synergy

2011
Research
Annual
Report

UNT | HEALTH SCIENCE CENTER

Research collaboration at all levels sets us apart

Welcome to the fifth edition of the UNT Health Science Center's (UNTHSC) annual research publication, Synergy. In this issue of Synergy, you will see many of our researchers discovering new ways to improve the health and well being of Texans.

The cover of Synergy highlights our new virtual reality equipment called the CAREN (Computer-Assisted Rehabilitation Environments) system. CAREN is a state-of-the-art rehabilitation system that incorporates a virtual reality environment with independently controlled treadmills that can tilt in any plane, mimicking any number of environments. UNTHSC investigators also will use the CAREN system in their research efforts to determine how individuals maintain balance on changing terrain. This understanding will improve our ability to minimize falls in older individuals and others with compromised functional status. Of the five CAREN systems in the U.S., UNTHSC is the only academic institution operating one.

This is but one example of how UNTHSC researchers, working to combat many diseases and disorders, are improving the health of our citizens. UNTHSC has committed to expand and lead research efforts in a number of areas, such as aging and Alzheimer's disease, primary care and prevention, and investigative genetics.

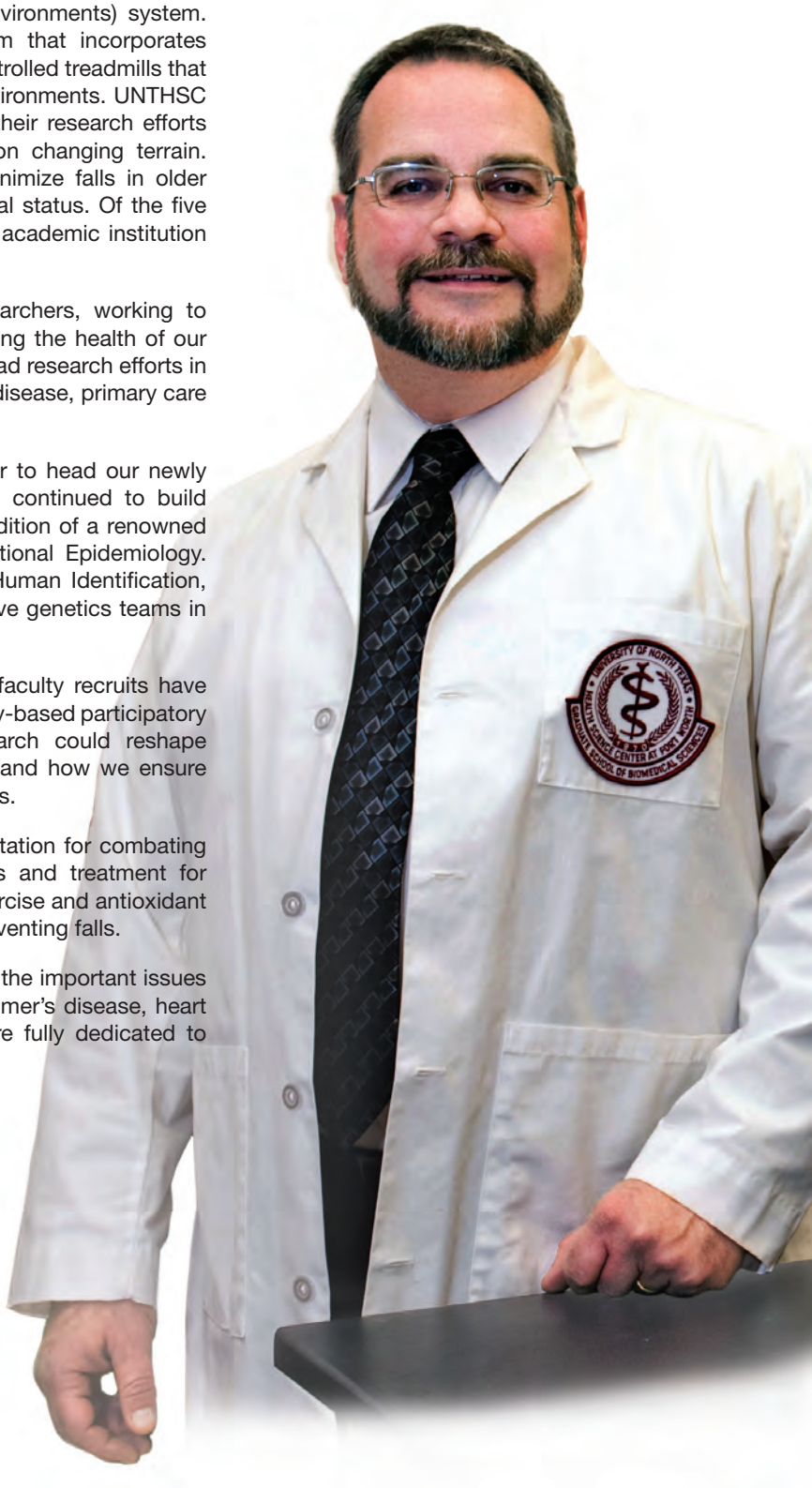
Last year, we recruited a long-time FBI researcher to head our newly formed Institute of Investigative Genetics. We've continued to build our world-class reputation in this area with the addition of a renowned bioinformaticist to head our Center for Computational Epidemiology. Combined with our leadership in the Center for Human Identification, UNTHSC truly has one of the strongest investigative genetics teams in the country.

In the area of primary care and prevention, new faculty recruits have solidified UNTHSC as a national leader in community-based participatory research. This rapidly developing area of research could reshape how we make discoveries in disease prevention, and how we ensure implementation of these findings in our communities.

Our researchers have earned an international reputation for combating aging at the cellular level, improving diagnostics and treatment for Alzheimer's disease, studying the interaction of exercise and antioxidant supplements in affecting cognitive decline, and preventing falls.

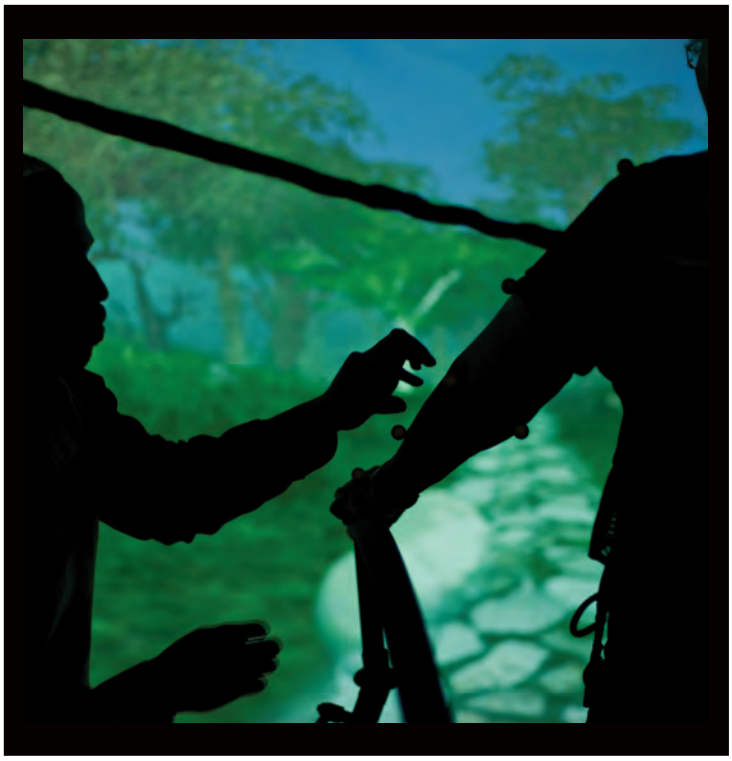
We appreciate your interest in learning more about the important issues our investigators are tackling. Whether it be Alzheimer's disease, heart disease, vision loss or diabetes, our scientists are fully dedicated to working together to improve lives.

Glenn H. Dillon, Ph.D.
Vice President for Research
glenn.dillon@unthsc.edu



Inside

Cover Photo: Janice Knebl, Nicoleta Bugnariu and Rita Patterson conduct research on the V-Gait CAREN system, new virtual reality equipment that addresses balance and movement impairments.



Welcome to the fifth annual research report for the University of North Texas Health Science Center. Research is an integral part of the institution's mission, intimately associated with student training and our commitment to the advancement of knowledge. Our scientists lead cutting-edge research, analysis and treatment of diseases, and they propel our discoveries from the bench to the bedside to the community for the betterment of all people.

Synergy is produced by the Research Office and Marketing and Communications Department at the University of North Texas Health Science Center, 3500 Camp Bowie Blvd., Fort Worth, Texas 76107-2699. (817) 735-2000. The publication is produced annually. Articles may be reprinted in their entirety with acknowledgment. Address requests for photographs or illustrations to the editor at news@unthsc.edu.

Staff

UNT Health Science Center Research Office

Vice President for Research
Glenn Dillon, PhD

Director of Strategic Research Initiatives
Peggy Smith-Barbaro, PhD

Marketing & Communications Vice President of Marketing & Communications
Jean Tips

Editor and Director of Public Relations
Dana Benton Russell, ABC

Photographers
Dana Benton Russell, ABC
Steel Shutter Photography

Writers
Dana Benton Russell, ABC
Sally Crocker
Matt Havlik
Cari Hyden
Nicole Lyons

Publication Design
Fish & Mojo

Production Coordinator
Amy Buresh-Schnelle

Risks of

Dennis Thombs' research into combining alcohol with energy drinks sheds new light on drinking in young people.

For Dennis Thombs, PhD, professor and chair of the Department of Social and Behavioral Sciences in the School of Public Health, the term "happy hour" has taken on a whole new meaning. For more than 20 years, Thombs has studied alcohol use by college students — especially so-called college-age binge drinking — leading to recent discoveries on the heavily-debated topic of alcoholic energy drinks.

Thombs and his research teams have interviewed almost 30,000 young people leaving bars after a night of partying, generally between the hours of 10 p.m. and 3 a.m., recording their drinking practices and intent to drive, as well as their breath alcohol concentration levels.

Early in 2010, his first-of-its-kind research evaluated the effects of alcohol mixed with energy drinks when consumed in bars. His conclusions noted that when caffeine is mixed with alcohol, people may perceive that they are less intoxicated than they really are, which may lead them to drink more or make inaccurate judgments as to whether they can drive safely.

His research indicated that bar patrons who consumed energy drinks mixed with alcohol were three times more likely to be highly intoxicated than those who drank only alcohol and four times more likely to drive.

Energy drinkers also drank for longer periods of time and left the bars later, which Thombs attributes to the caffeine stimulation that causes a "wide-awake" feeling, rather than a sleepy intoxication that other types of drinking may produce.

mixing caffeine & alcohol

"People are more apt to engage in risky behaviors," Thombs noted, "and they don't feel as impaired with regard to drinking and driving, even though they are. With as many as 28 percent of college-age drinkers mixing alcohol with energy drinks in a typical month, this phenomenon quickly has become a critical public health and safety issue, because students leave bars and make decisions that are skewed, based on how they perceive they are handling the effects of alcohol."

The Association of Schools of Public Health (ASPH) recently called this issue an emerging public health concern. Other studies report that students consuming caffeinated alcoholic beverages have double the risk of experiencing or committing sexual assault, riding with an intoxicated driver, having an alcohol-related accident or requiring medical treatment.

The most common alcohol/energy drink combination, Thombs says, is Red Bull and vodka. Red Bull is also frequently mixed with cherry vodka to create a popular drink called "Cherry Bomb." With Monster being one of the most popular drinks of teenagers, its manufacturer is now in competition with Red Bull to enter the bar market, Thombs says.

Students often begin "pre-drinking" before they go out and then continue at bars. They sometimes start with energy drink mixes early because they are tired and don't plan to go out until later in the evening, Thombs noted.

Can a healthy lifestyle protect against Alzheimer's?

It is commonly known that exercise and antioxidant intake can improve physical health. But could these factors decrease the chances of developing Alzheimer's disease?

Nathalie Sumien, PhD, assistant professor of Pharmacology and Neuroscience, recently received a two-year grant from the Alzheimer's Association to examine if a healthy lifestyle including exercising and taking antioxidant supplements will protect against declines in cognitive function.

In preliminary research, Sumien discovered that combinations of antioxidants such as vitamin E and coenzyme Q10, or vitamins E and C, have shown the most promise in reversing cognitive decline. Preliminary exercise research at the Health Science Center has shown that a moderate level of exercise training, such as easy jogging or swimming, can have a minor impact on cognitive function. However, recent studies have suggested a negative interaction of these two factors, where antioxidant intake abolished the beneficial effects of exercise.

Sumien's study will further explore the interactive effects of exercise and antioxidant supplementation on cognitive function in females. It will focus on whether exercise and consuming antioxidants have more of an impact when done early or later in life. Sumien is hopeful results of her study will allow her to determine whether antioxidant intake should be recommended for healthy aged and Alzheimer's patients engaging in moderate exercise.

Nathalie Sumien, PhD

Preventing cell aging could reduce age-related illnesses

Dong-Ming Su, PhD

It's inevitable. Everyone ages. Aging typically increases the chance of disease. Dong-Ming Su, PhD, associate professor of Molecular Biology and Immunology, is researching ways to prevent or delay the onset of diseases related to immune system aging.

The National Institutes of Health (NIH) have provided more than $2 million in support to Su to investigate molecular changes in the thymus, a gland located in the front of the neck that regulates the immune system. The thymus plays an active role in the aging of T cells, white blood cells that attack cells infected by bacteria, viruses or other disease-causing organisms.

T cells are part of the adaptive immune system, which is composed of highly specialized, systemic cells and processes that eliminate or prevent pathogenic challenges. This system is adaptive because it can prepare itself for future challenges, including infection, tumors or auto-immunity.

"As people get older, it becomes easier for them to get infection," Su said. "Influenza, cancer and rheumatoid arthritis are all examples of diseases caused from decreasing T cell function."

The thymus shrinks and fat begins to surround it, which prohibits the thymus from producing enough new T cells and fighting disease.

Cells in the thymus can be divided into thymic stromal cells and hematopoietic stem cells. Su's research team found that the stromal cells age more rapidly than the stem cells, which challenges traditional thinking.

"There is a need to change the condition of the stromal cells to provide a young microenvironment for hematopoietic stem cells," Su said. "We are working to find a way to rescue the stromal cells from aging and make the microenvironment younger. If the stromal cells do not age as quickly, the thymus will not shrink as quickly and would be able to produce new T cells."

Su said this could be accomplished through gene regulation, known as gene therapy, or through a stem-cell based therapy. While still in the early stages of lab research, Su said that gene expression could be stimulated through a simple injection.

"Although we are in the early stages of this research, this could ultimately change lives," Su said. "The consequences of this research could potentially increase life span and improve quality of life for the elderly."

America's obsession with texting

UNT Health Science Center School of Public Health researchers Fernando Wilson, PhD, and Jim Stimpson, PhD, published a report in the *American Journal of Public Health* showing that texting while driving resulted in an estimated 16,000 fatalities in the U.S. from 2001 to 2007. The report indicates that a growing percentage of distracted drivers in fatal crashes are males driving alone, and the accidents involve collisions with roadside obstructions.

Wilson, assistant professor of Health Management and Policy, and Stimpson, assistant professor of Social and Behavioral Sciences, analyzed traffic fatalities across the U.S. from 1999 to 2008 in what is being noted as one of the first efforts to place a scientific number on the amount of motor vehicle deaths resulting from cell phone use.

The report used data from the National Highway Traffic Safety Administration on motor vehicle deaths in each state and Federal Communications Commission reports on increasing cell phone ownership and texting volume over the targeted years. They noted that in 2002, one billion texts were sent every month on average, and this number skyrocketed to 110 billion by 2008. For every one million new cell phone subscribers, Wilson and Stimpson estimate a 19 percent rise in deaths from distracted driving. The recent and rapid increases in cell phone usage and texting may be responsible for thousands of additional road fatalities annually in the US.

Fernando Wilson, PhD, and Jim Stimpson, PhD

New research may prevent cell damage

The damage that results when a soldier takes a bullet in a limb or when someone is trapped in a car wreck often requires that the blood supply be cut off by applying a tourniquet to keep the victim from bleeding to death. Emergency medical responders administer fluids intravenously and stop the blood flow long enough to treat or repair the wound, then release the tourniquet to allow blood flow back into the injured limb to replenish necessary oxygen and nutrients.

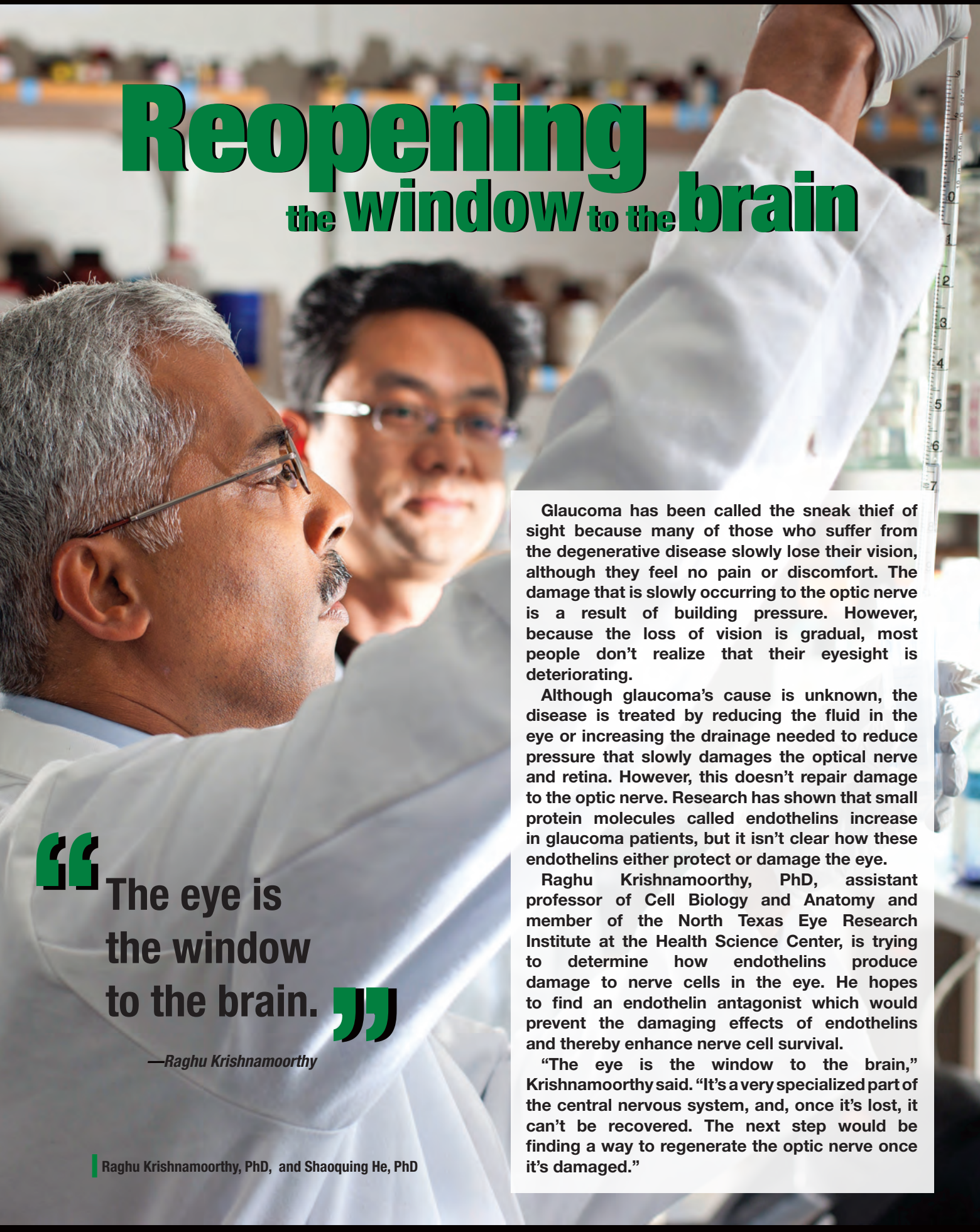
One would think that the most damaging part of the hemorrhagic injury was over, but negative effects occur when the tourniquet is released. As blood rushes into the oxygen-deprived tissue, reactive oxygen species (ROS) are formed. These highly reactive molecules can interfere with cellular function and damage muscles and other vital organs of the body, including the heart.

New research being conducted by DO/PhD student Hunaid Gurji may lead to changes in treatment for hemorrhagic shock by emergency care personnel.

Gurji's expertise in electrophysiology and cardiac performance has spurred him to continue research begun by his mentors Robert Mallet, PhD, professor of Integrative Physiology, and Albert Yurvati, DO ('86), professor and chair of Surgery, on the benefits of administering pyruvate to trauma victims as soon as possible.

Pyruvate is a naturally occurring organic acid and supplies energy to living cells. By administering pyruvate to trauma victims as they are transported from the trauma scene to a hospital, the researchers hope that pyruvate's anti-oxidant and anti-inflammatory effects will protect the heart and other tissues in the body from damage due to ischemia-reperfusion injury. In addition, pyruvate can act as an excellent metabolic fuel for the body's cells, supplying these cells with enough energy to maintain proper metabolism and cellular function. These combined effects of pyruvate will help guard cells from injury and allow quicker recovery.

Reopening the window to the brain



> "The eye is the window to the brain."
>
> —*Raghu Krishnamoorthy*

Raghu Krishnamoorthy, PhD, and Shaoquing He, PhD

Glaucoma has been called the sneak thief of sight because many of those who suffer from the degenerative disease slowly lose their vision, although they feel no pain or discomfort. The damage that is slowly occurring to the optic nerve is a result of building pressure. However, because the loss of vision is gradual, most people don't realize that their eyesight is deteriorating.

Although glaucoma's cause is unknown, the disease is treated by reducing the fluid in the eye or increasing the drainage needed to reduce pressure that slowly damages the optical nerve and retina. However, this doesn't repair damage to the optic nerve. Research has shown that small protein molecules called endothelins increase in glaucoma patients, but it isn't clear how these endothelins either protect or damage the eye.

Raghu Krishnamoorthy, PhD, assistant professor of Cell Biology and Anatomy and member of the North Texas Eye Research Institute at the Health Science Center, is trying to determine how endothelins produce damage to nerve cells in the eye. He hopes to find an endothelin antagonist which would prevent the damaging effects of endothelins and thereby enhance nerve cell survival.

"The eye is the window to the brain," Krishnamoorthy said. "It's a very specialized part of the central nervous system, and, once it's lost, it can't be recovered. The next step would be finding a way to regenerate the optic nerve once it's damaged."

Ann Schreihofer, PhD

Regulating blood pressure in the face of obesity

Thousands of Americans die each year from conditions stemming from high blood pressure. Although stress, dietary salt intake, tobacco use, alcohol consumption and lack of exercise are known to trigger high blood pressure, obesity is also an independent risk factor.

Ann Schreihofer, PhD, associate professor of Integrative Physiology, is studying how the brain regulates blood pressure in an obese population. Schreihofer's work focuses on how the brain regulates blood pressure under normal conditions to better understand how it is altered with high blood pressure. The metabolic syndrome that occurs with excessive weight gain is one of the hypertensive models under investigation in her laboratory.

Hypertension is the primary risk factor for death in America because high blood pressure increases the chance of developing heart disease, peripheral vascular disease and stroke. Obesity, a condition that affects one-third of the American population, also leads to bigger swings in blood pressure that are detrimental to normal cardiovascular function. Fat cells release chemicals and hormones that can act on the brain, and these are elevated when body fat accumulates. Schreihofer hopes her research will clarify how signals from fat cells affect the brain.

"When people continually struggle with obesity, they begin to feel hopeless," Schreihofer said. "Factors contributing to obesity are often misunderstood and there is more to it than not working hard enough to stay on a diet or exercise. People struggling with obesity need more than diet and exercise advice to deal with their obesity-related health issues. Regulating their blood pressure could give them hope and increase their chance for a longer, better life."

Schreihofer and her team are focused on studying a genetic model of obesity that stems from the mutation of the leptin receptor. Leptin, which is released by fat calls, normally acts within the brain to limit meal size. Without a functional leptin receptor hunger never abates, leaving the subject to continuously seek out and consume food. Eating more food changes the chemistry of the body and the brain. Once someone becomes obese, their brain does not react as well to stress, leading to changes in blood pressure.

"We are trying to determine causes for the inability to regulate blood pressure in the setting of obesity," Schreihofer said. "Once we understand how neurons in the brain change in an obese population versus their lean counterparts, we can ultimately find ways to help people."

Many medications have been developed for hypertension, but often they have negative side effects. Schreihofer hopes to understand what causes the brain to trigger high blood pressure, which may lead to therapies to alleviate obesity-induced over-activity in brain cells that regulate blood pressure.

Her research is funded by a four-year, $1.3 million National Institutes of Health grant.

"We are mid-way through the project. It is a basic science project, but in collaboration with others the work we do may be useful for future clinical trials to treat the deleterious consequences of obesity," Schreihofer said.

Help for adolescents with drug, psychiatric issues

Raquel Qualls-Hampton, PhD, and Monique Shuler

In 2008, more than nine percent of adolescents reported using illicit drugs, and studies estimate that 50 to 80 percent of these young people also have a psychiatric disorder. While innovative integrative treatment for both the drug use and the psychiatric disorders seems to be the answer, practitioners need reliable research findings to determine which practices are the most effective, particularly for low-income and minority adolescents.

Assistant Professor Raquel Qualls-Hampton, PhD, at the UNTHSC School of Public Health aims to analyze the effectiveness of these integrative treatments to determine if they influence treatment results. In fact, Qualls-Hampton received a grant from theprestigious Robert Wood Johnson Foundation (RWJF) to conduct her research.

The results from this 24-month, New Connections study should provide practitioners with guidance on the most effective integrative therapies for affected adolescents. Identification of effective integrative therapies is important. From clinical, access and policy perspectives, Qualls-Hampton believes that integrative therapies will be proven effective and become accessible, particularly for the vulnerable populations in critical need of these services.

New Connections is a national program designed to introduce new scholars to RWJF and expand the diversity of perspectives that inform the foundation's programming. New Connections seeks early- to mid-career scholars who are historically underrepresented ethnic or racial minorities, first-generation college graduates, and individuals from low-income communities.

"I am extremely proud to be among the junior investigators honored with this prestigious grant," says Qualls-Hampton. "This award will connect me to a network of experts established in research and evaluation related to health and health care, while providing me with an opportunity to evaluate a program that has far-reaching implications for adolescents with comorbid substance use and mental health conditions."

Esther Han evaluates an HIV patient in China.

Research on HIV in China

Esther Han, fourth-year Texas College of Osteopathic Medicine (TCOM) student, is currently researching the effectiveness of drug treatments on HIV and AIDS patients in Beijing, China. The study aims to determine the factors that may be associated with virologic failure in groups of HIV/AIDS patients on highly active antiretroviral therapy.

"We definitely had some interesting findings including a dramatic difference in virologic failure rates between patients in two counties in Henan Province that are about 70 kilometers apart," Han said. "We hope to get this study published soon."

Han is also involved with a project to identify factors including risky behaviors, ethnicity, age and gender that may be associated with incidences of the Hepatitis B and C viruses in intravenous drug users in China.

Han's research is funded by a year-long Fogarty International Clinical Research Scholars fellowship through the Fogarty International Center, a division of the National Institutes of Health. She is working in the Chinese Center for Disease Control and Prevention's Office of Virology and Immunology at the National Center for AIDS and STDs in Beijing.

Han said conducting research in the international setting and working with a Chinese team has been a learning experience.

"My learning curve was certainly steep when I arrived in late July," Han said. "Every day is a day of learning—from statistics and research design to learning statistical analysis software and learning how to delicately handle cultural differences that manifest themselves daily."

This is Han's second trip to China to research HIV and sexually transmitted diseases. Before starting medical school at TCOM, she spent a year researching HIV and AIDS in rural China as part of the U.S. Department of State's prestigious Fulbright Program.

After her fellowship, Han will return to TCOM to complete her fourth year. After graduation, she will pursue urology and plans to continue her research on HIV/AIDS and other viruses and their effects on the urogenital system.

New genomics research enhances many areas

Last year, the UNT Health Science Center added another dimension to its world-renowned Center for Human Identification when it created the Institute for Investigative Genetics. In addition to the Center for Human Identification, the new institute includes the Center for Biosafety and Biosecurity, and the Center for Computational Genomics (CCG), led by Ranajit Chakraborty, PhD, professor of Forensic & Investigative Genetics, who recently joined the UNT Health Science Center from the University of Cincinnati College of Medicine. The Institute for Investigative Genetics focuses on education, training, research, development and community engagement, which touch all missions of the Health Science Center from the students to clinical research to public health aspects.

The CCG enriches the research at the Health Science Center in many ways, as its researchers work side by side on statistical genetics, bioinformatics and biostatistics for biomedical and public health research. By applying genomic data in biomedical fields, the center provides training, research and services to improve the quality of life.

Recently evolved genomic tools can be used to understand resistance to drug responses and risks of specific environmental and lifestyle insults that can be influenced by genetic make-up. Research into these genetic effects supports the concept of individualized medicine, where a patient is treated based on genetic traits, expectations and proven reactions.

For example, radiation treatment estimates assume that all patients will respond to treatment the same way. However, Chakraborty's earlier studies show some genetic variants make some people more sensitive to radioactive exposures. The BRCA1 gene variants increase the risk of breast cancer and appear to indicate a high sensitivity to radiation. The center hopes to study the effects of family history and genetic make-up on the sensitivity to x-rays, CT scans, and mammography, as well as other exposures to radiation.

"Treatment works better if a patient isn't just a statistic," Chakraborty said, "but is treated as a person. That includes their health habits, spirituality, religiosity, environment and genetic heredity. Health disparities may not be as related to a socio-economic group as much as it is to a religious or disciplined group."

As part of his research, he works with Roberto Cardarelli, DO ('01), and Bandana Chakraborty, DrPH, at the Health Science Center's Primary Care Research Institute to determine indicators of chronic health effects beyond genetics. For example, do more faithful or religious people enjoy better health because of more disciplined behavior, which leads to less exposure to negative agents? His investigations into health disparities pull him into research at the Health Science Center's School of Public Health, as he searches for the answers to these questions.

In collaboration with the Osteopathic Research Center (ORC) and John Licciardone, DO, executive director of the ORC, Chakraborty is involved in researching low back pain and the role that genetics may play in treatment success. These genetic effects are called biomarkers and may be important to the effectiveness of many different treatments.

Chakraborty and his team also may find themselves analyzing familial DNA within state databases of criminal offenders. For example, Luther Franklin was identified as the Grim Sleeper murderer as the result of a familial relationship determined when his son Chris Franklin's DNA was entered into the offender database following a felony weapons charge. In Texas, the Twilight Rapist could also be identified using a similar method. Chakraborty currently is working with the states of Texas and New York to establish guidelines for use of familial DNA. Kansas and Louisiana are also likely to adopt similar guidelines.

Chakraborty's future research includes the possibility of matching highly heritable traits in genetic markers against eyewitness testimony. In such a situation, DNA markers can determine highly heritable traits that can then be compared to eyewitness accounts and composite drawings. With new tools and a more robust database of offenders, Chakraborty hopes to prevent false accusations and remove violent criminals from the street as soon as possible.

"The center's bread and butter is statistical modeling," Chakraborty concludes. "But I want to see it applied in a practical and useful way."

Joydeep Mallik, Blake Myers and Meredith Turnbough, PhD
Right: Ranajit Chakraborty, PhD

UNTHSC adds new DIMENSION to physical therapy

Rita Patterson, PhD, Nicoleta Bugnariu, PT, PhD, and Janice Knebl, DO

Physical therapy has been used for decades as a crucial component in the rehabilitation process of individuals who have suffered disorders and injuries of the musculoskeletal and/or nervous systems. It can help infants with birth defects to aid motor development and functional abilities; survivors of strokes to regain movement, function and independent living; patients with cancer to regain strength and relieve discomfort; patients with low back problems to reduce pain and restore function; and patients with diminished cardiac capacity to improve endurance and achieve independence.

UNT Health Science Center's Physical Therapy Department is taking a creative approach to address balance and movement impairments and help patients regain functional independence.

Nicoleta Bugnariu, PT, PhD, associate professor of Physical Therapy, will conduct clinical research using virtual reality equipment called the V-Gait Computer Assisted Rehabilitation Environments (CAREN) system. This system combines an instrumented self-paced, dual-belt treadmill with real-time motion capture and a three-dimensional interactive virtual environment.

"The dual belt treadmill is extremely beneficial for training balance and walking in stroke or amputee patients, as one side of their body may be weaker," Bugnariu said. "The patient is able to move at his or her own pace with each leg and the system can record their motion and force patterns so we are able to see any abnormalities or improvements over time. The treadmill is installed on a motion platform and its movement corresponds to the surface of the virtual environment. For example it can dip, slide or be rough just like a walking path going down or up a hill, or on an uneven terrain."

A motion analysis system with 12 cameras tracks and records all movements made by patients as they interact with the virtual environment.

The virtual environment can be delivered by two means: a 180-degree cylindrical screen or a head-mounted display. Virtual environments are tailored to each patient's needs, depending on the issues he or she needs to address. Patients receive advanced physical therapy while experiencing real-life activities such as opening a door, crossing a street, walking through a forest or driving a boat.

The parameters of the virtual application can be set so that small movements will open a door or push an object, although it might take a much larger movement in a real-life setting. As a patient's mobility improves, these parameters can be adjusted and tailored to help them gain the strength needed to be able to push, pull and walk outside of the virtual setting.

Markers stuck on the patient help track movements on the CAREN virtual reality system.

"This system provides a safe, controlled environment that empowers patients," Bugnariu said. "The movement of this system helps patients succeed in everyday activities, which is crucial to improving their balance."

The V-Gait CAREN will also help researchers determine how disease, age, neurological problems and brain injuries can affect sensory integration, as well as how the brain processes multiple sensory modality inputs into usable functional outputs. Bugnariu is specifically interested in the mechanisms of sensory-motor integration and their impact on balance. In collaboration with Janice Knebl, DO, chair of Geriatrics and professor of Internal Medicine, and Rita Patterson, PhD, professor of Manipulative Medicine, Bugnariu hopes that the results from this research will lead to better interventions for fall prevention in older adults.

"Patients who are mainly dependent on their visual sense to keep their balance usually look down while they walk," Bugnariu said. "When they have to look up, attend to other visual stimuli or perform a second task, they lose their balance and fall. But if we are able to train the mechanisms of sensory integrations and expand patients' use of other sensory inputs, balance control will be improved."

The Health Science Center is now one of only five locations, and the only academic institution, to house a system like this. The other four belong to the Department of Defense and primarily focus therapy on lower extremities. Bugnariu and Patterson will use the Health Science Center's system to help patients train both upper and lower extremities simultaneously during functional tasks.

Bugnariu is also collaborating with Advanced Arm Dynamics, and the Osteopathic Manipulative Medicine and Orthopaedic Surgery departments to explore the best ways to train upper-extremity amputees. These patients are often younger, will live longer and require use of their upper extremities throughout their lives.

"With this research we can definitely fill two gaps," Bugnariu said. "First, understanding the mechanisms of sensory-motor integration will lead to innovations in rehabilitation therapies for balance and mobility. Second, the use of virtual environments will allow for customized rehabilitation protocols that are not only fun and motivating for the patients, but are safer and more efficient in promoting recovery of function."

Nicoleta Bugnariu evaluates movements using computer programs.

Robert Barber, PhD

TARC research continues to reveal findings, bring hope

Since 2005 the Texas Alzheimer's Research Consortium (TARC) has been researching ways to improve prevention, early detection and treatment of the most common form of dementia.

TARC consists of five of the state's leading medical research institutions: the UNT Health Science Center, Baylor College of Medicine, the University of Texas Southwestern Medical Center, Texas Tech Health Science Center and the University of Texas Health Science Center San Antonio.

TARC has developed the first blood test for Alzheimer's disease. The test is based upon levels of 152 proteins in the blood serum. Work began on the test in 2005 and continues with patient enrollment and follow-up. If validated by TARC researchers in an independent group of patients and approved by the Food and Drug Administration, this cost-effective test will give physicians the ability to routinely screen many individuals. Patients who test positive for Alzheimer's disease on the blood test could be referred for more advanced neuro-imaging analysis.

This blood test has the potential to revolutionize diagnosing and treating Alzheimer's disease.

"Including those in the earliest stages of the disease is critical because Alzheimer's disease progresses in the brain for quite a while before symptoms become apparent," according to Robert Barber, PhD, associate professor of Pharmacology and Neuroscience at the Health Science Center and the TARC scientific coordinator.

All drugs and therapies that have been tested in clinical drug trials thus far have failed to prevent the disease or slow its progress. This could be because by the time individuals show clinical signs and symptoms, many cells in the brain have died, lessening the chance of any treatment successfully restoring cognitive function. Effective treatment may need to begin well before symptoms of the disease become apparent.

For this reason, all TARC sites, including the Health Science Center's Patient Care Center, have begun studying patients with mild cognitive impairment. These individuals do not have dementia but have cognitive impairment beyond what is considered normal for their age.

"Using the blood test as a first step in a multi-stage screening process could expand care dramatically. Currently, a diagnosis can only be made in a specialty clinic, usually in large, urban medical centers within developed countries. While advanced neuro-imaging and cerebrospinal fluid screenings are accurate, they are not widely available," Barber said. "The blood test could be administered annually to all individuals over 65 who are at an increased risk of Alzheimer's and could be performed nearly anywhere, resulting in increased access to care."

TARC is also working to expand its research studies to include patients in the earliest stages of the disease and the Hispanic population. The Health Science Center is enrolling patients and collecting biological samples and neuropsychological data.

TARC sites have enrolled more than 200 Hispanic patients in studies and plan to enroll more than 500 by September 2011. With Hispanics making up over one-third of the Texas population and Texas expected to become a majority Hispanic state between 2025 and 2035, expanded studies in this underrepresented group are needed. TARC will study cognitively normal individuals, Alzheimer's patients and early-stage Alzheimer's patients of Hispanic origin.

"We know that the Hispanic population has an increased incidence of Alzheimer's disease risk factors, such as diabetes, heart disease and hypertension," Barber said. "These factors, and the realization that the number of Hispanic Texans is increasing dramatically, make it imperative to study this underrepresented and at-risk group of Texans."

Barber said TARC's ultimate goal is to end this disease by developing and improving methods of treatment and prevention.

"This work is important to me because of the devastating effect Alzheimer's disease has on patients and their families," Barber said. "I have a strong interest in complex human diseases and AD has been the most resistant to the development of an effective treatment. Given the aging 'baby-boomer' generation, this single disease has the potential to bankrupt the health care system if effective preventive measures or therapies are not developed."

Does **testosterone** create ***more*** stroke damage in males?

As people age, the threat of a debilitating stroke increases. Rebecca Cunningham, PhD, research assistant professor in the Department of Pharmacology and Neuroscience at the UNT Health Science Center, is on a quest to determine if testosterone — especially in older men— contribute to the damage caused by ischemic stroke.

The research is looking into the biological effects of testosterone, the male hormone, on neurons in the brain and the reasons why males suffer worse effects from stroke. When these effects are better understood, Cunningham hopes to identify a novel therapy to lower the risk of ischemic stroke in men.

A stroke increases the likelihood of a condition termed oxidative stress, which has been shown to damage brain tissue. Androgens such as testosterone can further increase oxidative stress. Together they create a perfect storm that increases cell vulnerability.

"Testosterone decreases cell survivability by increasing calcium that harms the cell by overstimulation," Cunningham said. As part of her research, Cunningham creates oxidative stress on a cell similar to that caused by stroke and age. It also creates lost connections that can result in movement disorders similar to Parkinson's disease.

"We believe that testosterone only exhibits 'negative' effects on dopamine neurons in an impaired cellular environment, such as during aging and stroke," Cunningham concluded. "We hope to find a way to maintain the positive effects of testosterone while mitigating the negative effects."

Rebecca Cunningham, PhD

GoodNEWS and Healthy Harvest

Can healthy habits counter genetics?

Mark DeHaven, PhD

If you lived in a controlled environment, eating only nutritious meals and working out regularly with a trainer, would you reduce your risk for cardiovascular disease and diabetes — even if you are genetically predisposed for these diseases?

Mark DeHaven, PhD and founder of a groundbreaking study, says research shows that those who live in an environment where nutrition and exercise are carefully monitored can indeed reduce their risk for these diseases, even if their genes are working against them. It's a result of the epigenome — the chemical compounds, separate from the underlying DNA sequence, that tell the gene what to do. Scientists are discovering that epigenetic mechanisms allow organisms — human and otherwise — to respond to the environment and actually regulate gene expression.

But people live in an ever-changing world with all its stressors. DeHaven, UNTHSC's Health Institutes of Texas professor and director of the Texas Prevention Institute, is conducting the country's first large-scale faith- and community-based participatory research trial to determine whether people can reduce risk factors for chronic diseases while living in the real world. The study is funded by the National Institutes of Health's Heart, Lung and Blood Institute.

The program, called GoodNEWS (Genes, Nutrition, Exercise, Wellness and Spiritual Growth) shows great promise for reducing cardiovascular disease and diabetes risks.

"Our team has always been seeking ways to reduce risks for these diseases that can be implemented in a community setting, and that are effective," said DeHaven, who is working with black church congregants in South Dallas to determine if community-based efforts to encourage healthy diets and exercise reduce risk factors for heart disease, stroke and diabetes.

Care-related factors are commonly reported to account for only 10 percent of a person's risk of premature mortality, whereas lifestyle and behaviors represent 50 percent. Twenty percent is related to environment, and another 20 percent is genetics.

"This tells us that we do have a great deal of control over our health," DeHaven said. "Our study participants had always assumed they would die young because their relatives died young. Now they get it — they know that they can influence their risk factors for these diseases. They know they don't have to die young."

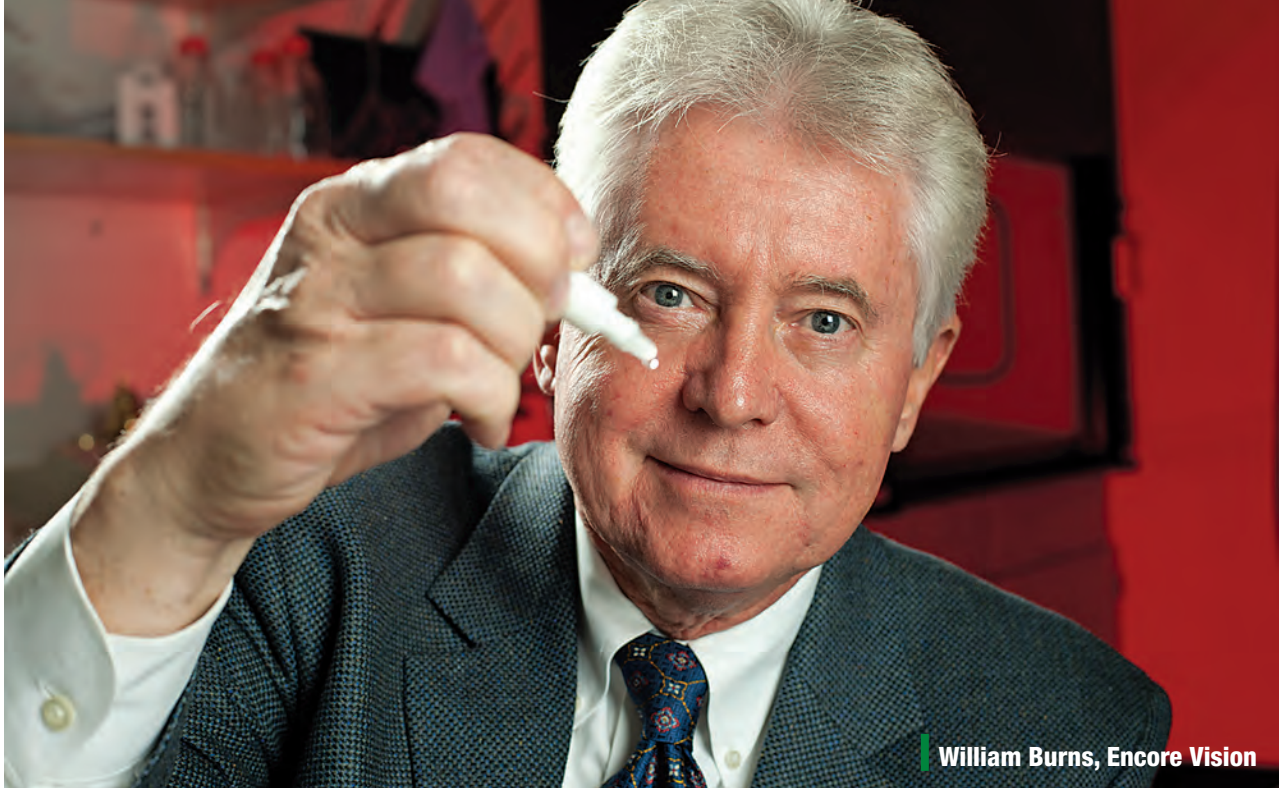
One barrier South Dallas residents face to a healthy lifestyle is a lack of stores selling fresh fruits and vegetables. There is one grocery story for every 35,000 South Dallas residents, DeHaven said, and most end up buying groceries at convenience stores that carry little produce.

After limited success in encouraging grocery stores to open in the area, DeHaven launched the Healthy Harvest Community Gardening effort.

Seven gardens have been developed, and three more are in planning — thanks in part to donations from Dallas developer and philanthropist Trammell S. Crow. Along with the UNT Health Science Center, other contributors and participants include PepsiCo, St. Philips Academy and Community Center, Paul Quinn College and several southern Dallas County congregations.

In most cases, the gardens begin when a church buys a condemned lot and removes the dwelling. Then the land is used to grow food, revitalize neighborhoods and provide a safe location for physical activity.

DeHaven is seeking funding for a similar program in Fort Worth.



William Burns, Encore Vision

Encore Vision gives insight into presbyopia

Encore Vision, a TECH Fort Worth company leasing laboratory space from the UNT Health Science Center, is developing an eye-drop treatment for presbyopia that may offer an alternative to reading glasses. Presbyopia, the inability to focus on nearby objects, has an age of onset around 40 to 45, and remains throughout life. Presbyopia makes it difficult to read a newspaper, do needlework or perform tasks requiring close-up work.

William Burns, CEO of Encore Vision, notes that as people age, they lose the ability to focus on objects less than an arm's length away. The new eye drop being developed delivers a drug that softens the lens, allowing the lens to better focus on nearby objects.

"We are supplying a derivative of an agent that is always present in cells of the eye," Burns said. "The drops will put more of that agent back in, allowing the chemical reduction of aberrant chemical bonds. This will soften the lens, restoring flexibility again and decreasing the viscosity of lens cells."

Encore Vision has completed the first phase of research and identified safe compounds that are derivatives of natural products of the eye. In the next development phase, toxicology studies will be conducted to identify safe dosing levels. Burns said they want to make sure that the product is comfortable, shelf-stable and sterile, and then clinical trials will begin. A portion of those studies will be conducted at the Health Science Center.

"We should know within the next two years how this is going to work in humans, the dosing frequency and duration of treatment required, and the safety evaluation through clinical trials and beyond," Burns said.

ZS Pharma receives $2M from Emerging Technology Fund investment

Another TECH Fort Worth Client leasing office space from the UNT Health Science Center, ZS Pharma, Inc., has received $2 million in an Emerging Technology Fund (ETF) investment from the State of Texas. This investment will provide ZS Pharma the funds to develop oral sorbents designed to reduce abnormally high levels of agents that build up in patients with either liver or kidney disease. At the Health Science Center, ZS Pharma will spend a portion of the ETF funding on activities to advance the commercialization of its technology.

ZS Pharma's core technology platform uses zirconium silicate crystals to specifically target ions and molecules, such as potassium, ammonium, urea and phosphate, that have built up in the body as a result of liver or kidney failure. There is currently no effective treatment for hyperkalemia, or high levels of potassium in the blood, and treatments that do exist are not suited for chronic conditions that require constant treatment. Taken with food, ZS Pharma's tasteless and odorless therapy should provide an alternative to hemodialysis, which is costly, demanding of the patient and potentially dangerous. The new advanced compound could be a significant medical breakthrough for treatment of acute and chronic hyperkalemia, providing a better quality of life and an alternative to dialysis and other expensive medical procedures.

The ETF investment fund was designed to attract Texas' top scientists and entrepreneurs in growing areas including life science technologies and pharmaceutical development.

Marianna Jung, PhD

Hypoxia may reduce sudden alcohol withdrawal distress

A recent Gallup poll indicates that Americans are drinking more than they have in the last 25 years. As a result, alcoholism continues to be a problem among adults and adolescents, and withdrawal from alcohol continues to disrupt lives as individuals and their families deal with both the physical and emotional trauma of weaning their bodies and minds from the effects of alcohol abuse. New research at the Health Science Center examines the effects of intermittent hypoxia — cycles of a moderately low level versus a normal level of oxygen — on the body's ability to adjust to alcohol withdrawal.

"When a patient is exposed to intermittent hypoxia over time, the body learns to adapt to the stress of low oxygen," said Marianna Jung, PhD ('97), assistant professor of Pharmacology and Neuroscience and principal investigator for the study, funded by the National Institutes of Health. "By introducing intermittent hypoxia for 20 days and training the brain to deal with stress, we hope to show that the brain can be protected from excessive stress of alcohol withdrawal."

At the suggestion of Fred Downey, PhD, professor and vice chair of Integrative Physiology, Jung is working with Robert Mallet, PhD, professor of Integrative Physiology, in testing the theory. During the first phase of testing, animal subjects exposed to intermittent hypoxia prior to experiencing sudden alcohol withdrawal were calmer and suffered less stress than subjects who were not subjected to hypoxia pre-conditioning. Subjects without hypoxia treatment were more hyperactive and more apt to suffer seizures during withdrawal. The second phase of testing showed a continued protective factor relative to the overt signs of alcohol withdrawal including tremors, rigidity and irritability. At this point, it's not clear if the residual effect of the hypoxia is true for all ethanol withdrawal-induced effects.

The hope is that further evaluation will result in therapies that can improve the recovery time for patients experiencing alcohol withdrawal.

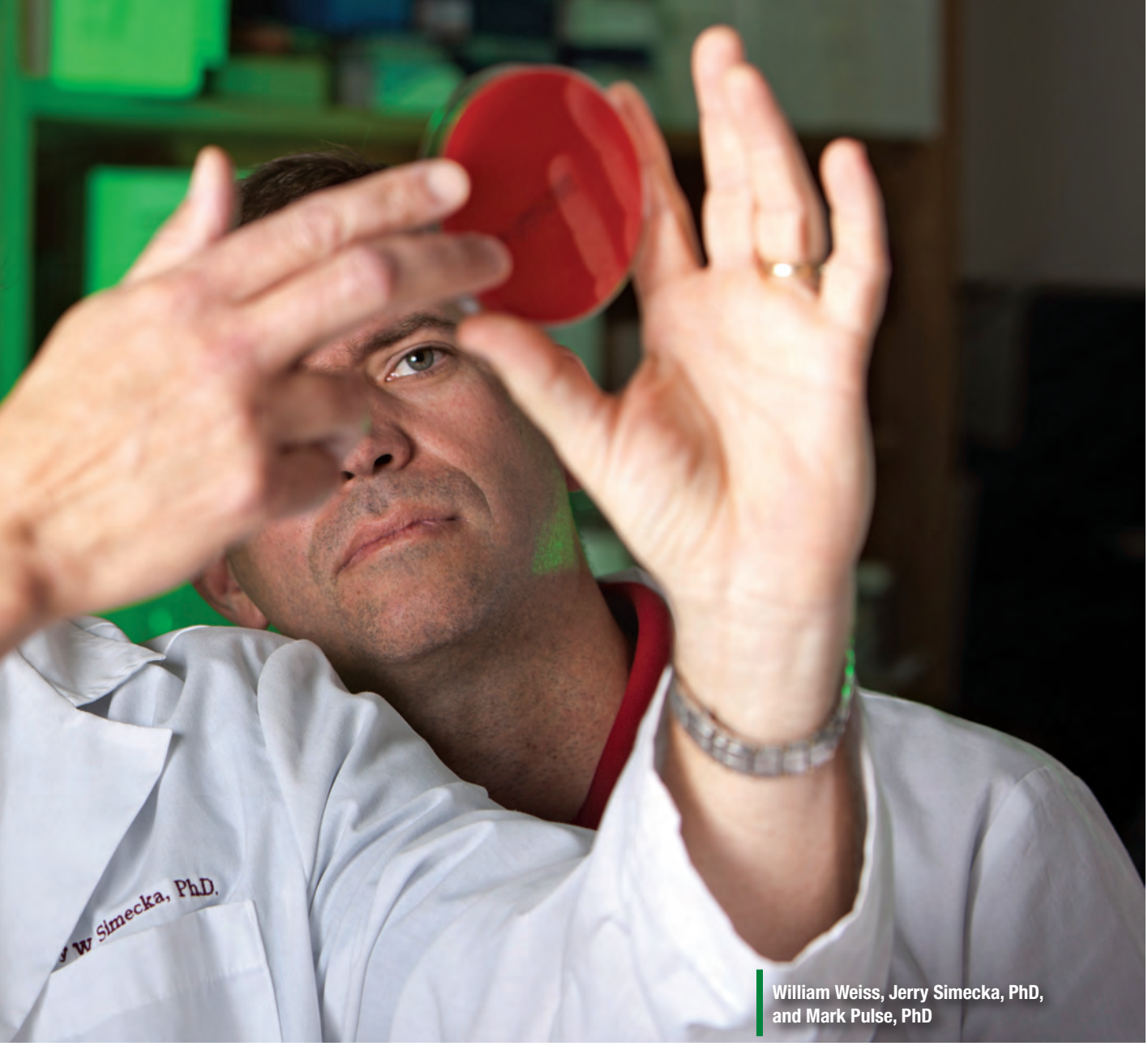
Setting the standard for drug testing

Before a new drug can be marketed and dispensed by a physician, it faces a long, circuitous route from the laboratory through rigorous testing and protocols. Commercial pharmaceutical companies need reliable, efficient testing of new and novel compounds at the bench level, in animal models and on into pre-clinical testing. That's where the UNT Health Science Center's Pre-Clinical Services has stepped up.

Part of the Department of Molecular Biology and Immunology, the group evaluates the efficacy and safety of pharmaceutical products before they become available to the public, merging academics and industry in the quest to discover and develop new drugs.

"We provide the expertise to help take a drug from laboratory to bedside," said Jerry Simecka, PhD, executive director of Pre-Clinical Services. "We work with companies and academic researchers to discover treatments for everything from skin infections to pneumonia. Some companies are hesitant to work with universities due to issues of intellectual property, but we have been able to address those concerns. As a result, we are building a world-wide reputation for solid work."

In state-of-the-art facilities, Pre-Clinical Services staff members guide the drug discovery process through protocol design, implementation and analysis. Together the staff — which has doubled in size to 12 in the past two years — has more than three decades of large pharmaceutical and specialized biotech experience in therapeutic efficacy models and drug discovery and development. Simecka expects to expand the operation and handle more than 50 projects per year.



William Weiss, Jerry Simecka, PhD, and Mark Pulse, PhD

"Some of these evaluations can be completed in one or two days," Simecka explained, "while others can take much more time. But through the process we've learned how to conduct the evaluations more efficiently and quickly."

Pre-Clinical Services has executed more than 100 contracts with biotech firms and pharmaceutical companies in the U.S. and Europe, as well as other universities across the country. Some studies are funded by grants, but many are commissioned by commercial organizations. Among the capabilities of the group is the ability to evaluate antibacterial agents and establish models of both acute and chronic bacterial infections.

Various additional studies and analyses can be performed in house. Infection models or other protocols can be established and adapted to meet more specific client needs. In collaboration with the Department of Laboratory Animal Medicine, Good Laboratory Practice (GLP) procedures were recently established. The GLP standards are in place to ensure the consistency, reliability and documentation required for submission of regulatory documents to the Food and Drug Administration prior to clinical trials.

"In the drug industry, there's been a huge shift. Companies have downsized and gotten away from the ability to perform pre-clinical studies," said William Weiss, director of Pre-Clinical Services. "That's why they need organizations like ours. They are looking for experienced people who know how to perform the pre-clinical work. We bring industry experience and provide the rationales."

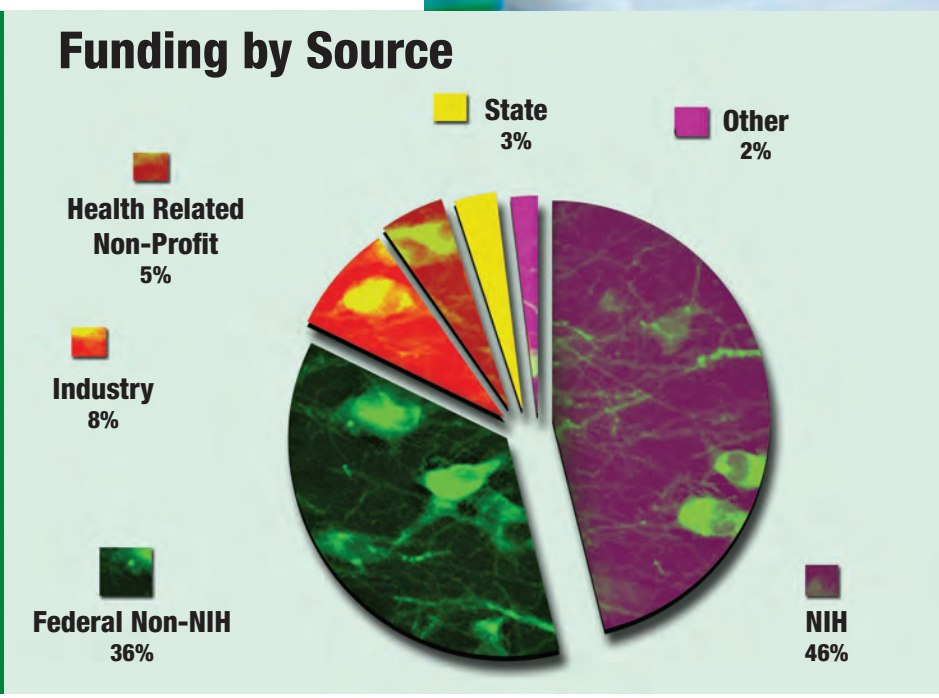
Research funding by the numbers

Research at the Health Science Center continues to grow, reaching an all-time high of nearly $40 million in 2010. Since 2000, our research expenditures have increased by nearly 300 percent.

Our scientists receive support for their research from a variety of funding sources. In 2010, over 70 percent of the research awards to UNT Health Science Center investigators were from the federal government. The majority of federal support was from the National Institutes of Health (NIH), considered the gold standard when judging quality of biomedical research. Whereas the federal stimulus bill infused drastically needed funding into the NIH research budget for 2009 and 2010, overall funding has been relatively flat on average for the past several years. Our growth in research funding from NIH dramatically exceeds the overall national average. This is strong evidence of the exceptional, high-quality research being conducted by our faculty at the Health Science Center.

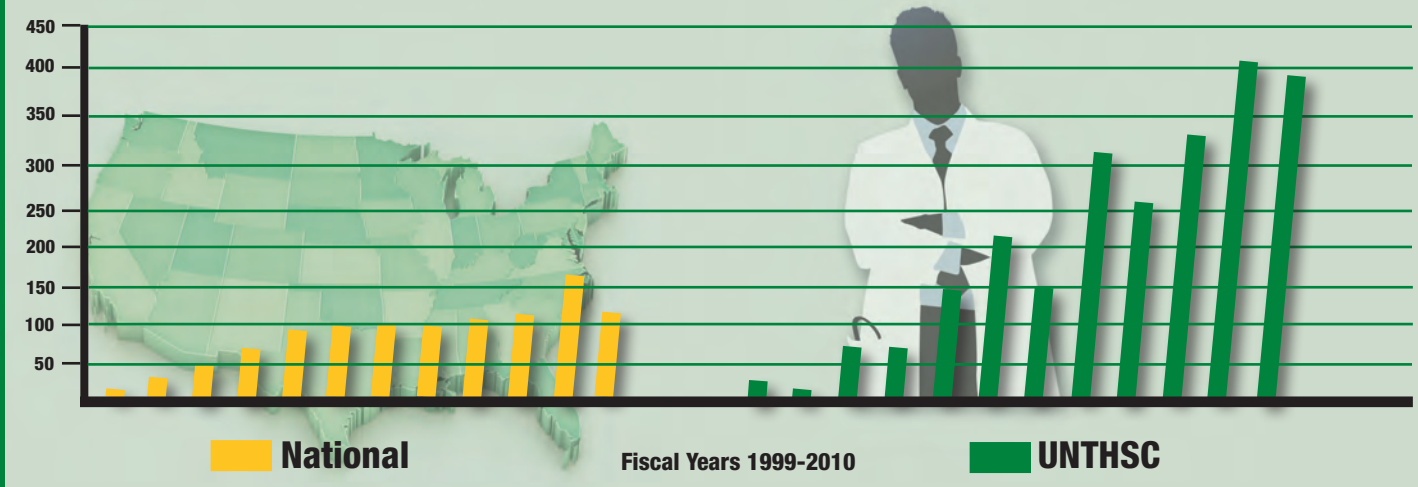
We are committed to creating solutions for a healthy community through research. Our investigators will continue to perform cutting-edge research in critical areas including aging and Alzheimer's disease, investigative genetics, cardiovascular disease, vision, cancer and disease prevention. Our emphasis on expanding translational research will help to increase the pace of discovery, and its conversion to new therapeutics and treatments.

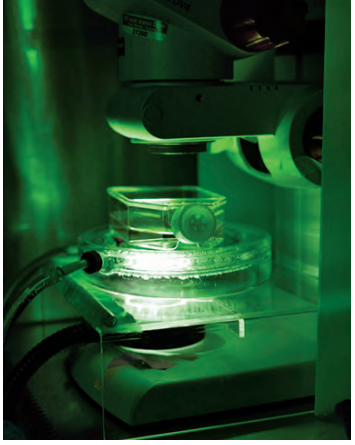
UNT Health Science Center. Our discoveries. Your Health.



2010 Research Funding

NIH funding growth
far exceeds national average





Health Institutes of Texas

The Health Institutes of Texas were designed to leverage the Health Science Center's growing expertise in public health, interdisciplinary scientific research, medical education and healthcare delivery. The ultimate goal is to use this model among various institutes to improve the health of Texans and beyond by reducing disparities, developing new treatments and therapies, and improving access to care in rural and underserved communities in Texas.

Cardiovascular Research Institute (CRI)

The CRI seeks to further our understanding of cardiovascular disease and improve the techniques used in the prevention, detection, diagnosis and treatment of cardiovascular disease and the rehabilitation of its victims by targeting myocardial infarction, hypertension, congestive heart failure and stroke.

Center for Commercialization of Fluorescence Technologies (CCFT)

Funded by an Emerging Technology Fund grant from the governor of Texas, the CCFT works to develop and commercialize new approaches for diagnostics and treatment using the emerging fields of nanophotonics and nanotechnology.

Center for Women's Health (Focused on Resources for her Health, Education and Research — For HER)

For HER is a collaborative, multidisciplinary organization created to address and meet the health care needs of women of all ages and ethnic groups.

Institute for Aging and Alzheimer's Disease Research (IAADR)

The IAADR focuses on early detection of Alzheimer's disease, estrogen's role in Alzheimer's and Parkinson's diseases, stroke therapy and identification of oxidation processes to measure brain aging, with several treatment drugs in clinical trials.

Institute for Cancer Research (ICR)

The ICR provides leadership in all aspects of cancer research, education and training.

Institute for Investigative Genetics (IIG)

The mission of IIG is to improve safety, security and quality of life through the application of genetics. The mission is met through the institute's three centers: the Center for Human Identification, the Center for Computational Genetics, and the Center for Biosafety and Biosecurity.

Mental Science Institute (MSI)

The mission of MSI is to foster a greater understanding of human thought and behavior through interdisciplinary research and education. The MSI conducts multidisciplinary research, and provides education and consultation in the mental sciences associated with human behavior.

North Texas Eye Research Institute (NTERI)

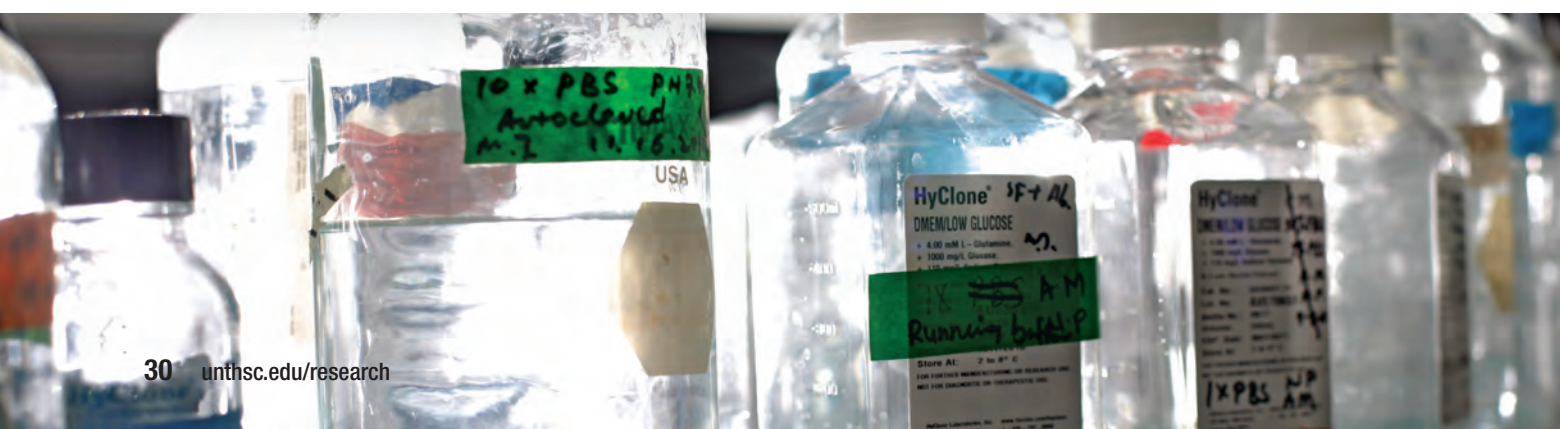
NTERI is dedicated to preserving vision and curing eye disease by using basic research, clinical research and medical education of clinicians and scientists to improve treatment of glaucoma, age-related macular degeneration, diabetic retinopathy and other vision disorders.

Osteopathic Research Center (ORC)

The ORC, housed at the Health Science Center campus, is the national center of collaborative research on the efficacy of osteopathic manipulative medicine through multi-center clinical trials, teaching research skills and promoting collaborative studies.

Texas Prevention Institute (TPI)

The Texas Prevention Institute is dedicated to conducting innovative translational research focusing on primary care and chronic disease prevention. It is composed of the Center for Community Health, the Primary Care Research Institute and the Texas Center for Health Disparities.



Walking the Talk

Walking the talk was a buzz phrase several years ago when leaders often paid lip service to a phrase or direction but didn't actually live by their words. But at the UNT Health Science Center, our researchers really epitomize the word "collaboration." Walking around our campus, I'm often struck by the collegial atmosphere here.

From graduate students studying the effects of pyruvate to clinical faculty working together with world-renowned researchers to physicians treating patients with new protocols, the UNT Health Science Center prides itself on the collaborative, multi-dimensional work environment and broad research relationships on campus. Our recent addition of virtual reality simulation therapy is the perfect opportunity to use our expertise in motion-related rehabilitation with the brand new physical therapy program to treat elderly patients under the care of a Reynolds grant expert.

The interrelationships here at the Health Science Center enrich our research and help us bring a broader understanding to a variety of research areas. Our intimate, tightly woven community and close proximity on campus lend themselves to information sharing, as well as testing and evaluation.

The addition of the Center for Computational Genomics creates an exciting group that will help analyze bioinformatics on everything from low-back pain in patients at the Osteopathic Research Center to biomarkers for prostate cancer and familial DNA samples in prosecuting criminals.

By bringing the brightest minds at all levels together, we create a unique opportunity to learn from one another, share new insights, present new questions and analyze a variety of different approaches and perspectives in our daily research.

It's not unusual to see a professor hail a physician or graduate student as each makes his or her way across campus, then proceed to confer about the latest new idea that could have far-reaching effects. These researchers, grad students and faculty are walking and talking and dreaming and doing. And the steps we are taking may lead to discoveries that will improve the journey for humankind.

There's a collegial energy and excitement on our campus that's contagious. And that's one virus that I hope continues to spread. Come experience it for yourself!

Scott B. Ransom, DO, MBA, MPH
President
UNT Health Science Center

UNT Health Science Center
3500 Camp Bowie Boulevard
Fort Worth, TX 76107-2699

Nonprofit Organization
U.S. POSTAGE
PAID
Denton, Texas 76201
Permit 455

synergy

2011
Research
Annual
Report

one last look

PDS_A013121Z-2/11L755