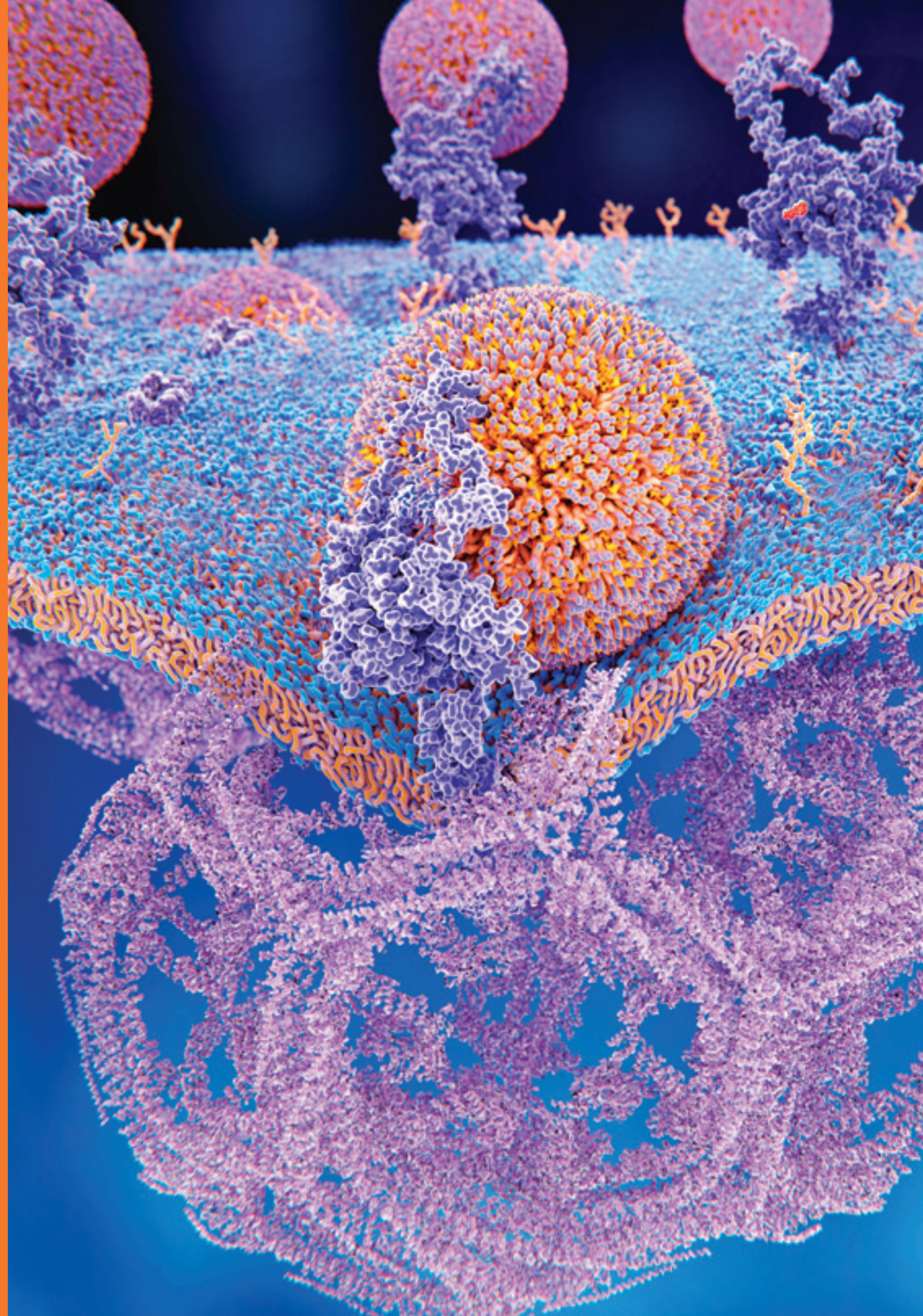
Advancing Scientific Discovery

A breakthrough takes patience, attention to detail, and painstaking trial and error. But the payoffs can be huge. Significant research advances by UTSW scientists this past year ranged from efforts to unleash the body's cellular recycling process to fight infections to reprogramming neurons in a novel way and in turn uncovering clues about a vulnerability in Parkinson's disease.



This image shows LDL receptors binding to a cell membrane. UTSW research has revealed how circulating LDL cholesterol enters artery walls, causing plaque.

Leading a national effort to develop new weapons against pathogens

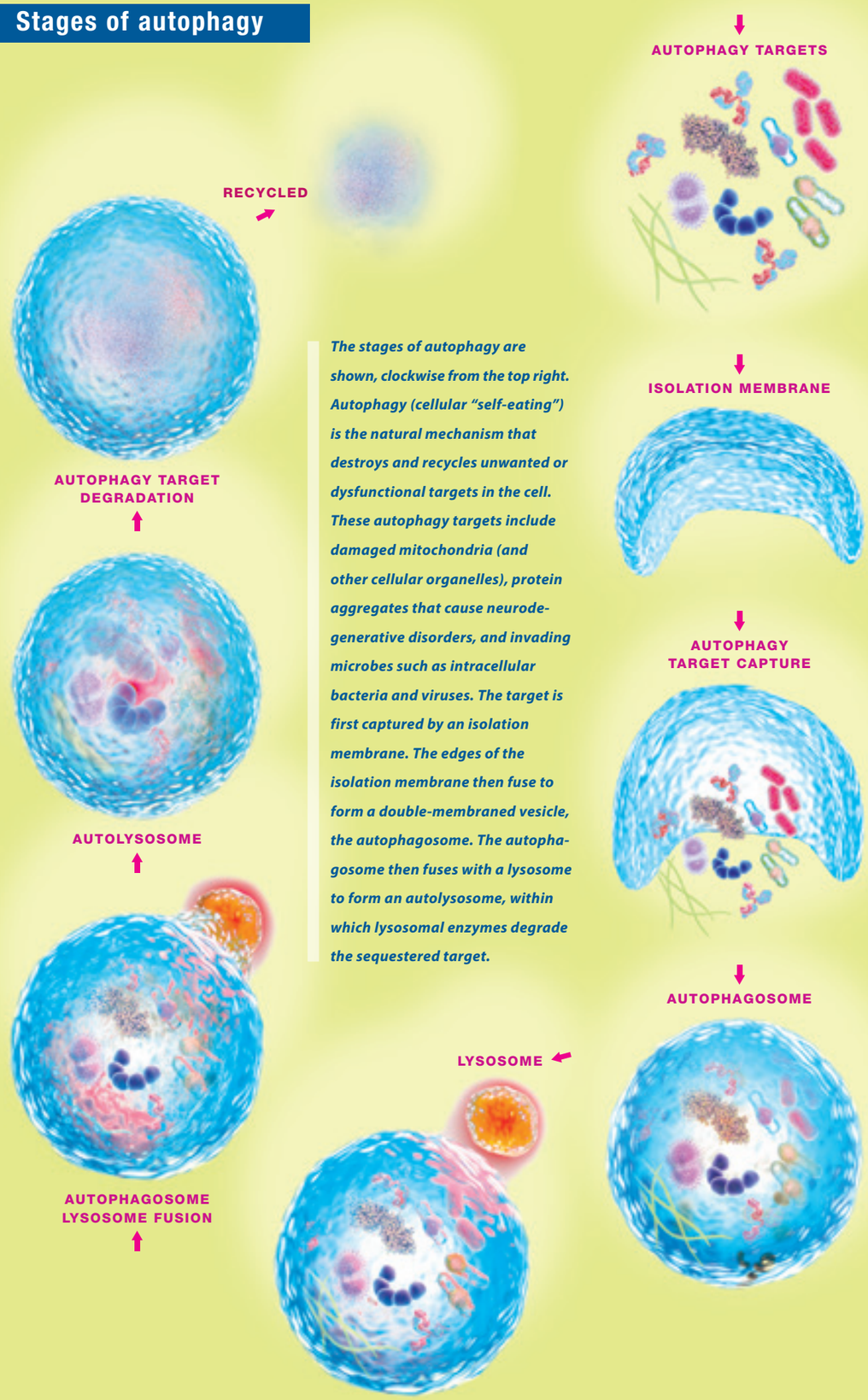
Amid growing concern about pathogens becoming more drug-resistant worldwide – and emerging new pathogens that have no current treatment – UT Southwestern is leading a five-year investigation into a promising new approach for controlling infections, funded by a grant of up to $37 million.

The National Institutes of Health (NIH)-funded program is headed by Dr. Beth Levine, Director of UT Southwestern's Center for Autophagy Research and a Professor of Internal Medicine and Microbiology.
Dr. Levine serves as Program Director over five separate research projects at UT Southwestern and across the country – all focused on the potential to exploit a cellular process known as autophagy, a natural mechanism that destroys invading bacteria and viruses.

"The process of autophagy takes place inside all human cells and is used to break down damaged parts of the cell," explained Dr. Levine, an internationally recognized expert in the field and a Howard Hughes Medical Institute Investigator. "Since the late 1990s, there has been a growing body of research showing that cells can also use autophagy to destroy pathogenic invaders and to regulate host immune responses to infectious diseases."

"During autophagy, the target to be destroyed is encased in a double-membrane compartment inside the cell called an autophagosome, which then merges with other compartments containing enzymes and acids

As part of a large NIH grant, Drs. Beth Levine and Michael Shiloh are investigating how to use a cellular recycling process called autophagy to improve defenses against bacteria and viruses.



to degrade the target," said Dr. Michael Shiloh, Associate Professor of Internal Medicine and Microbiology, who serves as the program's Associate Director. Dr. Shiloh holds the Professorship in Infectious Diseases, in honor of James P. Luby, M.D.

"Maximizing this natural defense could result in treatments effective against a broad range of pathogens – even before the cause of an illness is identified," Dr. Shiloh said. "That would make it a vital tool for combating a new outbreak or an act of bioterrorism requiring rapid response. Also, enhancing autophagy could kill infectious organisms that are resistant to traditional antibiotics."

Under the grant, awarded last year, UT Southwestern is working with five other research sites as a Center of Excellence for Translational Research supported by the National Institute of Allergy and Infectious Diseases: the Broad Institute in Cambridge, Massachusetts; Massachusetts General Hospital and Harvard Medical School in Boston; Vir Biotechnology Inc. in San Francisco; Washington University School of Medicine in St. Louis; and The Scripps Research Institute in La Jolla, California.

"The Center has been charged with investigating possible treatments for emerging and reemerging infectious diseases, in particular so-called 'priority pathogens' that are drug-resistant, have no treatment, or could be used by bioterrorists," Dr. Shiloh said.

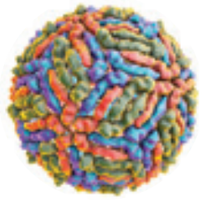
As co-leader of one of the projects, Dr. Shiloh is investigating use of autophagy to treat tuberculosis. This disease killed 1.6 million people worldwide in 2017 and has developed significant multidrug resistance, according to the World Health Organization, or WHO.

Dr. Levine leads a different project focused on how to ramp up autophagy within the body in order to augment host defenses against West Nile and other mosquito-borne viruses. In 2018, Dr. Levine's group published a report in *Nature* showing that genetically engineered mice with increased autophagy live longer and healthier lives. These findings raise the possibility that pharmacological strategies to increase autophagy, including in the setting of infectious diseases, may be well tolerated.

The new NIH grant follows a similar five-year award funded in 2013 in which UT Southwestern took part. Research conducted with the earlier funding generated several patents, licensing agreements, and promising compounds that can potentially be used to develop autophagy-inducing anti-infective agents, said Dr. Levine, who holds the Charles Cameron Sprague Distinguished Chair in Biomedical Science. With the new support, Drs. Levine and Shiloh are optimistic that even more breakthroughs to improve human health are possible.

In other work, UTSW research supported through a gift from Linda and Mitch Hart has indicated that autophagy enhancers may promote a healthy lifespan and longevity.

"If we can find ways to enhance autophagy in our cells, this could result in new treatments that would harness the body's own defenses to help fight infections," Dr. Levine said. "Moreover, such treatments could also be helpful to combat other diseases that may benefit from increased autophagy, such as certain neurodegenerative disorders and cancers."



Ramping up autophagy can augment host defenses against many types of bacterial or viral infections, such as the disease caused by the West Nile virus particle, pictured above.

Immunology advance provides clues to vitamin A infection link

Researchers have solved the longtime mystery about why people with diets deficient in vitamin A are more prone to skin infections. Last year, UT Southwestern investigators identified a previously unknown bacteria-killing protein on the epidermis that needs the vitamin to work, a finding that builds on the University's foundational research and growing expertise in immunology.

The research team discovered that one protein in the resistin-like molecule (RELM) family – RELMα – acts as an antibiotic to rapidly kill bacteria in mice. Both RELMα and the corresponding human RELM family protein, called resistin, are stimulated by dietary vitamin A.

"RELMα is the first example of an antimicrobial protein that requires dietary vitamin A for its bacterial killing activity. This finding gives us an important clue about how the skin defends itself against infection, and how skin defense is regulated by the diet," said Dr. Lora Hooper, Chair of Immunology and corresponding author of the study published in *Cell Host & Microbe* last year.

Dermatologists use synthetic vitamin A, called retinoid, to treat acne, psoriasis, and other skin conditions, although how those drugs work has long been a mystery.

Drs. Lora Hooper (left) and Tamia Harris-Tryon found that a bacteria-killing protein on the skin needs vitamin A to work, revealing why synthetic versions of the nutrient are effective against skin disease.

"The skin is the largest organ of the human body and is tasked with defending us against infection," said Dr. Tamia Harris-Tryon, Assistant Professor of Dermatology and Immunology. "If the skin immune system breaks down, infection results."

The team's experiments in human tissue and mice illuminate a previously unappreciated link between diet and innate immunity of the skin, suggesting why vitamin A derivatives are effective treatments for skin disease, said Dr. Hooper, a Howard Hughes Medical Institute Investigator and UTSW Professor of Immunology and Microbiology. Dr. Hooper has an additional appointment in the Center for the Genetics of Host Defense, holds the Jonathan W. Uhr, M.D. Distinguished Chair in Immunology, and is a Nancy Cain and Jeffrey A. Marcus Scholar in Medical Research, in Honor of Dr. Bill S. Vowell.

Using Dr. Hooper's colony of germ-free mice – raised from birth without exposure to germs – the researchers identified genes that are turned on when such mice are exposed to bacteria.

"Considering how often retinoids are used in dermatology, the implications of our findings are potentially vast," Dr. Harris-Tryon said. "This study gives us a better understanding of how diet impacts the ability of the skin to defend itself against bacterial infection – but more research will be needed to determine how these findings will impact patients with inflammatory skin diseases such as acne and psoriasis."

Dr. Philip Shaul (right) examines study data with postdoctoral researcher Dr. Linzhang Huang. Dr. Shaul's research team discovered how "bad" cholesterol enters artery walls to develop into heart-harmful plaque.

Investigation exposes how 'bad' cholesterol enters arteries

It could be called the great reveal: A study by UT Southwestern researchers has uncovered how cholesterol enters artery walls to cause the plaque that leads to heart attacks and strokes.

The study shows for the first time how a protein called SR-B1 (short for scavenger receptor class B, type 1) ferries particles of LDL – the so-called "bad" cholesterol – 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.

Low density lipoprotein, or LDL, cholesterol entry into the artery wall drives the development of atherosclerosis, more commonly known as hardening of the arteries – and atherosclerosis leads to heart attacks and strokes. Future treatments preventing the process of LDL entry may help decrease the occurrence of these life-threatening conditions, said Dr. Philip Shaul, senior author of the study published last year by *Nature*.

Cardiovascular disease is the leading cause of death worldwide, and coronary artery disease (which underlies heart attacks) and strokes account for more than 60 percent of those cardiovascular deaths in the U.S., according to recent statistics from the American Heart Association.

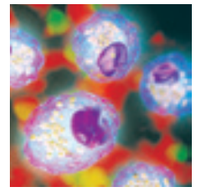
In the early stages of atherosclerosis, LDL that has entered the artery wall attracts and is engulfed by important immune system cells called macrophages that ingest, or "eat," LDL particles. LDL-laden macrophages become foam cells that promote inflammation and further the development of atherosclerotic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

However, in studies of mice with elevated cholesterol, the investigators determined that deleting the SR-B1 protein from the endothelial cells lining blood vessels resulted in far less LDL entering the artery wall. As a result, fewer foam cells formed, and atherosclerotic plaques 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, who holds the Associates First Capital Corporation Distinguished Chair in Pediatrics. "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 the abundance of SR-B1 and DOCK4 in areas of the mouse aorta that are prone to plaque formation with regions less likely to become atherosclerotic. They found higher levels of SR-B1 and DOCK4 in the disease-prone regions long before atherosclerotic



Foam cells are types of scavenger cells in atherosclerotic plaques that engulf LDL and accumulate lipid droplets.

plaques formed. This finding suggests that atherosclerotic lesions may be more common in particular artery sites because of the presence of more SR-B1 and DOCK4 at those locations, said Dr. Shaul, also Professor and Vice Chair for Research in the Department 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. In all three databases, SR-B1 and DOCK4 were more abundant in atherosclerotic arteries compared with normal arteries.

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 cells that line arteries in order to prevent atherosclerosis, Dr. Shaul said.

> "At the start of this work it was surprisingly unknown how LDL enters the artery wall to cause cardiovascular disease." – *Dr. Philip Shaul*

"If you could develop a drug that inhibits SR-B1 or DOCK4, or a gene therapy that silences them in those 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."

The dangers of hidden fat: Exercise is your best defense to fight it

Excess fat of any type can be bad for your health, but it's the deeper, hidden fat within the body that's most dangerous. To combat this type of fat, called visceral fat, exercise is a better defense than medication to fight it. UT Southwestern scientists made this discovery last year in research published in *Mayo Clinic Proceedings*.

"Visceral fat can affect local organs or the entire body system. Systemically, it can affect your heart and liver, as well as abdominal organs," said cardiologist Dr. Ian J. Neeland, Assistant Professor of Internal Medicine and corresponding author of the study.

Obesity affects nearly 40 percent of adult Americans, according to the Centers for Disease Control and Prevention, and can lead to heart disease, stroke, Type 2 diabetes, and certain types of cancer.

The UTSW research team wanted to find out whether exercise or medication was the best weapon to fight visceral fat. Changes in visceral fat were evaluated in 3,602 participants during a six-month period measured by a CT or MRI exam. Both exercise and medicines reduced visceral fat, but the effects of exercise were more significant per pound of body weight lost.

The majority of exercise trials were performed in the U.S. and Canada, while the pharmacologic trials included the U.S., Canada, Sweden, Japan, and four multinational cohorts.

"The location of fat in the body and the type of fat is important. If you just measure weight or body mass index (BMI), you can underestimate the benefit to your health of losing weight," said Dr. Neeland, a Dedman Family Scholar in Clinical Care. "Exercise can actually melt visceral fat."

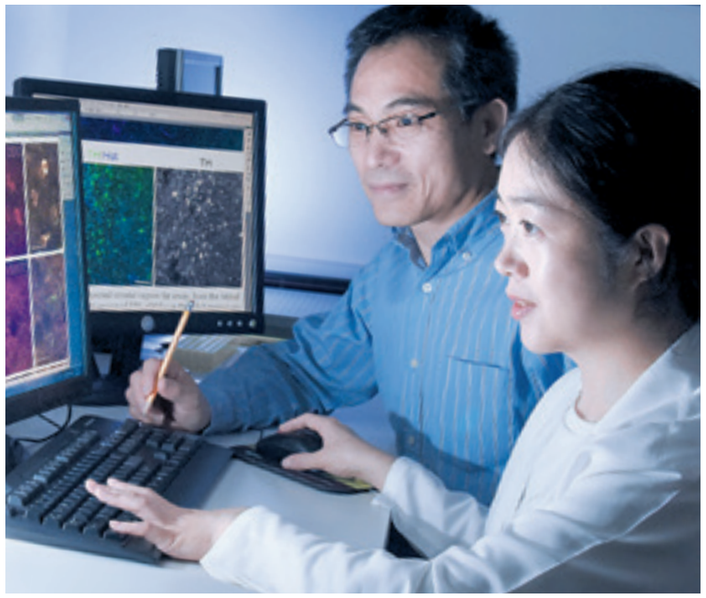
Dr. Neeland said researchers previously thought of fat as inert storage, but over the years this view evolved and fat is now seen as an active organ.

(Left) Dr. Ian J. Neeland's investigation found that exercise works better than medication to combat hidden, visceral fat.

"Some people who are obese get heart disease, diabetes, or metabolic syndrome – and others don't," Dr. Neeland said. "Our study suggests that a combination of approaches can help lower visceral fat and potentially prevent these diseases."

Basic research sheds new light on Parkinson's disease

While attempting to transform supporting brain cells into neurons, UT Southwestern researchers instead reprogrammed mature inhibitory neurons into a different type – nerve cells that generate the neurotransmitter lost in Parkinson's disease. The surprise discovery reveals new insights about this movement disorder.



Drs. Chun-Li Zhang (left) and Lei-Lei Wang unexpectedly reprogrammed mature inhibitory neurons into a different neuron type that is linked to Parkinson's disease. The research holds promise as a translational medicine discovery that could lead to new treatments for the incurable disease.

This basic research holds promise as a translational medicine discovery that may lead to new treatments for Parkinson's, an incurable neurodegenerative disease in which the brain cells progressively die.

The study, published in *Stem Cell Reports,* suggests mature neurons may be changed from one kind to another without relying on stem cells, contrary to the prevailing view.

"To find that we could manipulate neurons to change their identity in adulthood was truly unexpected," said Dr. Chun-Li Zhang, Professor of Molecular Biology and corresponding author of the study, adding that insights into neuronal plasticity and cell identity maintenance may someday lead to therapeutic strategies for treating neurological diseases through the reprogramming of local neurons.

The mouse study indicates that the brain's neurons are more changeable in adulthood than previously thought, said Dr. Zhang, also a W.W. Caruth, Jr. Scholar in Biomedical Research. The long-held belief was that a neuron's identity was sealed well before adulthood and that one kind of neuron could not morph into another variety, he added.

"Initially, I was a little disappointed that we altered the properties of medium spiny neurons and not the supporting glial cells we were targeting," he said. "But when we realized the novelty of our results, we were amazed. To our knowledge, changing the identity of resident and mature neurons had never been accomplished."

Boxing gives Parkinson's patients a fighting chance

Judy Danielson, who has Parkinson's disease, is fighting for her life. She is using a unique therapeutic strategy – boxing – and has already seen improvement. The rehabilitation program grew out of UT Southwestern research evaluating the benefits of exercise in Parkinson's patients.

"The first thing I thought of after being diagnosed was: This is not the plan I had for my life. This is not what my retirement was going to be," Ms. Danielson said.

While Ms. Danielson was visiting the UT Southwestern Gait Clinic, her therapist, Heather Mowry, suggested she check into the boxing program and research study designed to assist rehabilitation.

Ms. Danielson praised the program, saying she has seen a vast difference in her balance, her walking ability, her strength, and her emotional health. "It's about so much more than just boxing," she said.

Dr. Michael Braitsch, a 2016 UT Southwestern School of Health Professions alumnus, developed the noncontact boxing program that he hosts at Preston Hollow United Methodist Church in Dallas. The classes incorporate big dynamic functional movements, balance training, and aerobic exercise to improve cerebral blood flow and circulation throughout the body. After spending years in the financial services industry, Dr. Braitsch discovered his calling in helping patients like Ms. Danielson.

"In some ways, we're trying to fight back against impairments associated with Parkinson's. In other ways, we're trying to slow the progression of symptoms," Dr. Braitsch said.

UTSW Assistant Professor of Physical Therapy Dr. Staci Shearin joined the effort as Principal Investigator for the study. Both she and Dr. Braitsch have witnessed emotional and physical improvements in study participants.

"In our data, we've seen improvements in patients in several ways, including with functional strength and walking ability. We've seen some really cool results in functional mobility, especially in dual tasks – which is a really important skill for balance and safety for individuals with Parkinson's and their ability to do two things at once," Dr. Shearin said. "Exercise is probably one of the most important activities that can affect the progression of Parkinson's. We also find that the higher the intensity of exercise, the better the benefits."

UTSW School of Health Professions alumnus Dr. Michael Braitsch demonstrates boxing techniques to a class participant in a research study designed for patients with Parkinson's disease.

Because the neurotransmitter dopamine is lost in movement disorders like Parkinson's disease, many neuroscientists are interested in the possibility of someday creating new dopamine-producing neurons. Dopaminergic cells are important for controlling voluntary movement and emotions such as motivation and reward that drive behavior, Dr. Zhang explained.

For proper function, levels of the neurotransmitters GABA, dopamine, and others need to exist in a delicate balance in the brain, he said. Because dopamine is involved in reward behavior, including addictive behaviors, any potential treatment to increase dopamine levels would also need a way to keep the levels of other neurotransmitters in balance, he added.

The mature medium spiny neurons that changed their identities in this study usually produce GABA, an inhibitory neurotransmitter that targets other neurons throughout the adult brain, Dr. Zhang explained.

This work was supported by The Welch Foundation, The Michael J. Fox Foundation, The Decherd Foundation, and the Judith and Jean Pape Adams Charitable Foundation.

> "When we realized the novelty of our results, we were amazed. To our knowledge, changing the identity of resident and mature neurons had never been accomplished." – *Dr. Chun-Li Zhang*

Unlocking the cellular connections to neurodegenerative diseases

UT Southwestern research that delves into the way certain proteins respond under metabolic stress could have far-ranging applications to understanding the development of neurodegenerative disorders such as amyotrophic lateral sclerosis, or Lou Gehrig's disease.

"There's pretty good evidence that variants of the human ataxin-2 protein are associated with neurodegeneration, and now we might have some clues as to why," said Dr. Benjamin Tu, a Professor of Biochemistry and UT Southwestern Presidential Scholar.

Two studies from Dr. Tu's lab published last year in *Cell* revealed several key functions of the yeast version of this poorly understood protein.

Using various approaches, the researchers tied yeast ataxin-2 to autophagy – the so-called housekeeping process that recycles nutrients to the cell during times of stress. They also found important implication for maintaining the health of the cell's energy source, the mitochondria. Finally, the research revealed an important role in the cellular defense against reactive oxygen species, also known as free radicals. Under normal conditions, ataxin-2 molecules form assemblies that regulate a pathway to help cells deal with that oxidative stress.

"Assembly formation is critical for ataxin-2 to do its job, and when its function is compromised, cells and neurons are more likely to die," said Dr. Tu, a W.W. Caruth, Jr. Scholar in Biomedical Research who holds the Martha Steiner Professorship in Medical Research.

He emphasized that finding ways to sustain or increase these protective functions of ataxin-2 could someday lead to neuron-saving treatments. His lab is interested in identifying small, drug-like molecules for this purpose.

Dr. Benjamin Tu has been studying a protein linked to neurodegenerative disorders. His research suggests that increasing the protective functions of this protein could lead to neuron-saving treatments.

Perot Foundation's $25 million gift advances brain science

A generous donation given by Margot and Ross Perot Sr. last spring (just prior to Mr. Perot's death in July) will accelerate UT Southwestern's efforts to discover new treatments and potential cures for brain and other neurodegenerative diseases.

The Perot Foundation's gift of $25 million last year supports neuroscience translational research at the Peter O'Donnell Jr. Brain Institute. With this latest gift, cumulative support from the Foundation has grown to more than $90 million since the 1980s.

"Our family supports UT Southwestern because we strongly believe in its mission to give every person a chance to live a healthy, productive life," Mrs. Perot said. "Our investment in the people who expand and deliver knowledge to advance science, technology, and medicine has reaped tremendous dividends. We are hopeful that this gift will lead to new treatments for brain diseases and, ultimately, cures."

The gift will expand activities in UT Southwestern's Perot Foundation Neuroscience Translational Research Center, renamed so in the family's honor. The Center's goal is to facilitate and enhance quality clinical research within the O'Donnell Brain Institute by providing resources for scientists, clinicians, and patients in the facilitation of research protocols and clinical trials and helping researchers obtain funding from the National Institutes of Health and other sources.

The gift also will help transform the Center's current biorepository into a state-of-the-art biobank, which will house large volumes of biological samples, neuroimaging, and electrophysiological data. The biobank will bring better understanding of how to maximize treatment outcomes through personalized medicine.

"Ross and Margot have always been true visionaries, driven and inspired by the potential of what the world could become," said Dr. Daniel K. Podolsky, President of UT Southwestern, who 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. "Over many decades, they have generated excitement around our institution's mission and vision through their collaborations and philanthropic gifts. This extraordinary gift will usher in new eras of innovation and development and accelerate the translation of discoveries into new treatments and cures for brain diseases and disorders."

Members of the Perot family, from left: Katherine Reeves, Suzanne McGee, the late Ross Perot Sr., Margot Perot, Ross Perot Jr., Nancy Perot, and Carolyn Rathjen

Remembering UTSW benefactor and legend Ross Perot Sr.

One of UT Southwestern's most steadfast benefactors for more than three decades, legendary Texan Ross Perot Sr., passed away July 9 at the age of 89, leaving an enduring legacy.

An enormously successful businessman, political leader, and philanthropist, Mr. Perot was known for his loyalty and commitment to his country, community, and family – typifying the great American citizen. He was a man possessed of tremendous drive, enviable business acumen, and keen intellect, with a clear sense of when and how he might improve the human condition.

UT Southwestern benefited immensely from his generosity and leadership. Mr. Perot and his wife, Margot, and the Perot Foundation have contributed more than $90 million to UT Southwestern, including more than $50 million to the *Innovations in Medicine* campaign.

"Mr. Perot's extraordinary support for UT Southwestern enabled us to establish and provide exceptional educational opportunities for generations of future physician-scientists and deliver impactful research and care that has left a lasting impact on Texas and the nation," said Dr. Daniel K. Podolsky, President of UT Southwestern.

Mr. Perot founded and later sold two high-tech companies, Electronic Data Systems and Perot Systems. He also was one of the most successful independent candidates for the U.S. presidency, winning nearly 19 percent of the popular vote in 1992. He ran for President again in 1996 as a Reform Party candidate. Mr. Perot also authored several books, including *Ross Perot: My Life & the Principles for Success* and *United We Stand: How We Can Take Back Our Country.*

In philanthropy, Mr. Perot set his sights on supporting internationally renowned institutions and became impressed with UT Southwestern's advancement from its humble beginnings in the 1940s.

The Perots and their Foundation provided generous support for UT Southwestern's Medical Scientist Training Program (MSTP) as well as Gulf War syndrome research efforts. Most recently, the Perot Foundation established the Perot Foundation Neuroscience Translational Research Center at UT Southwestern. This latest expression of the Perot family's generosity is supporting translational research at the Peter O'Donnell Jr. Brain Institute to move science more quickly from the laboratory to the patient's bedside and transform research discoveries into improved and innovative drugs, devices, and treatments.

"Mr. Perot was a true friend to the Medical Center and a remarkable man whose inspirational leadership touched all who knew him," said Dr. Podolsky. "He will be deeply missed."

Acclaimed neurologist leads O'Donnell Brain Institute

The deep commitment of UT Southwestern's leadership and community supporters to create a premier center for the study and treatment of brain disease, along with the Medical Center's renowned scientific culture, made Dr. William T. Dauer consider the offer to become inaugural Director of the Peter O'Donnell Jr. Brain Institute a compelling and exciting opportunity.

"The commitment of both the University and the surrounding community, with Mr. Peter O'Donnell at the forefront, is really unparalleled in any environment I know of," said Dr. Dauer, an acclaimed physician-investigator in dystonia and Parkinson's disease who was recruited after a national search.

"The dedication to make this an important priority to change the lives of people with brain disease will be the key ingredient for success."

In July, Dr. Dauer joined UT Southwestern as Director of the O'Donnell Brain Institute and Professor of Neurology & Neurotherapeutics and Neuroscience. His responsibilities include integrating the work of scientists and clinicians in fields that include neurology, neuroscience, neurosurgery, physical medicine and rehabilitation, neuroradiology, and psychiatry.

"Dr. Dauer's broad experience as a neurologist and a scientist positions him to provide strong leadership as the Peter O'Donnell Jr. Brain Institute works to accelerate the translation of fundamental discoveries into cutting-edge treatments for a broad spectrum of brain disorders," said Dr. W. P. Andrew Lee, Executive Vice President for Academic Affairs, Provost, and Dean of UT Southwestern Medical School, who holds the Atticus James Gill, M.D. Chair in Medical Science.

Dr. Dauer was previously on the faculty at the University of Michigan as Director of the Movement Disorders Group and Director of the Morris K. Udall Center of Excellence for Parkinson's Disease Research. For nearly two decades, Dr. Dauer's groundbreaking research has been focused on the molecular basis of dystonia and the mechanisms of neurodegeneration in Parkinson's disease. His findings have elucidated the critical role of the torsinA protein in the progression of dystonia, which is marked by disabling, involuntary movements. Studies taking place under his direction at the Udall Center explaining the neurobiologic basis of falls in Parkinson's disease are being used to pioneer a novel therapy for this currently untreatable symptom.

Building teams across disciplines, among both scientists and clinicians, will be a key focus of the O'Donnell Brain Institute as it seeks to uncover the fundamental causes of brain disease and translate discoveries into treatments.

"UT Southwestern has a uniquely outstanding scientific culture," said Dr. Dauer, who holds the Lois C.A. and Darwin E. Smith Distinguished Chair in Neurological Mobility Research. "It's really the perfect place to bring together the best minds in the country, or even the world, to work on brain science with the important goal of improving the lives of people with brain diseases."

Established in 2015 with a gift from the O'Donnell Foundation, the O'Donnell Brain Institute brings together doctors and researchers from various disciplines to better understand the molecular workings of the brain and apply those discoveries to the prevention and treatment of brain, spine, nerve, and muscle disorders.

Artificial intelligence moves into clinical spaces to improve patient care

Imagine a future in which a patient's wristband can nudge his or her doctor by indicating they've been in the exam room for half an hour. Or where the clinic is wired for sensors that recognize patients as they walk in the door, getting temperatures, blood pressures, heights, and weights.

Far from science fiction, these clinic scenarios are real AI projects currently being developed at UT Southwestern's Medical Artificial Intelligence and Automation (MAIA) Laboratory.

"AI is going to transform health care. Nothing is comparable," said Dr. Steve Jiang, Professor of Radiation Oncology, Director of the MAIA Lab, Vice Chair of Radiation Oncology, and Director of the Division of Medical Physics and Engineering. "Almost everything we do in health care will be impacted by artificial intelligence – to improve the efficiency and quality of the work. AI helps humans do a better job, faster."

AI will never replace doctors – who will continue to provide the warm, human touch – but it will enable new physicians to work hand in hand with the latest technology to improve patient care and research.

Incorporating the latest teaching about artificial intelligence to benefit UTSW students, trainees, and fellows, and pursuing research using AI have become major focuses for Drs. Gaudenz Danuser (left) and Steve Jiang.

"The reality is when one of our current medical students hits his or her professional life – AI is going to be in the clinic," said Dr. Gaudenz Danuser, Chair of the Lyda Hill Department of Bioinformatics, Professor of Bioinformatics and Cell Biology, and holder of the Patrick E. Haggerty Distinguished Chair in Basic Biomedical Science.

To stay on top of this trend, a committee of faculty and administrators convened in late 2018 to evaluate adding AI to the UT Southwestern Medical School curriculum.

At a campus lecture last year, Dr. Danuser explained how companies like Facebook and Google are using AI to create profiles of users and their needs. In a similar way, he said, AI in medicine will help doctors process and understand data faster than a human brain can calculate such information.

In January 2019, the University added a lecture series to the Medical School curriculum introducing students to the basic concepts and applications of AI. A few months later, a Grand Rounds lecture series for the entire campus launched that brings in speakers to discuss AI topics.

"UT Southwestern is already developing sophisticated computer algorithms to guide diagnosis and treatment in oncology, cardiology, and other fields. AI has helped detect subtle patient abnormalities through imaging and can analyze large datasets to draw conclusions and predict likely patient outcomes," Dr. Danuser said.

"AI can learn from human experience and by itself by interacting with the environment," added Dr. Jiang, who holds the Barbara Crittenden Professorship in Cancer Research. "AI can improve patient safety by automatically detecting and preventing errors. The machine is never tired and will check everything, every detail. And it will learn from data from previously treated patients and become smarter and smarter from learning continuously."

> "Almost everything we do in health care will be impacted by artificial intelligence – to improve the efficiency and quality of the work." – *Dr. Steve Jiang*