what he loved, and he saw himself in Brett. Our family is thrilled that Brett continues to change lives daily at Parkland and carries a part of Gary's legacy with him."

Dr. Arnoldo said he intends to use the endowment to mostly support research led by early career investigators or fellows. Dr. Arnoldo is particularly focused on training future burn surgeons because of a shortage in the specialty. At a recent American Burn Association meeting, the group identified approximately 300 burn surgeons in North America.

"My legacy will be to try to identify the next generation of burn surgeons and develop them the way Dr. Purdue developed me so they can make the specialty better than it is now – and I know they will," Dr. Arnoldo said.

Dr. Arnoldo, now 61, said he'll likely continue performing surgery for the next decade. After that, he'd like to continue as a mentor to other surgeons.

Although he forged a nontraditional path to medicine, Dr. Arnoldo said many seeds were planted along the way that led him to his career. Determining your motivation is an important principle to live by, Dr. Arnoldo said, otherwise it is easy to get sidetracked. He said his mentor set that example.

"I saw Gary Purdue model that and it's one of the things that attracted me to working with him. He was just a really, really good human being. I still miss him; I still think about him a lot," Dr. Arnoldo said.

FOCUS: HEART

Researchers learn how 'bad cholesterol' enters artery walls to cause plaque

By Carol Marie Cropper

UT Southwestern researchers have determined how circulating "bad cholesterol" enters artery walls to cause the plaque that narrows the blood vessels and leads to heart attacks and strokes.

Since low density lipoprotein, or LDL, cholesterol entry into the artery wall drives the development of atherosclerosis, or hardening of the arteries, and atherosclerosis leads to heart attacks and strokes, future treatments preventing the process may help decrease the occurrence of these life-threatening conditions, said Dr. Philip Shaul, senior author of the study published online recently by *Nature*.

Cardiovascular disease is the No. 1 cause of death worldwide, and coronary artery disease (which underlies heart attacks) and strokes account for over 60 percent of cardiovascular deaths in the U.S., according to recent statistics from the American Heart Association (AHA).

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

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

The plaques narrow the artery and can become unstable. Plaques that rupture can activate blood clotting and block blood flow to the brain or heart, resulting in a stroke or heart attack. In studies of mice with elevated cholesterol, the investigators determined that deleting SR-B1 from the endothelial cells lining blood vessels resulted in far less LDL entering the artery wall, fewer foam cells formed, and atherosclerotic plaques that were considerably smaller.

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

In their studies, the researchers compared SR-B1 and DOCK4 abundance in areas of the mouse aorta that are prone to plaque formation compared with regions less likely to become atherosclerotic. They found higher levels of SR-B1 and DOCK4 in the disease-prone regions long before atherosclerotic plaques formed. This finding suggests that atherosclerotic lesions may be more common in particular artery sites because more SR-B1 and DOCK4 are present there, said Dr. Shaul, UTSW Vice Chair of Research and Professor of Pediatrics.

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

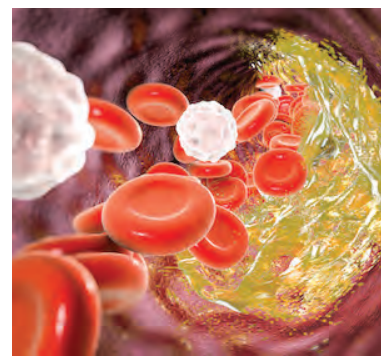


Illustration of cholesterol causing a narrowing of an artery

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

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

Dr. Chieko Mineo, Associate Professor of Pediatrics and Cell Biology, directed the project with Dr. Shaul, and Dr. Linzhang Huang, a postdoctoral researcher, was first author of the study. Co-authors include researchers at the Children's Medical Center Research Institute at UT Southwestern, New York University School of Medicine, and Cornell University.

The study received support from the NIH, the AHA, the Henrietta B. and Frederick H. Bugher Foundation, the Rally Foundation for Childhood Cancer Research, and The Children's Cancer Foundation Inc.

■

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

One-two punch helps solve greatest unmet need in cardiology

By Lori Sundeen Soderbergh

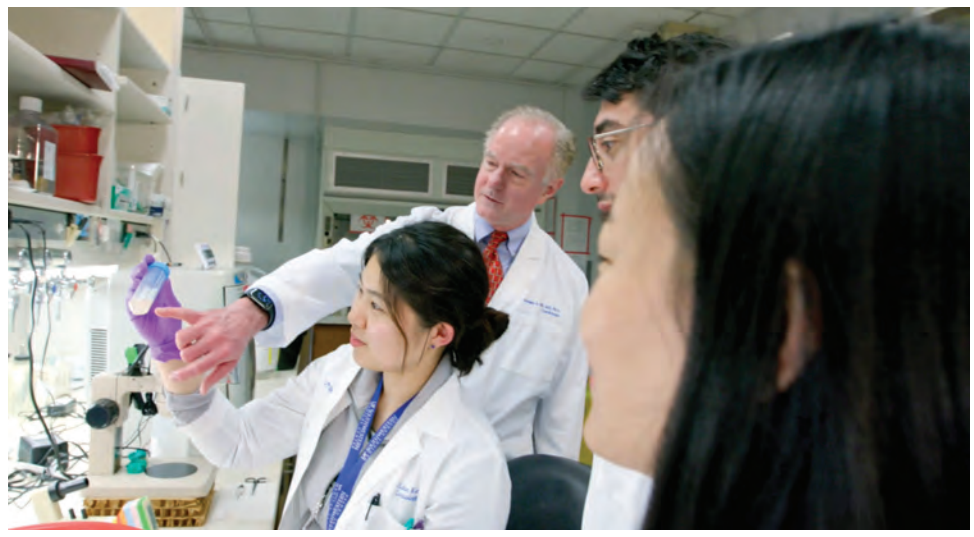
Nearly half of current hospital admissions for heart failure are caused by a type of the disease with no treatment options. Cardiology researchers at UT Southwestern are changing that reality with a fresh approach, detailed in an article recently published in *Nature*.

"There are two types of heart failure. One is called HFrEF, for which we have a number of therapies, including medications, devices, and transplants. The other – HFpEF – has zero options," explained Dr. Joseph Hill, Chief of the Division of Cardiology. "HFpEF is the single greatest unmet need in cardiology. Finding a new way to examine it represents a significant advance, as it provides a model necessary to develop and test therapies that could save lives worldwide."

The Centers for Disease Control and Prevention estimates that 5.7 million people have heart failure in the U.S.

One type of the disease – heart failure with preserved ejection fraction (HFpEF) – is a lethal disorder for which there are no effective clinical therapies. The heart muscle becomes too stiff to pump blood efficiently. Most HFpEF patients are obese, have diabetes, and have metabolic syndrome.

A second type is heart failure with reduced ejection fraction (HFrEF), which functions differently. In HFrEF, also known as systolic HF, the heart muscle is not able to contract adequately and, therefore, expels less oxygen-rich blood into the body. Previous heart failure models of HFpEF focused on raising the levels of an enzyme called NO, or nitric oxide synthase.



From left: researcher Soo Young Kim, Chief of Cardiology Dr. Joseph Hill, researcher Gabriele Schiattarella, and cardiology fellow Dr. Dan Tong.

However, in HFpEF, there is actually too much of the NO enzyme. A strike on this target – with a medical inhibitor, for example – would solve the problem. According to Dr. Hill, who is also Professor of Internal Medicine and Molecular Biology, there are already FDA-approved drugs that inhibit this NO-synthesize enzyme, which could facilitate developing new treatments rapidly.

Dr. Hill's team looked at current, ineffective models of HFpEF and concluded that none correctly mirrors the realities they see clinically in human patients. They found that combining a high fat diet with a drug that raises blood pressure gave them a "two-hit" model, like a one-two punch to the disease. Next, the team examined results of their model at the cellular level and compared them with human cells. They found that they had replicated the human condition, providing scientists an accurate biological picture that can greatly advance the development of new treatments.

Millions of people worldwide have both obesity and diabetes. The research team believed that these two conditions would lead to HFpEF – a hypothesis they confirmed by duplicating the disease conditions and examining changes at the molecular level.

"Heart failure is one of only two forms of cardiovascular disease that is increasing. It's exploding around the world," said Dr. Hill, who is also Director of the Harry S. Moss Heart Center at UT Southwestern and Editor-in-Chief of *Circulation*. "We dance around the edges of it, treating patients' diabetes, blood pressure, and other conditions. With this model, we'll be able to get to the underlying cause so we can get to the root of the problem."

The UT Southwestern researchers are currently taking steps toward moving into human clinical trials based on findings in their preclinical two-hit model. With time, they expect that all heart failure patients will have treatment options.

The National Heart, Lung, and Blood Institute, part of the National Institutes of Health, helped fund the study. Researchers from Johns Hopkins University and the University of Chile also contributed to the study.

■

Dr. Hill holds the James T. Willerson, M.D. Distinguished Chair in Cardiovascular Diseases and the Frank M. Ryburn, Jr. Chair in Heart Research.

More online: To read more and watch a video, go to **utsouthwestern.edu/newsroom/articles/year-2019/two-hit-model.html**.

Translational researcher Busch receives Hartwell biomedical support

By Patrick Wascovich

Patients with severe heart or lung disease sometimes need a mechanical intervention much like heart-lung bypass in a form of treatment known as extracorporeal membrane oxygenation (ECMO). ECMO pumps blood throughout the body, sometimes for weeks, delivering oxygen to tissue while the heart/lungs heal or while waiting for transplant.

However, during this lifesaving process it is difficult to closely monitor the brain to ensure it gets a sufficient blood supply. The dangers can be extreme. The brain naturally maintains adequate blood flow in healthy people. In critically ill patients on ECMO, those mechanisms can be disrupted, leading to injury from blood flow that is too high or too low.

With support from The Hartwell Foundation, Dr. David Busch is applying optical spectroscopic tools in an effort to change dire statistics and consequences.

"More than 30,000 children in the United States have received ECMO. Tragically, only about 1 in every 3 of these young patients survive without some long-term brain damage," said Dr. Busch, Assistant Professor of Anesthesiology and Pain Management at UT Southwestern. "Many of the fatalities suffer catastrophic brain injury. Our study seeks to provide clinicians a tool to enable real-time individualized adjustment of ECMO settings to optimize the health of the patient's brain."

Dr. David Busch

Dr. Busch's ECMO autoregulation work was one of 12 investigations selected to receive a 2018 Hartwell Individual Biomedical Research Award from the private foundation based in Memphis, Tennessee. The award provides $100,000 support for three years.

"We are very pleased but not surprised by The Hartwell Foundation's selection," said Dr. Charles Whitten, Chairman of Anesthesiology and Pain Management. "Dr. Busch, a Fulbright and Whitaker scholar, is a researcher who is bringing basic science into the clinical arena."

The Hartwell Foundation annually invites a very limited number of U.S. institutions to nominate candidates from their faculty who are involved in early stage, innovative, and cutting-edge biomedical research that has not yet qualified for significant outside funding.

Selection criteria include the transformative nature of the proposed innovation, the institutional commitment to provide encouragement and technical support, and the extent to which funding the investigator will make a difference.

"Our approach is to be unique, selective, thorough, and accountable," said Dr. Fred Dombrose, President of The Hartwell Foundation. "We provide an opportunity for those we support to make a difference and to realize their hopes and dreams."

Dr. Busch, who holds a secondary appointment in Neurology and Neurotherapeutics, said he plans to initially deploy this new technology at Children's Health for children on ECMO and then expand to other critical and chronic pediatric illnesses with compromised blood flow.

"Blood flow in the brain may be critically dependent on the ECMO pump settings, yet currently there are no good ways to monitor the adequacy of flow during ECMO. Clinicians fall back on measurements like blood pressure of the whole body instead of measuring brain health directly," he said. "I model the light transport in tissue to enable direct measurement of the blood flow, volume, and oxygen content in the brain or other organs. This technology, 'diffuse correlation spectroscopy,' is available at only about five pediatric hospitals worldwide."

By receiving this Individual Award, UT Southwestern also qualifies for a Hartwell Fellowship that provides $50,000 in postdoctoral support for two years to a worthy candidate who holds a Ph.D. or equivalent doctorate and will pursue further specialized training in biomedical research rather than extend or complete clinical training.

■

Dr. Whitten holds the Margaret Milam McDermott Distinguished Chair in Anesthesiology and Pain Management, which was partially used to support Dr. Busch's early research.

Graduate School alumna's passion for neuroscience leads to Ida Green Award

By Nyshicka Jordan

Neuroscientist Dr. Bishakha Mona wants to find out how sensations such as pain or itch are transmitted to the brain – an answer that resides in the neurons. In her enthusiasm for scientific discovery, she wants others to be just as curious about why those cells matter and care about the clinical potential of such findings.

"What scientists are trying to do is help people and develop therapies by better understanding disease and their development. We are trying to increase awareness about the importance of scientific research," Dr. Mona said.

In April, Dr. Mona was awarded the Ida M. Green Award. The honor is given to a female student of the UT Southwestern Graduate School of Biomedical Sciences who has demonstrated scholastic excellence and outstanding citizenship in line with the values and mission of the Medical Center.

Dr. Mona, a native of Bihar, India, traveled to the United States to pursue her research career goals at UT Southwestern. She comes from a family of physicians – her mother is a gynecologist, her father an anesthesiologist, and her little sister a physician who has yet to choose a specialty. Dr. Mona's decision to become a research scientist was one her parents did not embrace at first.

"They really wanted me to become a doctor and practice medicine," Dr. Mona said. "Now they understand that I am not running away from saving lives, just taking a different approach."

While she had always been interested in neuroscience, Dr. Mona became particularly captivated by the function of the brain while attending college at Birla Institute of Technology and Science, Pilani.

In her dissertation research, she reported on developmental mechanisms of neuronal cell fate specification in spinal cord circuit formation. (This is the process by which neurons become what they are – for example, how a stem cell becomes a particular type of neuron that may provide inhibitory or excitatory information into a network.) These discoveries were published in a first-author study in *Developmental Biology* and a co-first author article in *eLife*. Future research discoveries in the field could potentially mean new therapies for patients with a wide range of conditions, from psoriasis to spinal cord injuries.

Besides her dedication to research, Dr. Mona is committed to supporting younger scientists. She started mentoring girls as a college student in India, and in Texas, she has worked with high school girls through MAGIC (More Active Girls in Computing), an organization that supports girls' interests in STEM fields.

Rust E. Reid, Vice President of the Cecil and Ida Green Foundation, and Kathleen M. Gibson (right), President and CEO of Southwestern Medical Foundation, present the 2019 Ida M. Green Award to Dr. Bishakha Mona.

"When I was a young student, I didn't really have female role models like that. That is why I would like to encourage young minds and provide guidance wherever I can," she said.

Today, she is glad there are more women in science and academia to provide inspiration for girls to pursue careers in science. "I believe in empowerment of women and I want to be a person driving that," she said.

At UT Southwestern, Dr. Mona has displayed leadership by organizing events to help trainees improve their science communication skills. She also was involved in the 2014 creation of the Science Policy, Education, and Communication Club and has served as President since 2016.

"Dr. Mona is a role model for other graduate students as she generously shares her time and efforts with community service while maintaining robust research accomplishments," said Dr. Jane Johnson, Professor of Neuroscience and Pharmacology and Dr. Mona's dissertation adviser.

Dr. Mona graduated in May and has stayed on at UT Southwestern. In addition, she has taken a position with a nonprofit foundation that provides funding for research in cancer prevention. In the future, she wants to further educate the public on the role of research by managing a scientific nonprofit.

The Ida M. Green Award is presented by Southwestern Medical Foundation and includes a $2,000 prize.

"Like Ida Green, Dr. Mona serves as a wonderful role model for women," said Kathleen M. Gibson, President and CEO of Southwestern Medical Foundation. "Her perseverance and intellect, combined with her service in helping other young women in science, is to be celebrated. While Dr. Mona's accomplishments are remarkable on their own, they are even more powerful when leveraged by mentoring others in their scientific progress. We are very proud to have Dr. Mona as the winner of the 2019 Ida Green Award."

■

Dr. Johnson holds the Shirley and William S. McIntyre Distinguished Chair in Neuroscience.

Drs. James Amatruda and Genevieve Kendall use zebrafish as a model to study childhood cancer. Ongoing support from multiple sources provides nearly $470 million annually to fund innovative research programs such as this at UT Southwestern.

Ranking Continued from page 1

according to the 2019 Nature Index listings. Other peer institutions on the global listings include Harvard, Stanford, Yale, MIT, and the National Institutes of Health in the United States, along with the Chinese Academy of Sciences in China, the University of Oxford in England, and the Max Planck Society in Germany.

"This respected ranking reflects UT Southwestern's consistent strength in publishing research that advances our scientific understanding of disease at the biological, cellular, and molecular levels, which is fundamental to illuminating viable pathways to propel therapeutic treatments," said Dr. W. P. Andrew Lee, Executive Vice President for Academic Affairs, Provost, and Dean, UT Southwestern Medical School. "Faculty success evolves from UT Southwestern's emphasis on cultivating an atmosphere of rigorous science through multidisciplinary collaboration where scientists can perform at their best."

UT Southwestern faculty members have received six Nobel Prizes, and its faculty includes 22 members of the National Academy of Sciences, 17 members of the National Academy of Medicine, 16 members of the American Academy of Arts and Sciences, 15 Howard Hughes Medical Institute Investigators, and two recipients of the prestigious Breakthrough Prize. The Medical Center houses one of HHMI's 12 principal laboratories nationwide, has four HHMI Faculty Scholars on campus, and has more than 100 early career researchers, who have come to UT Southwestern through the Medical Center's acclaimed Endowed Scholars Program in Medical Science, subsequently establishing themselves as leaders in their fields.

"Research is conducted every day in hundreds of labs across campus, in which established faculty members, early career researchers, postdoctoral fellows, and graduate students work tirelessly to discover the underlying causes of disease and ways in which we can improve health and extend life," said Dr. David Russell, Vice Provost and Dean of Research.

The UT Southwestern Graduate School of Biomedical Sciences, with more than 950 predoctoral and postdoctoral students, educates biomedical scientists, engineers, clinical researchers, and counselors. The Graduate School has two Divisions: Basic Science and Clinical Science, which together offer 12 programs leading to the Ph.D. degree – Biological Chemistry; Biomedical Engineering; Cancer Biology; Cell and Molecular Biology; Clinical Psychology; Genetics, Development and Disease; Immunology; Integrative Molecular and Biomedical Sciences; Molecular Biophysics; Molecular Microbiology; Neuroscience; and Organic Chemistry. In addition, an M.S. degree and graduate certificate are offered in Clinical Science.

■

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

Dr. Russell holds the Eugene McDermott Distinguished Chair in Molecular Genetics.

Breaking ground for two towers on North Campus were (left to right): longtime donors Peter O'Donnell Jr. and Annette Simmons; former cancer patient Morgan Aaron and her mother, Dawn; and UT Southwestern's Dr. Daniel K. Podolsky (President), Dr. Joseph Takahashi, and Dr. Carlos Arteaga.

Buildings Continued from page 1

care. Our researchers, working with learners, will also be able to make discoveries to improve the treatment, cure, and prevention of all the forms of brain disease that affect 50 million Americans," he said.

He thanked event attendee Annette Simmons and her late husband, Dallas businessman Harold C. Simmons, for longtime, generous support that has furthered cancer research and care at UT Southwestern. He also thanked Edith and Peter O'Donnell Jr. for their decades of giving and generosity to help launch the O'Donnell Brain Institute to advance brain science. When it was time to lift the shovels of soil, Annette Simmons and Mr. O'Donnell were called on to share in the moment.

The Research Tower will help UT Southwestern attract the best and the brightest research talent, top-flight faculty, and the most outstanding Ph.D. students in the country, said Dr. Joseph Takahashi, Chair of Neuroscience. "More space means we can take on more projects and discoveries," he told the crowd, and unite researchers, faculty, students, and clinical specialists from the O'Donnell Brain Institute.

Great strides are being made in treating and curing cancer, added Dr. Carlos Arteaga, Director of the Simmons Cancer Center, which will be expanding from the clinical buildings nearby. He said the new facility would triple current cancer care capabilities on campus, providing added space for multidisciplinary care, private treatment rooms, genetic counseling, imaging, physical medicine, clinical trials, supportive care, and telemedicine.

"We expect this outpatient cancer care tower to be not only the exceptional destination for those with a cancer diagnosis in Dallas and in surrounding areas seeking the latest standards of care, but also a shining light of clinical investigation, innovation, and progress," Dr. Arteaga said.

Toward the end of the event, Dr. Podolsky introduced Morgan Aaron and her mother, Dawn, to share their personal stories of how far UT Southwestern's cancer and brain treatments have already come.

Morgan was 28 years old in 2016 when she was diagnosed with stage 4 breast cancer that had spread to her brain, resulting in five brain tumors.

Within days of her diagnosis, Morgan's UT Southwestern care team comprised of Dr. Barbara Haley, Dr. Toral Patel, and Dr. Robert Timmerman had performed the treatment that saved her daughter's life, said Dawn. "Today Morgan is healthy. She is cancer-free."

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

■

Dr. Arteaga, also Associate Dean of Oncology Programs and Professor of Internal Medicine, holds The Lisa K. Simmons Distinguished Chair in Comprehensive Oncology.

Dr. Haley, Professor of Internal Medicine, holds the Charles Cameron Sprague, M.D. Chair in Clinical Oncology.

Dr. Patel is Assistant Professor of Neurological Surgery and Neurology and Neurotherapeutics.

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. Takahashi, also Professor of Neuroscience, holds the Loyd B. Sands Distinguished Chair in Neuroscience.

Dr. Timmerman, Professor of Radiation Oncology and Neurological Surgery, holds the Effie Marie Cain Distinguished Chair in Cancer Therapy Research.

UTSW researchers find form drives function in cancer proliferation

By Deborah Wormser

A new study finds that the protein responsible for the crawling movements of cells also drives the ability of cancer cells to grow when under stress.

The protein is actin, which is also a key component of the contraction apparatus of muscles. The link between cell movement and signaling is through the cell's actin cytoskeleton – chains of actin that dynamically assemble and disassemble to aid locomotion in cancerous and noncancerous cells.

Although the actin cytoskeleton was known to be involved in the spread, or metastasis, of cancer cells, the fact that the cell migration machinery can drive cancer cell growth has never before been described, said Dr. Gaudenz Danuser, UT Southwestern Chair of the Lyda Hill Department of Bioinformatics and Professor of Bioinformatics and Cell Biology. Dr. Danuser is the corresponding author of the study in *Developmental Cell* that identifies a novel role for actin in cell signaling.

The study demonstrates that form drives function in a mechanism that behaves one way in both noncancerous cells and in unstressed cancer cells but acts differently in cancer cells that encounter stressors such as chemotherapy or the need to adapt to a new environment. When encountering such stresses, the actin mechanism affects signaling to promote drug resistance or aggressive metastatic growth.

Drs. Ashwathi (Abbee) Mohan (left) and Gaudenz Danuser

In their studies, the researchers took human skin cancer (melanoma) cells that contained a mutation in the *Rac1* gene linked to chemotherapy-resistant tumors and used CRISPR/Cas9 gene editing to snip out the single-base pair mutation and revert it to the normal gene. In a petri dish, cells with the mutation continued to grow when exposed to chemotherapy, while cells with normal *Rac1* could not – even though both kinds of cells remained cancerous. When injected into mice, cells carrying the mutation made much larger metastatic nodules than cells carrying the normal version of the gene. Interestingly, cancer cells with or without the mutation grew at the same rate, as long as they were not exposed to chemotherapy or remained in the primary tumors. Hence, it is the stress of a new environment that turns on cell growth in the mutated cells, the researchers said.

In 2012, laboratories at Yale and at MD Anderson Cancer Center independently isolated the *Rac1* mutation in melanoma. About 10 percent of melanoma patients carry the mutation.

"In 2014, the MD Anderson group showed that this mutation is among the culprits behind chemotherapy resistance in skin cancer cells," said study lead author Dr. Ashwathi (Abbee) Mohan, who recently received her Ph.D. from the Cancer Biology Graduate Program and UT Southwestern's Medical Scientist Training Program. The UTSW study identifies for the first time a reason for the mutation's ability to encourage drug resistance and the growth of cancer cells – and it's a structural one.

By combining gene editing, molecular cell biology, advanced live-cell imaging, and computer vision, the researchers learned that when cells with the *Rac1* mutation are stressed, the actin cytoskeleton creates enlarged sheet-like protrusions called lamellipodia. Noncancerous cells or cancer cells without the mutation extend much smaller lamellipodia to initiate migration. "These sheets – lamellipodia – (in stressed cancer cells that have the mutation) are so massive that they sequester and turn off tumor suppressor molecules, which otherwise would control cell growth," Dr. Mohan said.

"It resembles catching the signaling molecules in a net. This raises the possibility of restoring the chemotherapy response by blocking the assembly of these dense actin sheets," she added.

Beyond controlling cell shape and enabling cell migration, the actin cytoskeleton is also actively involved in regulation of cell signaling, Dr. Danuser added. The Danuser lab is now working to better understand how cancer cells know when to turn on and off this form-driven signaling machinery.

"If we can figure out how the cells access this pathway, we can block what we have found to be a critical escape route that cancer cells use to resist drug treatment," Dr. Danuser said. "This study reaffirms the concept that cell shape is instrumental in driving signaling – that by simply spreading out, cell signals can be silenced and sequestered. Cancer exploits this ability to drive both drug resistance and metastasis."

The study received funding from the National Institutes of Health, the Human Frontier Science Program, and The Welch Foundation.

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Dr. Danuser holds the Patrick E. Haggerty Distinguished Chair in Basic Biomedical Science.

New screening approach helps identify sources of rare genetic diseases in children

By Katie Regan

Scientists at the Children's Medical Center Research Institute at UT Southwestern (CRI) are using a new approach to pinpoint the causes of rare genetic diseases in children and identify treatment options faster than with traditional methods. The new approach combines DNA sequencing and a chemical analysis called metabolomics to identify mutant genes that cause defective metabolic pathways in patients.

"We hope our new technique will increase the speed with which we can pinpoint the defective gene in patients evaluated in our clinics at Children's Health," said Dr. Ralph DeBerardinis, Professor at CRI and of Pediatrics at UT Southwestern, where he is Chief of the Division of Pediatric Genetics and Metabolism. He also directs CRI's Genetic and Metabolic Disease Program (GMDP).

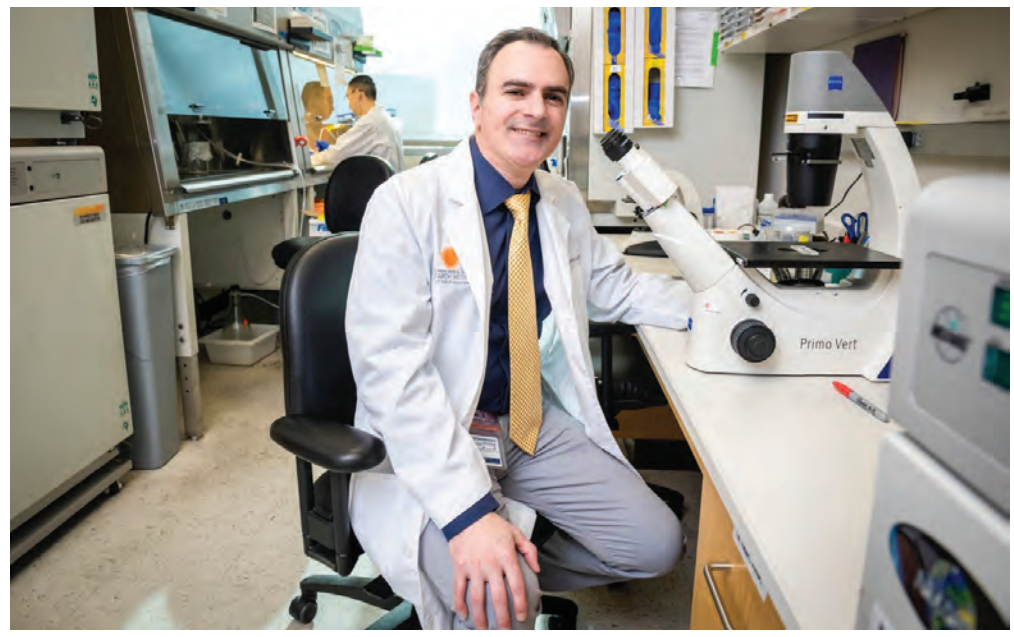
"Pinpointing the mutation allows us to provide useful information to the family about the disease and its risk to other family members. In some cases, the information either points to an existing therapy or helps us to devise new ones," Dr. DeBerardinis added.

Diseases with a genetic basis account for a large number of illnesses and mortality in children and result in about 25 percent of pediatric hospital admissions. The largest subset of these genetic diseases are known as inborn errors of metabolism (IEMs). Although individually these diseases are rare, collectively they affect a disproportionate number of children, he said. IEMs are caused by defects in genes that help the body metabolize or break down the sugars, proteins, and fats in food. Defective metabolism can lead to chemical imbalances that can cause death or permanent disability in children, unless identified and treated at a young age.

Encouragingly, many IEMs are treatable through dietary modifications and medical therapy once the genetic basis of the disease has been identified. A handful of IEMs are diagnosed through newborn screening, but the majority are diagnosed only after a child becomes ill. Because these diseases are so rare, it can take months or even years to establish the correct diagnosis, and the process often involves invasive procedures like muscle or liver biopsies.

"IEMs are traditionally hard to identify," Dr. DeBerardinis said. "Many of these diseases have overlapping symptoms, so even if you suspect an IEM, it is often difficult to pinpoint the problem. There are over 400 known IEMs and several thousand genes involved in human metabolism. Identifying the mutated gene in a child with an IEM – particularly a new or recently discovered disease – is like hunting for a needle in a haystack."

In the study, published recently in *Cell Reports*, researchers identified the gene responsible for a rare IEM that causes abnormal brain development, seizures, and severe metabolic acidosis. To find the gene, they used a combination of DNA sequencing and metabolomics, a technique that can detect hundreds of small chemical compounds in the blood. Researchers compared the level of each metabolite found in the patients to healthy subjects using a technique called untargeted metabolomic profiling. This technique allowed researchers to detect 20 times as many metabolites in the blood as would a conventional metabolic screen. This approach provided researchers with a granular view of the metabolic alterations in the patient.



Dr. Ralph DeBerardinis

Dr. Min Ni (third from left) and colleagues

Researchers then used advanced DNA sequencing techniques to look for mutations among the nearly 20,000 human genes. Next, they combined the list of metabolic alterations and the list of mutated genes to determine which mutation could explain the metabolic differences present in the patient.

"Performing metabolomics in parallel with DNA studies makes it possible to pinpoint disease-causing mutations much faster than the DNA studies alone," said Dr. Min Ni, lead author of the study and Assistant Professor at CRI and of Pediatrics at UT Southwestern. "In this case, it helped us determine that the patient had a genetic defect in one enzyme known as LIPT1. We were able to confirm our new screening technique worked by using cultured cells from the patient and a mouse model to show that the mutation we identified in the patient caused the metabolic disturbances and prevented normal development."

Dr. DeBerardinis credits the unique setup of the GMDP for the discovery. "With support from Children's Health and UT Southwestern, we've tripled the size of our clinical group and built a research program to handle human genomics and metabolomics data. Our scientists and doctors work side by side to evaluate patients, learn about their diseases, find new mutations, and think creatively about developing better treatments. Seeing patients in the clinic keeps our research focused and ensures we are asking the right questions. In the past five years, we have identified new disease genes, provided accurate diagnostic information to families, and, in a few cases, helped patients find better treatments tailored to their mutations. We are very excited about what we will learn in the next few years."

A practicing physician, Dr. DeBerardinis is a Howard Hughes Medical Institute (HHMI) Investigator and is also affiliated with the Eugene McDermott Center for Human Growth and Development and the Harold C. Simmons Comprehensive Cancer Center, both at UT Southwestern.

The National Institutes of Health, the HHMI, The Welch Foundation, and donors to the Children's Medical Center Foundation supported the research.

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

Takahashi

Continued from page 1

over the last 25 years. I share the credit for this prize with all my students, postdocs, and staff who contributed to this work."

In the 1990s, Dr. Takahashi's lab was analyzing hundreds of mice with random genetic alterations and looking for any that displayed abnormal circadian behaviors. His team gave mice access to running wheels and noticed they ran every 23.7 hours, except for one: a mouse that used the wheel on a 25-hour cycle. After breeding the mouse and determining its altered circadian behavior was genetic, Dr. Takahashi's team spent three years tracking down which gene was altered and named it *Clock*.

Dr. Takahashi's lab went on to discover that *Clock* is intertwined with an extensive list of biochemical pathways. It's even involved in metabolism, as the group found while investigating why mice with *Clock* mutations become obese with age. Dr. Takahashi is now researching whether the gene may also influence lifespan.

"UT Southwestern is proud to have this international leader in neuroscience discovery as a member of its faculty," said Dr. Daniel K. Podolsky, President of UT Southwestern. "Dr. Takahashi's research has given us fundamental insights into how circadian rhythms affect human health and behavior, and it provides avenues for new approaches to such diverse and prevalent conditions as insomnia, diabetes, and cancer."

Dr. Takahashi is also a Professor of Neuroscience with UT Southwestern's Peter O'Donnell Jr. Brain Institute.

■

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

More online: To read the full story and view a video on this story, go to **utsouthwestern.edu/newsroom/articles/year-2019/takahashi-circadian-rhythms-award.html**.

CLASS NOTES

IN MEMORIAM

Medical School

James R. Matthews, M.D. ('57)
Jerold Dennis Michaelson, M.D. ('67)

Housestaff

Briant Gray Herzog, M.D. (Obstetrics and Gynecology)
Stuart Ronald Stone, M.D. (Obstetrics and Gynecology)

MEDICAL SCHOOL

Class of 1987: Mark Hancock, M.D., joined the medical staff of the Dreiling/Schmidt Cancer Institute at Hays Medical Center, a part of The University of Kansas Health System.

Class of 1988: Peter A. McCullough, M.D., M.P.H., was named Editor-in-Chief of *Reviews in Cardiovascular Medicine*. For over a decade, Dr. McCullough has served on the editorial board and as Co-Editor of the journal. Dr. McCullough oversees cardiology training, education, and research for Baylor Health Care System and is Vice Chief of Medicine at Baylor University Medical Center in Dallas.

Class of 1996: Kellie Flood, M.D., was recognized as one of Alabama's premier geriatrics health professionals by the American Geriatrics Society (AGS). She was honored at the AGS 2019 Annual Scientific Meeting. Dr. Flood serves as an Associate Professor at the University of Alabama at Birmingham (UAB) as well as Associate Chief Medical and Quality Officer for Geriatrics and Care Transitions at UAB Hospital.

Class of 1999: Sanaz Cordes, M.D., was named Chief Executive Officer of DotCom Therapy, an industry leader in teletherapy for speech, occupational, and behavioral health services. Dr. Cordes is a known advocate for female entrepreneurs in the venture-backed health tech space. Prior to joining DotCom Therapy, Dr. Cordes was the founder and principal at Value Prop Shop, a consulting firm focused exclusively on working with health tech startups.

GRADUATE SCHOOL

Class of 1981: Raymond DuBois, M.D., Ph.D., FAACR, was awarded the Margaret Foti Award for Leadership and Extraordinary Achievements in Cancer Research by the American Association for Cancer Research for his studies in the early detection, interception, and prevention of colorectal cancer. Dr. DuBois is the Dean of the College of Medicine at the Medical University of South Carolina (MUSC) and a Professor in the Departments of Biochemistry, Molecular Biology, and Medicine. In addition to his appointment at MUSC, Dr. DuBois is an Editor-in-Chief of *Cancer Prevention Research* and serves as Vice Chair of the Stand Up To Cancer Scientific Advisory Committee.

FORMER HOUSESTAFF

Fellowship alumnus Jonathan D. Leffert, M.D., was elected Chancellor of the American Association of Clinical Endocrinologists at the 28th Annual Scientific & Clinical Congress in Los Angeles.

Residency alumna Suzanne Rybczynski, M.D., was appointed to Associate CMO of Kennedy Krieger Institute, an internationally renowned organization with the mission of improving the lives of children and adolescents with disorders and injuries of the brain, spinal cord, and musculoskeletal system. Dr. Rybczynski was most recently Medical Director of the Institute's Pediatric Rehabilitation Unit and is also a clinician at Kennedy Krieger and an Assistant Professor of Pediatrics at the Johns Hopkins School of Medicine.

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.

Patients, donors celebrate life at Transplant Reunion

By Nyshicka Jordan

On the 14th floor of the T. Boone Pickens Biomedical Building, Jackie Kelly and Jackie Schoonover chatted like the good friends they are. But there was something very special, and very powerful, at the heart of this gathering.

Gratitude overtook the room as "the two Jackies" joined dozens of transplant patients, organ donors, and their families, who all came together April 26 to attend the annual UT Southwestern Transplant Reunion.

The celebration of life is made possible each year because of the selfless decisions made by donors or their families.

"None of us would be in this room tonight if there weren't organ donors. So, it's important not just to sign up on your driver's license, but also consider being a living donor if you're ever called upon," said Dr. Parsia Vagefi, Chief of the Division of Surgical Transplantation and Associate Professor of Surgery.

Dr. Vagefi joined UT Southwestern in 2018, and under his leadership, liver and kidney transplant volume increased by 66 percent that first year. UTSW's living-donor programs offer better outcomes because live donation allows patients to undergo surgery sooner, with organs from the healthiest of donors. At the event, several attendees shared their transplant journeys.

Kidney donor Jackie Schoonover and kidney recipient Jackie Kelly have celebrated their transplantation journey each year since 2012 at the Annual Transplant Reunion.

More online: For the full story and more photos, go to *Center Times Plus* at **ct.utsouthwestern.edu**.

A tale of two Jackies

Jackie Schoonover felt powerless. It was 2005, and her sister was dying of cancer.

"I was by her bedside when she took her last breath, and I stood helplessly – I couldn't help her," Ms. Schoonover said, choking back tears.

Years later, in 2012, she found herself in a position to save a friend. She seized it.

She and Jackie Kelly had met in church years before. Mrs. Kelly's health battle began in 2002 when her kidneys started to fail and she was placed on dialysis. She improved and was removed from dialysis six months later, but then her kidneys failed again five years after that.

When she found herself close to death three times, several of Mrs. Kelly's family members and Ms. Schoonover offered to donate a kidney. The latter was the right match.

Almost seven years after their 2012 operations, both women say they are in good health and that the experience drew them even closer. "We're sisters for real," Mrs. Kelly said.

Ms. Schoonover said she's hopeful her act can inspire others to consider live donation.

"You have to know within yourself this is something you want to do. Donating is not for glory – it's because you're able to help someone," she said.

Now the women have a bond they call spiritual. Last year, Mrs. Kelly published a book about her experience called *Going Through: The Journey*.

Paired match

Longtime friends Julie Harrell and Tod Hollis were first-timers to the reunion, having undergone transplantation last September. Mr. Hollis met Mrs. Harrell's husband in the Army, and their families remained close. So when Mrs. Harrell needed a kidney transplant, Mr. Hollis didn't hesitate.

"It was the right thing to do, and a pleasure and honor to do it," Mr. Hollis said.

Although Mr. Hollis had originally planned to donate directly to Mrs. Harrell, they were not a compatible match. Instead, Mr. Hollis' kidney was sent to a recipient in Minnesota, and their donor's kidney was sent to Dallas for Mrs. Harrell in a paired exchange or "kidney swap."

"It was a humbling experience that people would be willing to do that," Mrs. Harrell said.

She had previously been diagnosed with polycystic kidney disease, so Mrs. Harrell knew one day she would need a kidney transplant. Her mother also had the condition and had to have a transplant more than 20 years before. Because of her history, Mrs. Harrell had been prepared mentally for her fate – except she had always expected the organ would come from a deceased donor. She said she initially felt guilty about accepting such a generous offer from her friend.

"It was very hard for me to take a kidney from somebody living," Mrs. Harrell said. "But Tod and everyone convinced me that it was a gift he wanted to give."

Giving thanks

In 2018, UTSW physicians performed 289 heart, kidney, liver, or lung transplant surgeries. The Transplant Reunion is not only an opportunity to celebrate survival, but a chance for patients to thank everyone involved in their care.

Gynovel Henry, a heart transplant recipient, shared his story as a reunion speaker.

Mr. Henry's heart was weakened when he contracted rheumatic fever in 1984 as a teenager. He had heard about UT Southwestern's reputation for quality care, so in 2005 he moved from Phoenix to Dallas specifically to be cared for here. By January 2018, his health deteriorated, landing him in the hospital, where he remained until his heart transplant that March.

Looking back on all the trials of his health battle, Mr. Henry said he is particularly grateful to the medical teams who have cared for him, and during his speech, he specifically gave a shoutout to his UTSW nurses and physicians.

"This isn't about me; this is about the work that they do," Mr. Henry said. "They put a lot of time and work into what they do. They have families, just like us. They have ups and downs, just like us. Sure, they come here and do their jobs, but they come here to save lives."

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Dr. Vagefi holds the Ernest Poulos, M.D. Distinguished Chair in Surgery.

Celebrating decades of service

More than 80 longtime UT Southwestern employees – including two who have worked here 45 years – gathered at the Quarter Century Club luncheon held in their honor during Employee Recognition Week in May.

45-year-service honorees Gwen Griffin, left, and Bernadine "Bernie" Wafford enjoy the event.

Mary Ann Kelly, Cassandra Watkins, Andrea Casteel, Kimberly Taylor, Judy Newell, and Charlotte Washington pose for a photo.

Steve and Jeanne Seitz celebrate 40 years of UTSW service together.

Dr. Daniel K. Podolsky, President, congratulates Pattina Traylor.

FOCUS: BRAIN

Exploration of the ultimate frontier: The brain

This spring's Carolyn P. Horchow Women's Health Symposium focused on brain research.


First-time symposium attendee Shelly Heins poses a question to Drs. Camp and Czysz.

By James Beltran and Carol Marie Cropper

UT Southwestern scientists have discovered a molecular origin of Alzheimer's disease, led national efforts to improve depression treatment, and now are developing gene therapies for children with the rarest of deadly neurological diseases. These are a few of the distinguishing achievements of faculty associated with the Peter O'Donnell Jr. Brain Institute, which is seeking to position UT Southwestern as a national leader in brain research and care.

UT Southwestern's commitment has evolved into a billion-dollar initiative that is putting scientists closer to understanding some of mankind's most perplexing and devastating conditions.

President Dr. Daniel K. Podolsky discussed the O'Donnell Brain Institute's progress and goals at the Carolyn P. Horchow Women's Health Symposium this spring, an annual campus event that this year focused on talks from O'Donnell Brain Institute scientists on topics ranging from solving the mysteries behind everything from Alzheimer's disease and memory to depression, brain cancer, and autoimmune disease.

Dr. Podolsky provided a retrospective on why the O'Donnell Brain Institute was created in 2015, noting that new technologies had emerged that could lead to improved treatment of brain disorders – which the World Health Organization has estimated affect up to 1 billion people.

"Of course, important contributions to understanding and treating the brain will be made at many of our peer institutions around the world in the coming years," Dr. Podolsky told guests in opening the event. "But UT Southwestern is committed to being in the vanguard. The Peter O'Donnell Jr. Brain Institute is driving an ambitious vision and top priority at UT Southwestern. And we're making the investments to deliver on that vision."

Old foes in a new light: Inquiries into Alzheimer's disease

For the more than 5 million Americans with Alzheimer's, as well as for caregivers, this common form of dementia is devastating – a disease with no cure and eventual loss of mental function.

Today, treatments can only help lessen symptoms, said Dr. Marc Diamond, Director of the Center for Alzheimer's and Neurodegenerative Diseases at UT Southwestern's O'Donnell Brain Institute. But despite the disease's grim trajectory, the leader in Alzheimer's research told those attending the Symposium that he is optimistic.

Dr. Diamond's vision for the future? "We will no longer really see dementia in the clinic the way we do now. We will pick up the fundamental processes that lead to dementia long before a person actually experiences the symptoms."

And: "We're going to be giving an effective treatment to stop the disease."

Alzheimer's is by far the most common cause of neurodegenerative dementia in older people, Dr. Diamond said, although dementia can also be caused by strokes, Parkinson's disease, and even vitamin deficiencies, especially vitamin B12, a nutrient found only in animals. Depression or chronic sleep disturbance can look like dementia, he added.

In Alzheimer's, an abnormal transformation of the protein tau has been linked as a causal factor. "We know that when Alzheimer's strikes, that the protein changes its shape and it starts behaving abnormally inside the brain cells," he said.

When tau changes shape, Dr. Diamond explained, it exposes amino acids previously hidden inside that cause it to begin attaching to other tau molecules. Abnormally shaped tau then moves from one cell to another, he said, creating chains of abnormality as it goes, "kind of like falling dominoes in the brain."

This process starts in an area of the brain tied to memory, leading to Alzheimer's dreaded effect on the mind, said Dr. Diamond, also Professor of Neurology and Neurotherapeutics and Neuroscience.

Lab tests have borne out this theory. If bad forms of tau are introduced into the hippocampus of a mouse brain, the result is like an infection that spreads through the brain.

Already, an immunotherapy/antibody he developed several years ago to attack bad tau is in phase two clinical trials. Many pharmaceutical companies are working with this approach in hopes of developing treatments against tau and other proteins that form abnormal tau assemblies in the brain, Dr. Diamond said.

Dr. Marc Diamond

"We've got active programs going on in the Center for Alzheimer's and Neurodegenerative Diseases to try to attack the formation of these abnormal assemblies in the first place," he added. "What we're doing is developing small molecules that will stabilize the protein in its healthy form and prevent it from converting."

"We're also developing next-generation immunotherapies that are based on our knowledge of the unique structures that cause the different diseases (involved in dementia). So we're actually trying to make personalized vaccines that would be given much like a flu shot to attack this problem," Dr. Diamond said, adding that this strategy has already worked in mouse models.

Elsewhere, clinical trials are underway using antisense oligonucleotide inhibitors – a genetic approach – to turn off Alzheimer's development in genes.

With the Centers for Disease Control and Prevention (CDC) projecting the number of people with Alzheimer's to almost triple by 2050 as the U.S. population ages, success on any of these fronts could be lifesaving for millions.

Pathfinders: Illuminating the landscape of mental health

It's an exciting time in the field of mental health, with new treatments emerging and promising research underway.

Just this March, the Food and Drug Administration approved a new drug for treatment-resistant depression that relies on a completely new approach and is capable of creating results within days – even hours in some patients – said Dr. Andrew Czysz, a fourth-year psychiatry resident and one of the Symposium presenters. The drug, esketamine, is administered as a nasal spray in conjunction with an oral antidepressant.

The drug is generating excitement for its quick impact and all-new approach. Unlike many existing antidepressants that work on the neurotransmitters serotonin, norepinephrine, or dopamine to treat chemical imbalances in the brain, esketamine affects a different brain chemical called glutamate, Dr. Czysz said. "It's a completely new mechanism."

Depression is highly treatable and is becoming more so with such new treatment options, added Dr. Mary "Molly" Camp, Assistant Professor of Psychiatry, who co-presented with Dr. Czysz. In a landmark study done at UT Southwestern and elsewhere and reported in the *American Journal of Psychiatry* in 2006, 67 percent of the adult outpatients treated during the study for major depression achieved remission. The patients moved through up to four progressively more intense treatment options as they tried to attain remission. In the first stage, patients received only a single antidepressant, and about a third of the patients responded at this stage. But if that did not work, the initial medication might be changed and either a second antidepressant or cognitive therapy was added to the treatment mix.

Sometimes, Dr. Camp said, success takes time and a succession of medications. But more than 30 kinds of antidepressants are now on the market, and other treatment options include psychotherapy, transcranial magnetic stimulation (which uses magnets to create electrical currents in the brain), and electroconvulsive therapy, she said.

Electroconvulsive therapy, formerly known as electroshock therapy, is "extremely safe" and "one of, if not the most, effective treatments for treatment-resistant depression," she added.

Another treatment still in the research stage is magnetic seizure therapy. In this treatment, a patient undergoes controlled seizures similar to those in electroconvulsive therapy, but perhaps with fewer side effects, Dr. Czysz said. "There's something we don't quite understand that's very therapeutic about a controlled seizure in people with mood disorders. Some people liken it to rebooting the brain."

In addition to such medical interventions, those suffering from depression can use exercise to improve their mood, Dr. Camp said.

Dr. Andrew Czysz and Dr. Mary "Molly" Camp

Inflammation could be one reason stress affects the brain, Dr. Czysz said. Chronic stress can lead to inflammation and changes in immune function, in turn associated with major psychiatric disorders, he said. "Exercise really is one of the best anti-inflammatories out there," he noted.

Studies are underway to tailor treatment for depression based on a patient's level of an inflammation biomarker, C-reactive protein, Dr. Czysz added. Early results using the information to choose the right antidepressant have been promising.

Part of what makes people more susceptible to depression is genetic; those born with a short variation of the serotonin transporter gene can be at increased risk, he said. But, Dr. Czysz told attendees, this effect is only seen in those who have also experienced maltreatment.

"If you had no maltreatment, this particular gene that you had didn't matter," he said. According to the research, "It was only the individuals who had experienced maltreatment and had the short version of the gene that had this dramatically increased risk of developing depression."

Since early life events can have a profound impact on mental illness later in life, UT Southwestern is involved in two longitudinal depression studies researchers hope to continue for 10 years. One examines biologic factors that impact whether someone with depression gets better or worse; the other involves studying what factors lead to depression or resilience in adolescents.

FOCUS: BRAIN

Brain Continued from page 10

'Et tu, Brute?' Neurologist takes Shakespearean approach to explain autoimmune disorders

As one of the world's leading experts on rare autoimmune diseases, Dr. Benjamin Greenberg knows the intricacies of the nervous system and the web of terms that defines it.

Yet, when describing autoimmune disease to lay folk, he kindly offers explanations that are more Shakespearean than scientific.

In a Symposium lecture titled "Et tu, Brute?" Dr. Greenberg described the molecular "Brutus" that attacks healthy cells and causes rare conditions such as transverse myelitis or more common ones like multiple sclerosis.

"The autoimmune system is supposed to be your friend; it is supposed to protect you from harmful viruses and bacteria," Dr. Greenberg said. "And when it gets confused and commits murder of one of its own, it is an act of betrayal akin to Brutus and Julius Caesar."

Dr. Benjamin Greenberg

Dr. Greenberg, Associate Professor of Neurology and Neurotherapeutics and Pediatrics, a Distinguished Teaching Professor, and Director of the Perot Foundation Neuroscience Translational Research Center, described how autoimmune diseases can manifest in a variety of symptoms, from seizures to movement disorders. They can also be mistaken for mental illness, similar to a case in the *Brain on Fire* autobiography and film about a journalist who was mislabeled as having a psychotic disorder until she was diagnosed with autoimmune encephalitis.

"The symptoms depend on which part of the nervous system gets damaged," Dr. Greenberg said. "We need to be on alert for Brutus, looking for that betrayal in the immune system."

Identifying Brutus among the billions of cell types in the immune system has not always been an easy task, in particular with multiple sclerosis. But advances have enabled scientists to identify unique genetic signatures and track where antibodies are attacking healthy cells.

In the case of multiple sclerosis, research led by UT Southwestern's Dr. Nancy Monson, Associate Professor of Neurology and Neurotherapeutics and Immunology, has identified a pattern of antibodies attaching to neurons. This was surprising considering 150 years of MS research that described this disease based on damage to myelin, the protective coating around nerve fibers.

"We're following this unexpected discovery to better understand multiple sclerosis," Dr. Greenberg said. "The condition may have more to do with the world of neurodegeneration than we thought."

A variety of treatments have been developed to reduce the inflammation stemming from autoimmune disorders, including steroids and plasma exchanges in which the harmful antibodies are removed. But scientists have yet to establish an effective treatment that can restore some of the body function lost after severe attacks on the immune system.

Dr. Greenberg is hopeful a clinical trial he will launch this year will establish the first such treatment. The trial will use stem cells – called progenitor cells – to try to reverse the paralysis in patients whose spinal cords were inflamed by transverse myelitis. If successful, the clinical trial could lead to similar therapies for more common conditions.

The trial is funded in part by Q Therapeutics, the Transverse Myelitis Association, the Lyda Hill Foundation, and the M.R. and Evelyn Hudson Foundation.

Dr. Brendan Kelley

Memory loss: When to worry, when to forget about it

Memory experts at UT Southwestern commonly see patients concerned about developing dementia. The patients may notice taking longer to remember details, or perhaps they've forgotten an event entirely.

"But when should we worry, and when should we forget about it?" asked Dr. Brendan Kelley, a memory disorders expert and Vice Chair for Clinical Operations at UT Southwestern. "Sometimes memory issues are simply part of normal aging."

Dr. Kelley, Associate Professor of Neurology and Neurotherapeutics, acknowledged that while no objective measure of normal aging has been established, studies show that certain cognitive functions gradually change later in life in many patients who don't develop dementia.

Taking a couple of minutes to remember someone's name, for instance, may not require medical attention. But dense amnesia, uncharacteristic poor judgment, or decreased problem-solving skills might be signs of trouble.

Because Americans are living longer and have greater awareness of Alzheimer's disease, more patients are seeking medical help when they experience symptoms.

"Conditions that are associated with aging are of increasing personal and societal importance," Dr. Kelley said. "Fortunately, there are many ways that we can decrease the risk of developing cognitive impairment."

He noted memory disorders are strongly associated with lack of sleep, hypertension, high blood pressure, and diabetes, among other factors.

Exercise and healthy eating, such as the Mediterranean diet, are two primary strategies for reducing risk, he said, but only if they're implemented early enough.

"If you're going to start exercising after you already have Alzheimer' disease, you've waited too long," Dr. Kelley said. "The best treatment is prevention."

UT Southwestern scientists test new strategies to attack brain cancer cells

Dr. Elizabeth Maher foresees a day when brain cancer no longer amounts to a death sentence. She anticipates a time when vaccines might prevent the entire ordeal.

Her optimism stems from the insight scientists are gaining into the vulnerabilities of cancer cells – their need for sugars and fats for fuel and their predictable locale in the brain while dormant.

"Every tumor is unique, but there are common themes," Dr. Maher said. "Our goal is to identify and target these shared weaknesses."

Dr. Maher, an oncologist who specializes in brain tumors, was the final speaker at the annual campus event that this year included lectures from O'Donnell Brain Institute faculty members.

She explained the notable progress in cancer treatment and research, including new technologies that have enhanced brain imaging and drug-testing capabilities. Although such improvements have contributed to a 25 percent drop in the U.S. cancer death rate since the early 1990s, Dr. Maher acknowledged much work remains to achieve the ultimate goal of prevention.

Dr. Elizabeth Maher

"We have to do the thinking upfront and be smarter in our approaches," said Dr. Maher, Professor of Internal Medicine and Neurology and Neurotherapeutics who also directs UT Southwestern's translational research program in Neuro-Oncology, part of the Annette G. Strauss Center for Neuro-Oncology. "One day we will vaccinate for cancer, and I intend for it to be in my lifetime."

She elaborated on the difficulties of treating glioblastoma, an aggressive brain cancer that – even with chemotherapy and radiation – results in short survival. The disease isn't curable through surgery because its cells don't grow as a lump; instead they migrate through the brain.

But scientists are testing new strategies that utilize insight into how and when cancer cells migrate and divide.

Dr. Maher cited two major research projects at the O'Donnell Brain Institute and Harold C. Simmons Comprehensive Cancer Center that may lead to potential therapies: One is focused on finding ways to remove the sugar and fats that cancer cells feed on while dormant and the second involves understanding how the cells move in the tight spaces of the brain.

"The imaging shows these cells hiding in plain sight," she said. "The problem is, we don't yet know how to kill them when they're dormant and not dividing."

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Dr. Diamond holds the Distinguished Chair in Basic Brain Injury and Repair.

Dr. Greenberg is a Cain Denius Scholar in Mobility Disorders.

Dr. Maher holds the Theodore H. Strauss Professorship in Neuro-Oncology.

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

More online: To read the full stories and watch speaker videos, go to *Center Times Plus* at **ct.utsouthwestern.edu**.

Nominata Continued from page 1

"Then my high school teacher got me interested in understanding biological activities, encouraged me to pursue my studies, and gave me the confidence to try for college."

Mr. Du excelled academically, placing second out of 160,000 students on the national college entrance exam in his province. He was accepted to Tsinghua University, described as the MIT of China. There he trained in several laboratories, including one run by a world-renowned structural biologist.

"In China, the only way for children from the poor countryside to change their destinies and improve their futures is to get an education, especially college," he said.

Mr. Du is a fifth-year graduate student in the UT Southwestern laboratory of Dr. Zhijian "James" Chen – Director of the Center for Inflammation Research, Professor of Molecular Biology, and a Howard Hughes Medical Institute Investigator. Mr. Du recently presented the Nominata Lecture, describing his work on innate immunity to an audience of faculty members and fellow graduate students.

"It's such an incredible honor to receive this award and to share my research in a University lecture," he said.

He said he chose UT Southwestern for graduate school because of its international reputation.

"My mentor, Dr. Chen, is one of the best scientists in the whole world to study cellular signaling using traditional biochemical approaches, and he made several fundamental discoveries on innate immune signaling pathways," Mr. Du said.

Mr. Du's thesis work focuses on the activation of innate immune signaling by DNA-induced liquid phase condensation of cyclic GMP-AMP synthase (cGAS), the cellular sensor of DNA discovered in 2012 in the lab of Dr. Chen, who became UT Southwestern's newest Breakthrough Prize winner based on that advance.

When he arrived for a graduate school rotation in the Chen lab, Mr. Du was given the tedious but important research needed to characterize single- and double-stranded DNA of different lengths, DNA/RNA hybrids, as well as DNA from different species and organelles within the cell to determine those to which the DNA sensor cGAS reacted most strongly.

The experiments required careful planning and long hours in the lab. By working through the winter holiday, he moved the project to an advanced stage before leaving to complete his other rotations, then returned to continue the painstaking work.

His observations caused him to suspect that cGAS might be undergoing protein liquid-liquid phase separation, a physical chemistry process he had encountered during a rotation in the laboratory of Dr. Michael Rosen, Chair of Biophysics and a pioneer in showing that liquid-liquid phase separation is vital for a variety of biological processes.

Next, Mr. Du conducted experiments that confirmed the activation of cGAS via DNA-induced liquid phase separation. He also identified a switch-like threshold effect that helped explain how cGAS can detect and respond to infection from pathogenic DNA while avoiding reacting to low amounts of self-DNA in the cytoplasm, said Dr. Chen, who is also a member of the Center for the Genetics of Host Defense.

As a result, Mr. Du became lead author on a two-author study with Dr. Chen published in *Science* last year that found cGAS forms droplets (foci) that act as tiny bioreactors creating molecules to stimulate innate immunity – the body's first response to infection. "I should stress that Mingjian single-handedly conceived and executed all the experiments that led to the exciting discoveries reported in his *Science* paper," Dr. Chen added.

Dr. Chen said he expects Mr. Du's findings to greatly facilitate the design and development of cGAS inhibitors, therapeutics that have the potential to treat autoimmune diseases such as lupus.

"It is very likely that several other proteins involved in innate immunity and inflammation also have similar liquid phase separation behavior and I believe his paper will have a great impact in the immunology field," Dr. Chen said. "In summary, Mingjian is a highly talented, extremely driven student who has the potential to become a next-generation scientific leader."

Mr. Du plans to return for a sixth year. After graduate school, he intends to pursue postdoctoral work in neuroscience.

"I'm fascinated and obsessed with fundamental questions such as how memory is initiated, consolidated, and recalled. Additionally, a role of quantum physics in consciousness has been implied, and I'm also very interested in studying that possibility," he added.

He hopes his parents, who still live in China, will be able to visit when he graduates and said that they support him and are proud of his accomplishments, though it is hard for them to understand his work. Mr. Du visits them every year or two.

"Sometimes tears come from my mom and she says that she misses me on video chat, but this gives me the momentum to work hard," he said.

In addition to Mr. Du's honor, Dr. Bishakha Mona of the Genetics, Development, and Disease Graduate Program received a Dean's Discretionary Award for research excellence and superior ability to communicate her science. Dr. Bishakha, the recipient of the 2019 Ida M. Green Award in April, recently completed her Ph.D. in the laboratory of Dr. Jane Johnson, Professor of Neuroscience.

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Dr. Chen holds the George L. MacGregor Distinguished Chair in Biomedical Science.

Dr. Johnson holds the Shirley and William S. McIntyre Distinguished Chair in Neuroscience.

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

More online: Read the full story and watch a video on *Center Times Plus* at **ct.utsouthwestern.edu**.

Community health fair provides free screenings, sports physicals

By Patrick Wascovich

Alexander Sanchez and Carlos Mendoza rolled up their eighth grade sleeves and got down to the puzzle at hand: extracting DNA from strawberries.

"We're interested in engineering, but this was cool," said Carlos, a student at Thomas J. Rusk Middle School.

This must've been music to the ears of Mehraban Kavoussi, then a first-year student at UT Southwestern Medical School. He was working with the two Rusk students at UT Southwestern Medical Center's annual Carnaval de Salud.

The April 27 event, organized and run by UT Southwestern students and faculty and staff volunteers, is in its 15th year of providing free health care services, information, and lifestyle strategies to hundreds of families from underserved populations in Dallas. It is part of the UT System's "United to Serve" initiative.

Through projects like the strawberry DNA and other interactive booths, UTSW's educational mission was effectively delivered, allowing students to learn more about science, health, and the human body – perhaps without even realizing it.

"The Science Zone offers a unique opportunity to learn about the science of the human body, face to face with UT Southwestern students," said Dr. Alice Jean, a recent Medical School graduate and one of this year's event co-directors. "That type of relaxed and interactive environment really makes the subjects approachable and fun for patrons of all ages."

Carnaval de Salud keeps growing by the year, as nearly 200 people lined up prior to the 9 a.m. opening at the school. By midafternoon that Saturday, the hallways were still bustling and more than 600 people had taken part in UTSW's community outreach.

"It's absolutely wonderful," said Elisa Simmons, who brought along daughters Alecia, a sophomore at Lancaster High School, and Jasmin, a student at Cedar Valley College. "There's so much useful information, and it's presented in a family-friendly way."

Jacqueline Escobar, meanwhile, wasted little time in Rusk's East Gym, first getting a hands-on feel for CPR before moving to the first-aid station to bear hug a mannequin for Heimlich experience. Her youngest, 20-month-old Samantha, had already given Mrs. Escobar and older daughter Kimberly, 11, ample reason for practical training.

"She's twice had choking incidents," Mrs. Escobar said. "At Samantha's age everything, not just food, goes in the mouth. You never know when you'll need it, but getting this experience helps."

Third grader Vhinu Womeni (left) takes a closer look, along with medical student Angela Zhang.

School of Health Profession students Rayna Jeter (left) and Jamala Christopher offer tips for healthy dishes.

An attendee learns how to suture by practicing on a banana peel.

Students from the Medical School, UT Southwestern Graduate School of Biomedical Sciences, and UT Southwestern School of Health Professions plan and coordinate the fair, which featured about 75 stations and involved more than 500 volunteers this year. Afterward, students proactively follow up with community members who participated.

"Carnaval de Salud provides a welcoming environment where patrons can undergo basic health screening, learn about common medical conditions, and enjoy fun and educational activities for the whole family," said Dr. Claire Mauvais, a recent Medical School graduate and event co-director. "UT Southwestern students work together to reach all ages, emphasizing preventive care and providing resources to encourage healthy lifestyle choices in our community. It's great for everyone involved."

This year's event, themed "Into the Wild," featured free health screenings for several common conditions such as diabetes, high blood pressure, and high cholesterol. Dallas ISD student-athletes like Jukeen Bellows who needed a health screening could get a free sports physical and learn about local health resources. Jukeen, a junior at Emmett J. Conrad High School, got his football physical even before summer training. "We're here, it's free, and he's now ready to go," said his mother, Janeeka Bellows.

For young kids, the fair had carnival activities, arts and crafts, and more than 20 drop-off boxes for a chance at prizes.

Participants milled around two tables featuring some of the day's popular giveaways: the UTSW Police gave out flying discs and wristbands, and a team from the School of Health Professions offered healthy recipes and ingredient options.

"I've gotten some great recipes and tips," said Tiffany Thomas, who is raising her nephews, middle-schoolers Nicolas and Cadyn Rogers. "I've told my nephews that if you go too hard, you can lose steam and not achieve your goal. We've been shown practical approaches to meals that take little dietary steps. Now we have a better chance to succeed."

More online: To view a video and more photos from the event on *Center Times Plus*, go to **ct.utsouthwestern.edu/ctplus/stories/2019/carnaval-de-salud.html**.

A 15-year legacy of service

Carnaval de Salud's enduring popularity showcases the continued need for access to care, as well as the need to engage the community to promote health and a healthy society that enables achievement of full human potential.

Guided and shaped by the Medical Center's institutional pillars of education, discovery, and healing, this culture flourishes because leadership understands that community engagement can serve as the key entry point for many to connect with UTSW's health care system and link them to resources that can enhance their future well-being.

"United to Serve's impact on participants and its incredible structure of service-oriented learning enables students to develop robust experiences in community and public health by effectively applying medical knowledge for the betterment of our community," said Dr. Bethany Werner, event co-director and a recent Medical School graduate. "All in all, this exemplifies UT Southwestern's commitment to increasing access to care and enhancing the public's awareness of the importance of healthy living and prevention."

Babies who arrived early celebrate life with hospital staff who worked to save them

By Carol Marie Cropper

Nurse Miosotis Mejia looked out on the growing crowd of squirming, laughing, crying, running children at William P. Clements Jr. University Hospital recently and proclaimed the chaos one of her favorite events.

The joyful ruckus was part of UT Southwestern's annual Preemie Party, hosted by the hospital's Neonatal Intensive Care Unit (NICU). "We look forward to it every year," said Ms. Mejia, a NICU nurse. "It's so much fun. It's so rewarding."

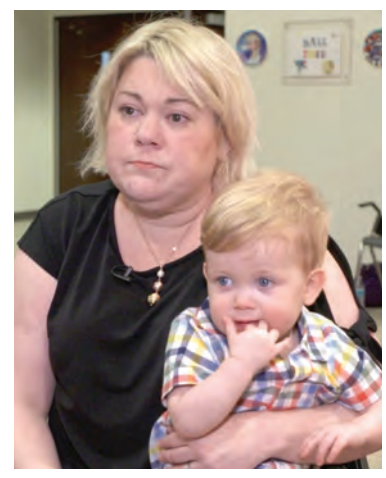
The April 28 party reunited about 100 former preemie (prematurely born) patients and family members with the NICU nurses and other medical staff who cared for them at Clements University Hospital.

"We had some babies that we worked so hard on and we weren't sure they were going to make it. But then they did and they came back and they're running around," Ms. Mejia, a former preemie herself, said with a smile.

Ms. Mejia helped organize the event, which featured a bounce house, cake, and visits from "Spider-Man" and "Elsa" of Disney's "Frozen" fame.

But the main attractions were children like Celeste Salgado, whose arrival into the world was alarmingly early. She was born at 24 weeks gestation, just inside the cutoff for survival, and weighed 15 ounces – not even a pound. But at the Preemie Party, Celeste was there, doing well, and set to turn 10 years old the day after the party. It was her family's ninth year in attendance.

Sisters Celeste Salgado (left) and Isabel Salgado attended the party. Ten-year-old Celeste was born at 24 weeks gestation, just inside the cutoff for survival.



Amy E. Davidson Williams holds her 17-month-old son, Osbourn.

Waylon Irizarry, another 24-weeker, was also among the preemies taking it all in. Now just shy of 11 months old, he spent his first 99 days in the NICU at Clements University Hospital. "We were very worried that we would lose him because he was so little," said his mom, Jessica Irizarry, as she wrestled with the boy wiggling on her lap. "He's doing amazing now. He's not on any medications. He is a normal baby."

Nearby, Amy E. Davidson Williams was holding her 17-month-old son, Osbourn. "My husband and I wanted a baby for a really long time," she said. "I was 41 when I got pregnant."

Everything seemed fine until she went in for a routine prenatal checkup at 30 weeks and learned she had preeclampsia, a type of high blood pressure that affects some pregnant women and can cause liver or kidney damage and, in the worst cases, death.

"My OB said, 'You have to have him now to save you both,'" Ms. Williams recalled. After the birth, "When they said, 'He weighs 3 pounds and he's unable to breathe on his own,' the world sort of stopped turning for me."

But Osbourn was a fighter. "Now, he's wonderful," she said. "He's doing really well with some motor and communication skills issues. He wants to get into everything. He is just a very happy and sometimes very naughty – but in a good way – little boy."

She had a special reason for making the trip back to Clements University Hospital for the party. "It's important for me and for him to know where he was born, how he was born, and how many people are responsible for him being here.

"We don't go to church every Sunday," Ms. Williams said, "but we pray every night, and every night since he was born we pray for the people in the NICU who saved him."

About 1 in 10 babies are born preterm (before 37 weeks gestation), according to the Centers for Disease Control and Prevention (CDC). Preterm birth and low birthweight is the second leading cause of infant death in the United States, reports the CDC.

Babies delivered early are at increased risk of having underdeveloped lungs, bleeding in the brain, intestinal inflammation, and heart problems, said Dr. Rashmin Savani, Chief of Neonatal-Perinatal Medicine and Professor of Pediatrics at UT Southwestern.

The American College of Obstetricians and Gynecologists now recommends that moms try to carry their babies to at least 39 weeks, recognizing that important organs such as the brain, lungs, and liver are still developing at the 37-week threshold, Dr. Savani said.

Parkland Memorial Hospital, the public hospital affiliated with UT Southwestern, was able to push its preterm birth rate down from 10.4 percent to 4.9 percent – half the earlier rate – after increasing prenatal care, according to a study published in *Obstetrics & Gynecology* in 2009. Clements University Hospital currently has lower infection rates than other NICUs nationwide, thereby allowing for lower complication rates in these vulnerable infants.

Dr. Becky Ennis, Medical Director of the NICU and an Associate Professor of Pediatrics, was also on hand for the celebration.

"It's one of the best parts of our jobs," Dr. Ennis said of the event. "We take care of these babies for months. They feel like family to us. It's wonderful to see how they grow."

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Dr. Savani holds The William Buchanan Chair in Pediatrics.

More online: To read the full story and watch a video on *Center Times Plus*, go to **ct.utsouthwestern.edu/ctplus/stories/2019/nicu-preemie-reunion.html**.