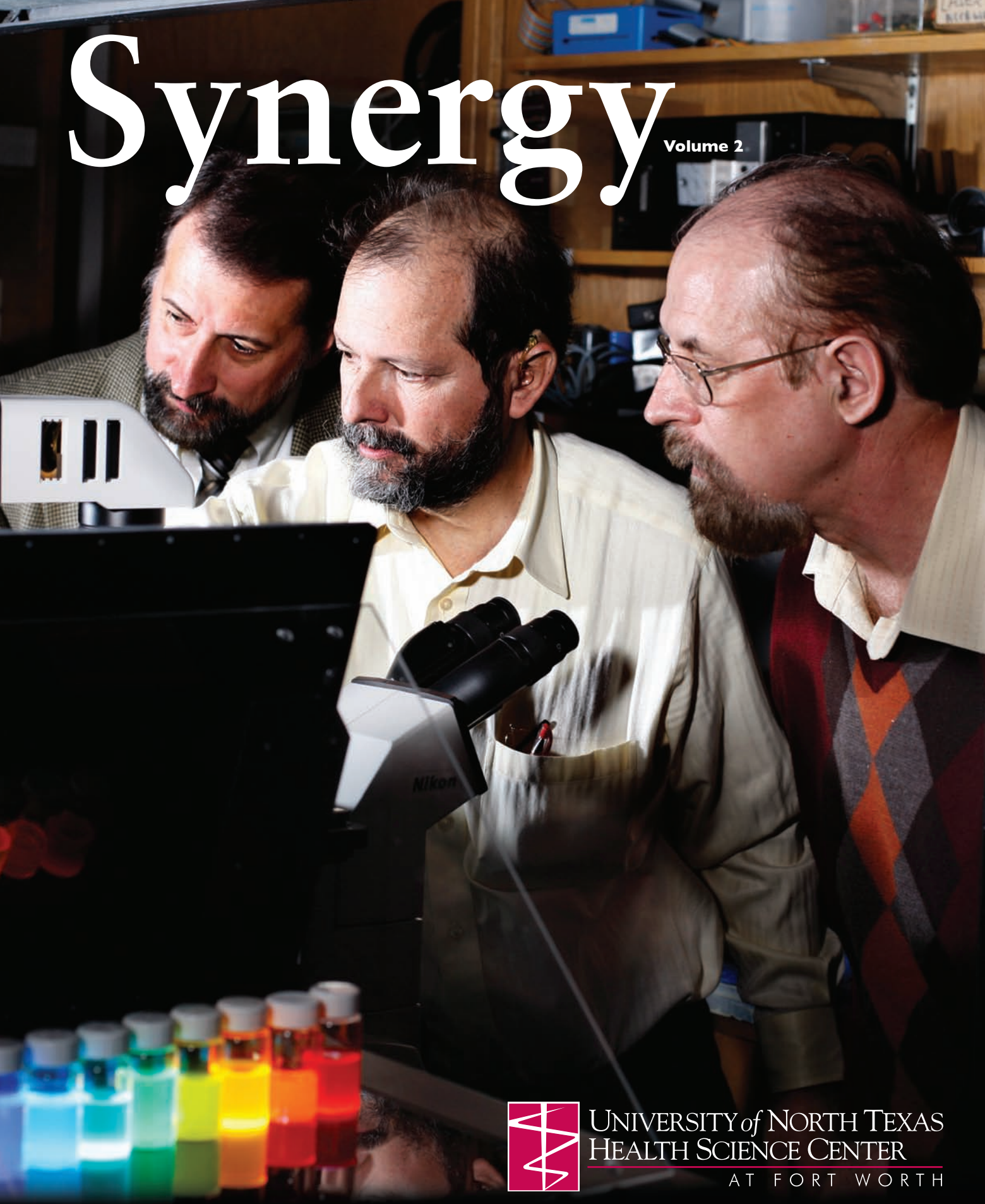
Synergy

Volume 2



UNIVERSITY of NORTH TEXAS
HEALTH SCIENCE CENTER
AT FORT WORTH

2008 Research Annual Report

Welcome

Welcome to our second annual Synergy Research Annual Report for the University of North Texas Health Science Center. This year has been the first complete year for our new president, Dr. Scott Ransom. Our institution has been reinvigorated with enthusiasm for the future under his leadership. His vision is for us to become a top 10 health science center with research as an important part of our mission.

This year he launched the Health Institutes of Texas, a new initiative that focuses on translational research in taking what we learn at the bench to rapidly bringing this to the bedside, where we will have great impact on the health of our population. During this past year, we have recruited some of the best research talent to complement our already excellent, world-class faculty. Areas of research that were strengthened by some of these additions include aging and Alzheimer's research, neuroscience and visual science, cancer research, cardiovascular research and physical medicine. These individuals are bringing well established and internationally recognized research programs to the Health Science Center.

The Health Science Center continues to house the national Osteopathic Research Center, which provides important mechanistic research studies on the relationship between structure and function using osteopathic manipulative medicine in the treatment and prevention of various diseases. This research is well funded from private sources, as well as from the National Institutes of Health.

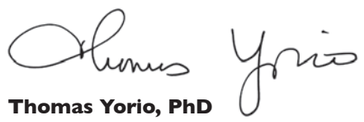
We also continue to make headlines with our Center for Human Identification. This Center provides the important link for families searching to identify loved ones who have been missing — often for a number of years. Our group has been working closely with the FBI, U.S. Department of Justice, National Institutes of Justice and local law enforcement to help solve these mysteries using our world-class DNA identity laboratory.

Our Institute for Aging and Alzheimer's Disease Research continues to have a major impact on this terrible, debilitating disease. Our research group has focused on drug development for the treatment of dementia and has several candidate drugs in the pipeline. We are very hopeful that some of these will reach clinical trials and begin to benefit patients suffering from this dreaded disease.

Recently, we recruited a group of cancer researchers who have discovered a protein that may be crucial in the development of cancer. Their basic research is quite startling and has shown tremendous promise in preventing and treating a variety of cancers. We are in the process of trying to move this discovery into a clinical trial as quickly as possible so that we can begin to save lives.

This year we also have a feature in Synergy that looks at some of our graduates titled "Where are they now?" In this report, you will meet several of our graduates and learn of their successes. Some of these individuals we actually have recruited back to the Health Science Center to now serve as faculty. Talk about giving back! We are proud of our graduates, and this feature, I think, shows you why.

In summary, we have had another outstanding year in research. The features in this report focus on some of the new people and their research. We hope, like us, you find the research exciting and promising. We can't wait to bring you reports of our extraordinary accomplishments for 2008.



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Inside

Cover Photo: *Drs. Karol Gryczinski, Julian Borejdo and Ignacy Gryczinski focus on new frontiers in fluorescence technology.*

Welcome *to the second 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 researchers lead cutting-edge research, analysis and treatment of diseases, and propel our discoveries from the bench to the bedside for the betterment of all people.*

Staff

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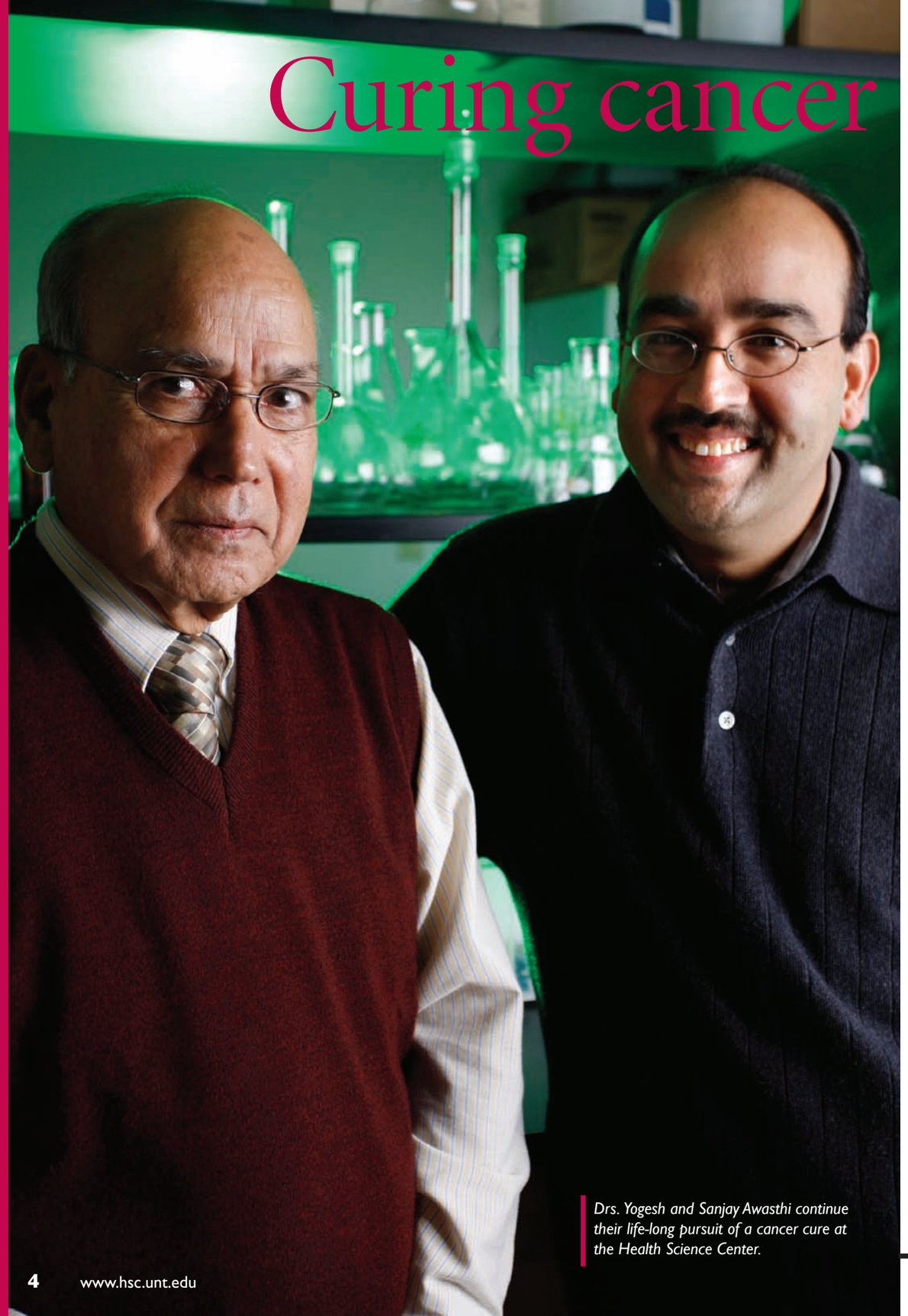
Curing cancer one patient at a time



Drs. Yogesh and Sanjay Awasthi continue their life-long pursuit of a cancer cure at the Health Science Center.

In January, the Health Science Center launched a new institute for cancer research in partnership with the Center for Cancer and Blood Disorders. The Institute for Cancer and Blood Disorders combines the expert cancer knowledge and research at UNTHSC with the real-life needs of clinical cancer patients throughout North Texas with the goal of curing cancer.

Father and son researchers Drs. Yogesh and Sanjay Awasthi are on a life-long quest — to find a new cancer treatment that won't harm the body but will kill cancers. They believe they are close to finding the gold at the end of that rainbow.

Their quest, which has spanned some 25 years, has brought them to a likely suspect – a protein called RLIP76. It's this protein and its potential to "turn off" vital signaling processes within cancer cells that may hold the key to developing a revolutionary approach to cancer treatment.

The Awasthis' quest began in India, when Yogesh, DrPH, received his doctorate in natural plant chemistry and began to pursue his passion to reduce the toxicity of environmental cancer-causing agents. After moving to the United States, the elder Awasthi first identified the existence of the RLIP76 protein in 1983. What he didn't realize at the time was his son's keen interest in his research.

"When Sanjay was 14 years old, he began to secretly visit my research lab at night," Yogesh said. "He would talk to fellow researchers and began some of his own experiments. That is what ultimately led to his identification in 1999 of RLIP76 as a multifunctional protein and transporter that responded to any stress applied to the cell."

In September 2007, Sanjay, who earned his MD from UT Southwestern Medical Center, joined the Health Science Center to continue his fight against cancer. Yogesh and his fellow researchers, formerly at the University of Texas Medical Branch at Galveston, have been critically involved in supporting and furthering the work of Sanjay and his fellow Dallas-Fort Worth-based researchers. He and his team joined his son at the Health Science Center late last fall combining their efforts to fight cancer.

Sanjay, a board-certified oncologist and researcher, compares RLIP76 to car exhaust stored in a tube on the side of the cell. When the cell is stressed, the tube attaches to the wall of the cell and pours out noxious chemicals. This biochemical change sends signals that result in inflammation and cancer cell growth. Interrupt that signaling process by reducing or eliminating the RLIP76 protein through the use of enzymes, and the changes in the cell stop. The cancer stops growing and dies. Ultimately the patient survives and returns to a healthy, normal life.

The Awasthis are buoyed by exhaustive animal trials that showed a reduction and ultimate elimination of tumors in mice that were given the protein inhibitor and in some cases that received complementary chemotherapy. That has led them to the Health Science Center and the prospect of conducting clinical trials.

"My father and I are extremely excited about joining the Health Science Center family because the institution is highly recognized for its research biologists and its successful track record in sponsoring and conducting clinical trials," Sanjay said. "Our work is at a critical point, and our association with the Health Science Center will help our research move forward to the next level.

"There are several groups around the world who are focused on this particular protein. We were the first to show that the protein was a transporter, and now we have demonstrated that by eliminating the protein, cancers die. This opportunity at the Health Science Center has come along at just the right moment for us, for our research and for the cancer patients who may some day benefit from it.

"The technology and equipment we have at our disposal here will enable us to show in pictures that this is a protein that walks, shakes and moves – that it is a transporter," Sanjay said.

"In a way, this protein has brought my son and me full circle," Yogesh explained. "What began as my interest in plant toxicity and the environment has led us to work together in the lab at Fort Worth where we may be able to refine and introduce a completely new approach to cancer treatment."

Cooling those hot flashes

With an increased focus on women's health, the Health Science Center Created For HER (Focused on Resources for her Health, Education and Research), a collaborative organization that addresses and meets the health care needs of women of all ages and ethnic groups. Encompassing education, community outreach, research and clinical care through UNT Health, For HER includes new research on hormones, including estrogen and progesterone, as part of the menopause research at the heart of new grants and research at the Health Science Center.

Insomnia, hot flashes, irritability. Ask a woman over age 50 about the symptoms of menopause, and she'll recite them in a flash. But aside from these annoying symptoms, a woman's risk for diseases, including heart disease, osteoporosis and Alzheimer's disease, increases significantly after the menopause. Because the levels of hormones such as estrogen and progesterone decline after the menopause, does this decrease render the body more vulnerable to diseases commonly associated with aging? If so, can hormone therapy reduce such risks? And which hormones will benefit which individuals? That's what a team of scientists from the University of North Texas Health Science Center at Fort Worth intends to answer.

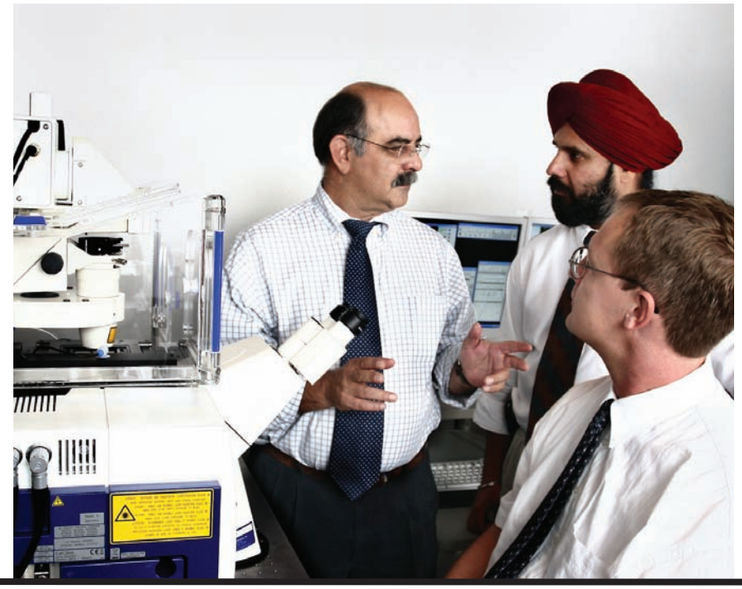
For years, physicians have prescribed hormone therapy to reduce the discomforts of menopause. But research efforts, including those at the Health Science Center, suggest that such hormones also may reduce brain dysfunction and the risk of diseases associated with the aging process, including Alzheimer's disease.

A few years ago, results of a major clinical study (the Women's Health Initiative) concluded that hormone therapy was not effective and may create adverse effects. As a result, physicians and their female patients began to avoid hormone therapy for fear of causing more damage than benefit.

In reality, the data did not warrant such broad generalizations, and, in an effort to clarify the apparent controversy, a team of researchers at the Health Science Center, led by Dr. Meharvan Singh, is studying how estrogens and progestins affect the brain. Singh is the project director for the collaborative research team that received a $5.6 million grant from the National Institute on Aging (NIA), a division of the National Institutes of Health (NIH), in August 2007 to study the novel mechanistic targets of steroid hormones in the brain. This is the third NIH-funded program project grant awarded to the Pharmacology and Neuroscience Department, a feat achieved by few other departments in the country. This program of research takes a multi-pronged approach toward tackling issues relevant to our understanding of how hormones, particularly estrogen and progesterone, affect the brain.

The team of Drs. Singh, James Simpkins, Peter Koulen, Laszlo Prokai, Katalin Prokai-Tatrai, ShaoHua Yang, Michael Forster, Michael Gatch and Shande Chen from

Researchers Dr. James Simpkins and Dr. Meharvan "Sonny" Singh work with Dr. Peter Koulen on hormone and Alzheimer's disease research.



"Through this research, we hope to give women more options, not rob them of choices."

— Dr. "Sonny" Singh

the Health Science Center, along with Dr. Dominique Toran-Allerand from Columbia University in New York, will address which estrogens or progestins are best at protecting the brain (for example, natural vs. synthetic progestins) and which may help the brain stay healthy.

"We work well together," Singh said. "This project is really a collaborative effort, where the program as a whole is truly greater than the sum of its individual components.

"Through a better understanding of the biology of these hormones, we may understand the consequences of not having these hormones around after the menopause. Then, we can use this knowledge to develop safer and more effective means of treating diseases whose risks increase following the menopause," Singh said. "Through this research, we hope to give women more options, not rob them of choices."

In addition to the $5.6 million NIH grant, Singh also received a recent grant from the Alzheimer's Association to study the effects of progesterone on the levels and regulation of a family of proteins, called neurotrophins, whose function is altered in Alzheimer's disease.

By understanding the basic mechanisms by which these proteins are regulated, Singh hopes to provide the foundation for new and innovative means of treating diseases like Alzheimer's disease.

Singh, together with Stan Hall, chief executive officer of Sendera Discovery, also received a Small Business Technology Transfer (STTR) grant from the National Institute on Aging. This partnership was developed based on Singh's other research relating to how a class of hormones, called androgens (which include testosterone), affect brain health. The goal of this project is to develop a diagnostic test to define risk associated with androgen therapy. Dr. Singh hopes that this eventually will allow physicians to determine if a patient is a good candidate for androgen therapy.

The Health Science Center's pharmacology and neuroscience department is in the top 10 percent of research grant dollars per faculty members and the top 20 percent of all research centers in the U.S.[1]

The NIH funds grants, cooperative agreements and contracts that support the advancement of fundamental knowledge to meet its mission of extending healthy life and reducing the burdens of illness and disability. NIH P01 grants support integrated, multi-project research projects involving a number of independent investigators who share knowledge and common resources.

[1]Based on 2005 Association of American Medical Colleges data for pharmacology departments.

Author! Author!

The following books were published by Health Science Center faculty during the past year:

- *BioMechanics in Ergonomics*, **Shrawan Kumar**, published by CRC Press.
- *Disparities and Access Barriers to Health Care Among Mexican American Elders*, **Alberto Coustasse**, Fernando Trevino, published by Springer.
- *Health-Seeking Behavior in Ethnic Populations*, Tyson Gibbs and **Sue Gena Lurie**, published by The Edwin Mellen Press.
- *Medical School Leadership Strategies*, Robert N. Golden, Richard N. Fine, Lee Goldman, Arthur Levine, **Marc B. Hahn**, published by Aspatore Books.
- *Ocular Therapeutics: Eye on New Discoveries*, **Thomas Yorio**, Abbott F. Clark and Martin B. Wax, published by Academic Press.
- *Oxidative Stress and Clinical and Biomedical Implications*, **Robert Mallet** and **Albert Olivencia-Yurvati**, published by Nova.
- *Risk Assessment for Environmental Health*, March G. Robson, William A. Tuscano and **Terry Gratton**, published by Jossey-Bass.

New light on the future

Drs. Karol and Ignacy Gryczinski use fluorescence technologies for commercial ventures and research.

Two years ago, two brothers from Poland, both with PhDs and an interest in fluorescence spectroscopy, came to the Health Science Center to further their work in this promising area. Today, they are spearheading the business applications through the Center for Commercialization of Fluorescence Technologies (CCFT).

Ignacy Gryczynski, PhD and professor of cell biology and genetics, and Zygmunt "Karol" Gryczynski, PhD and professor of molecular biology and immunology, are taking this new technology out of the research arena and developing new applications for the world of medicine.

"The major goal of the CCFT is to merge modern fluorescence with nanotechnology in order to create new research and developmental frontiers for modern medical diagnostics, biotechnology, genomics and proteomics," Karol said. "Use of optics and nanostructure engineering to amplify the fluorescence signal at a molecular level enables the development of new advanced tools needed for research and medical diagnostics of the 21st century."

Fluorescence is the emission of light from molecules that have been electronically excited by physical, mechanical or chemical mechanisms. The process reveals fundamental information about molecules and the interactions among different molecules. Fluorescence is produced by essential physiological functions in our bodies – proteins, DNA, RNA, etc. Processes such as genetic coding, cell growth or cell death are regulated by a well-defined set of macromolecular interactions. Cancer or cardiovascular disease results from a dysfunction from some of these processes.

The focus of the Gryczynskis' research in the CCFT is broad, covering many aspects of fluorescence. The brothers see several important practical applications of their work in the future, including the development of ultra-sensitive assays for cardiac markers, assays for early cancer detection, single molecule gene sequencing, novel imaging technologies for tissue imaging, and angiography.

"The purpose of the CCFT is to attract and develop the most promising technologies, especially nanotechnologies, to the stage that will result in their practical applications," Karol explained. "One of the CCFT's principal activities is to provide state-of-the-art fluorescence equipment and expertise to researchers in the Dallas/Fort Worth area and throughout Texas. The idea of the Center is not only to advance research but also to stimulate the transition of new emerging technologies to local commercial partners."

The role of the CCFT is to accelerate practical applications of the technologies, mostly related to medical and biomedical applications. Often, many years of testing and trials are required before they can be used commercially.

Ignacy sees a bright future for the CCFT. "Karol and I agree that the next phase of research in fluorescence involves advances in plasmonic fluorescence. Future biomedical diagnostics in the next 10 years will be dominated by nanophotonics and nanoplasmonic fluorescence applications. New detection technologies and devices for disease diagnostics and tissue imaging will dominate the medicine of tomorrow. Other growing areas for ultra-sensitive detection are biohazards and bioterrorism."

The Gryczynskis see more nanophotonic applications being developed for medicine. For them, creation of the CCFT with advanced nanotechnology and optics within the Health Science Center is ideal because it will support the future needs for more advanced training of new physicians.

"Ten to 15 years ago, facilities like the CCFT were clearly associated with physics or engineering departments," Karol said. "Today the interaction between physicists, engineers and medical doctors mandate advanced cross-training across these disciplines. We believe the diagnostic devices that will emerge from research such as ours are likely to resemble those seen in today's futuristic movies such as Star Trek."

Research Grant Updates

Relating L-Dopa *and* Parkinson's

For many years the good news for those suffering from Parkinson's disease was that there was a drug that was useful to treat their ailment — levodopa, commonly known as L-dopa.

The bad news, especially for young patients with early-onset Parkinson's, was that prolonged use of L-dopa caused motor side effects including tremors and involuntary movements. These side effects are generally referred to as levodopa-induced dyskinesia (LID).

Robert R. Luedtke, PhD and professor in the department of Pharmacology and Neuroscience, and his team of researchers are using money from a Community Fast Track program grant from the Michael J. Fox Foundation to investigate various drugs — D2-like (D2/D3) dopamine receptor agonists — and their ability to counter LID by binding to D3 dopamine receptors.

"There are three pathways in the brain that communicate using the neurotransmitter dopamine," Luedtke explained. "These systems are known to be involved in movement coordination, emotion, mood and memory. A deterioration of the nigrostriatal pathway is thought to be involved in the symptoms associated with Parkinson's disease. Therefore, the communication between one neuron making dopamine and another neuron expressing dopamine receptors becomes weakened. Levodopa is typically prescribed as a building block for making dopamine in the cell."

L-Dopa research could lead to treatments for Parkinson's disease.

The focus of Luedtke's research is to investigate the possible use of D3 dopamine receptor-selective drugs to delay or diminish LID. Currently, it is unclear if the binding to the D2 or D3 receptor is responsible for the therapeutic effects of these drugs, but recent studies suggest that drugs that bind only to the D3 receptors may alleviate the symptoms of both Parkinson's disease and LID.

Luedtke's team has focused on identifying and characterizing compounds that affect the D3 dopamine receptor subtype. These drugs have been developed in collaboration with the Division of Radiological Sciences of the Mallinckrodt Institute of Radiology at Washington University School of Medicine and the Medical Chemistry Section at the National Institute on Drug Abuse-Intramural Research Program (NIDA-IRP) in Baltimore.

"The goal is to determine if our novel D3 receptor-selective compounds are able to attenuate the symptoms of L-dopa-induced dyskinesia using a model of human LID," Luedtke said.

Luedtke's team already has identified several pharmacotherapeutic agents in the treatment of L-dopa-associated involuntary movements. These studies provide new insights into the role of the D3 dopamine receptor subtype in fine motor coordination and the pathology of dyskinesias that arise in patients with Parkinson's disease after chronic treatment with L-dopa.

In addition, Luedtke and collaborators at Washington University and Arizona State University, recently received a grant to investigate the use of D3 dopamine compounds to reduce the reinforcing properties of psychostimulants, including cocaine and methamphetamine.

"When we engage in rewarding behaviors, such as smelling flowers or listening to music or spending time doing things we enjoy, there is a release of dopamine in the nucleus accumbens," Luedtke said. "Unfortunately, people can abuse or over-stimulate this reward center by using psychostimulants."

In a recent TIME magazine article (July 16, 2007), Frank Vocci, director of pharmacotherapies at the National Institute on Drug Abuse (NIDA), was quoted as saying, "One particular group of dopamine receptors, called D3, seems to multiply in the presence of cocaine, methamphetamine and nicotine, making it possible for more of the drug to enter and activate nerve cells. Receptor density is thought to be an amplifier. Chemically blocking D3 interrupts an awful lot of the drugs' effects. It is probably the hottest target in modulating the reward system."

Therefore, Luedtke explained, the focus of the research around this new grant will be based on the hypothesis that D3 receptor subtype selective compounds may have potential as a new generation of D3 receptor-based pharmacotherapeutics for the safe treatment and/or management of individuals who abuse psychostimulants.

Dr. Robert Luedtke and researchers Rakesh Kumar and Lindsay Riddle research the premise that D3 receptor compounds may treat individuals who abuse psychostimulants.

Research Grant Updates

Helping Latino kids live healthier

Researcher's commitment to help Hispanic children live healthier lives brings her into the community. Dr. Ximena Urrutia-Rojas strives to being healthy living practices to vulnerable neighborhoods in Fort Worth, Texas.

Ximena Urrutia-Rojas, PhD, isn't your typical university health science researcher. In her quest to improve the lives of Hispanic children, she seizes every opportunity to maximize funding to support her community-based research efforts involving awareness and primary prevention that result in practical applications for the general population.

Currently, Urrutia-Rojas is in the middle of a three-year study funded by the FITFUTURE© Childhood Obesity Impact Project, sponsored by the United Way of Tarrant County. The community participatory project aims to reduce and prevent obesity and related chronic metabolic diseases such as diabetes in Latino and African-American children. The study involves researchers and staff from the Health Science Center's School of Public Health and John Peter Smith Health Network: Department of Family Medicine.

Urrutia-Rojas, a native of Chile, explained that this research project provides the opportunity to continue to expand her research agenda — to contribute towards the Texas community goal of reducing and preventing obesity, as well as related chronic diseases in children.

"The purpose of FITFUTURE© is to motivate children and their families to understand the importance of achieving an appropriate weight, decreasing obesity and making a commitment to a healthier lifestyle," Urrutia-Rojas said. "The target population is third-grade students and their families at Mitchell Boulevard Elementary School in Fort Worth. The school is composed primarily of African American and Latino children. These populations have been identified to be at the greatest risk for obesity in childhood."

The study's primary goals are to:

- conduct an intervention/control trial study to prevent and reduce childhood obesity at two elementary schools over three years; and
- implement the three main components of the intervention — increased nutrition education for children during school; nutrition education for the parents; and increased opportunities for physical activity.

The study's main objectives are to:

- increase the amount of physical activity at the family level;
- improve healthy/nutritional food choices and portions at the family level; and
- enhance family commitment to a healthier lifestyle.

"By the end of the first year of the study, more than 75 percent of the third-graders at Mitchell Boulevard Elementary (the intervention school) and almost two-thirds of the third-grade students at Maude Logan Elementary (the control school) were enrolled in the study," Urrutia-Rojas said. "The students had measurements of body mass index (BMI), body fat and waist circumference assessed three times under the study protocol. Analysis of

Students at Mitchell Boulevard Elementary School integrate exercise into a health life style and stay fit for the future.

Ximena Urrutia-Rojas (third from right, back row) works with young people at Mitchell Boulevard Elementary School in Fort Worth to help improve their health and fitness.

study data indicate that at the end of the first year of the intervention, participants at Mitchell Boulevard are benefiting from the study. The BMIs of children at Mitchell Boulevard are increasing at a slower rate than those of the children at Maude Logan. The waist circumferences and body fat percentages of children at Mitchell Boulevard have decreased or remained the same, while these same indicators are increasing among children at Maude Logan."

The study organizers developed a multi-pronged approach to implementation and maintenance of the project. JPS Shapedown was selected as the prevention program for the obesity impact project because it incorporates parents and the community and provides a minimum of approximately 30 minutes of classroom time per class per week, which is vital in addressing the problem. JPS Shapedown was developed by the nutrition department of JPS Health Network to teach children and their parents to manage weight problems and obesity. The program was designed by registered dieticians and is based on nutrition, science, exercise, education and behavior modifications. Topics and activities focus on self-esteem, communication, behavior change, nutrition and fitness.

"Each week at Mitchell Elementary during their class time, all four third-grade classes receive nutrition education class, conducted by the registered dietician," Urrutia-Rojas explained. "Emphasis is on exercise, motivation and implementing established daily activities. I am pleased that seven third-graders signed up for the 2007 Cowtown Marathon, and four participated for the first time. In addition, all fourth-, fifth- and sixth-graders participated in the Fit Student Contest.

"Parents and their children had the opportunity to come together to learn about healthy nutrition at the 'Taste of Spring' cooking class, the 'How Sweet It Is' class on sugar and the 'Shake The Salt Habit' class," Urrutia-Rojas said.

While the study is far from complete, organizers, children and their parents are pleased with the promising results achieved so far. The expected study outcome, according to Urrutia-Rojas, is that the children and their families who are participating in the study and going through the intervention will embrace healthier lifestyles — increased physical activity and eating healthier foods.

"These newly adapted behaviors have the potential to produce changes for their lifetime and therefore prevent overweight and obesity and related chronic diseases," Urrutia-Rojas said. "Ultimately, the whole community and society at large benefit from these outcomes."

Pyruvate treats trauma

Albert Olivencia-Yurvati, DO, and Robert Mallet, PhD, have teamed up to determine the benefits of using pyruvate, a naturally occurring compound which acts as an anti-oxidant and a fuel source, in trauma victims and battlefield casualties.

With critical trauma injuries, especially to arms, legs, hands and feet, a tourniquet usually is applied immediately to stop the bleeding. Once the injury is stabilized (with stitches, surgery or other means), the tourniquet is removed, allowing blood to course back into the limb. While blood flow is essential, the oxygen carried in blood can damage the tissue when it rushes back into the blood vessels of the injured limb.

"In the field, there can be benefits from administering pyruvate immediately," said Olivencia-Yurvati, chief of surgery, who earned his doctor of osteopathic medicine degree from the Health Science Center in 1986 and is handling the clinical research, which initially was funded by a grant from Health Science Center President Scott Ransom as part of his commitment to collaborative research on campus.

Preliminary studies of intravenous pyruvate show that it can help prevent damage to tissue if administered within an hour of the injury. The compound also may have anti-inflammatory applications by reducing swelling and oxidative stress in surgery patients, especially those undergoing cardiovascular surgery.

"Pyruvate can help the heart work more effectively and maintain blood pressure, in addition to preventing tissue damage and maintaining cardiovascular health," Mallet said. "However, it must be administered intravenously; oral doses aren't effective."

As part of their research, Mallet and Olivencia-Yurvati have teamed up with the North Texas Research Alliance for Urgent Medical Assistance (NTrauma) at the University of North Texas at Denton to test pyruvate's effects using a heart-lung model and machine. NTrauma scientists are investigating vascular growth and injury, consequences of poor tissue oxygenation, limb reperfusion techniques, and wound repair and healing.

"We believe some of the most immediate and critical uses for pyruvate may be for the military treating casualties in the field," Olivencia-Yurvati said. "Civilian emergency medical and trauma teams could also see benefits in treating trauma injuries by incorporating this compound in resuscitative fluids."

Myong-Gwi Ryou, Dr. Albert Olivencia-Yurvati, Dr. Robert Mallet and Devin Flaherty test the effects of pyruvate on trauma injuries and cardiovascular surgery using this heart lung machine at the Health Science Center.

Osteopathic treatment meets technology

Dr. Michael Smith, left, and Dr. Kendi Hensel use the circle bed to measure changes in a pregnant woman's physiology at different stages of her pregnancy.

Health Science Center researchers combine osteopathic manipulative treatment with technological measures of treatment to benefit patients.

How do shifts in weight and center of gravity affect the way a person walks? Can osteopathic manipulative medicine change how a person's body systems interact enough to adjust for these shifts? Can these changes affect the outcome of pregnancies?

The national Osteopathic Research Center (ORC) at the Health Science Center seeks answers to these questions and more through the Osteopathic Heritage Foundation Physical Medicine Core Research Facility (PMCRF) — a laboratory for collaborative research for orthopedic and manipulative medicine specialists in biomechanics and human performance.

As part of the Health Science Center's Health Institutes of Texas, the PMCRF researchers and practitioners study osteopathic manipulative medicine, orthopedic surgery, and other aspects of musculoskeletal disease and somatic dysfunction.

The first two members of the PMCRF team started at the Health Science Center in late 2007, and between them, more than 55 years of research and work in biomechanics will give this institute a solid foundation on which to build the future of musculoskeletal disease diagnoses and treatments.

Shrawan Kumar, PhD, has 30 years of research experience in biomechanics and physical therapy, with most of his work focused on musculoskeletal maladies of the trunk and back. He holds two U.S. patents for his inventions of biomechanical devices related to the treatment of spine mobilization and manipulation, with three prototypes of technology for assessment, treatment and training for patients with back disorders currently under review by the patent sub-committee of the University of Alberta.

Kumar has held more than $1.85 million in work-related grants over the lifetime of his career in both individual and joint projects. He has taught courses in design, development and teaching of courses in tissue biomechanics, electromyographic kinesiology and rehabilitation ergonomics.

Rita Patterson, PhD, has focused her research on the biomechanics and kinematics of human joints and projects designed to increase knowledge about the human musculoskeletal system. Currently, she has two grants pending approval of the National Institutes of Health — "Hand Grasp Patterns after Traumatic Brain Injury" and "Intrinsic-Extrinsic Muscle Function in the Hand."

Patterson has held more than $2.6 million in other grants over the lifetime of her work, including work as principal investigator on projects studying the function of the dorsal wrist in injured and normal states, and motion analysis assessment in brain-injured patients.

Researchers at the ORC began the center's biomechanics study in early 2007 with a project incorporating osteopathic manipulative treatment (OMT) and measures of vital signs and body changes in pregnant women — including heart rate, blood pressure, fluid volume shifts between body compartments and gait — to determine if OMT can help ease the stress of pregnancy on a woman's body. The five-year project is funded by both the American Osteopathic Association and the National Institutes of Health.

Subjects' biomechanic function measurements include a walk on a 14-foot-long, portable mat with 16,128 embedded sensors. The mat, called a GAITRite, captures electronic footprints instantly, and sensors in the mat measure cadence, step length, velocity and other gait parameters.

Kendi Hensel, DO and assistant professor at the Health Science Center's departments of Family and Community Medicine and Osteopathic Manipulative Medicine, said measuring a pregnant woman's gait before and after OMT can help determine if the treatment helps her by adjusting her biomechanical systems enough to compensate for the localized weight gain that accompanies pregnancy. Previous studies have shown stress in the pregnant mother can lead to fetal stress, which causes meconium staining of the placenta – a primary factor of elevated risk in delivery.

"We take physical measurements at 30 and 36 weeks, before and after OMT treatment," Hensel said. "It's during this last part of pregnancy when the baby grows significantly. This study will help us see how this weight gain changes a woman's gait and how much the gait changes after OMT."

Reducing stress in both the mother and baby can help lower risks during pregnancy and delivery. Pregnant OMT patients historically have reported easier, less painful pregnancies and deliveries.

"This is just a small sampling of what biomechanics can do," Hensel said. "This is just the beginning of this kind of work here."

Leading primary care research

Imagine a health system designed for primary care physicians to translate their knowledge of local health issues from neighborhood clinics to global health care solutions.

Dr. Roberto Cardarelli

NorTex, the North Texas Primary Care Practice-Based Research Network, allows physicians and health researchers to recruit actual clinic patients for studies, then disseminate their research findings beyond the health professionals to the local community through newsletters, churches and other avenues.

NorTex will lend its participating clinics and physicians' knowledge in this approach to UT Southwestern by partnering in their recently awarded $34-million, five-year Clinical Translational Science Award (CTSA) from the National Institutes of Health (NIH). By creating the new Primary Care Research Institute, NorTex will help revamp the way primary care research is done in North Texas and beyond.

"We were approached by UT Southwestern and asked to be a partner because of our research network and the need for a practice-based research model as part of the grant," said Roberto Cardarelli, DO, MPH, and founder and director of NorTex and the new Primary Care Research Institute. "This large NIH grant will create an incredible infrastructure for all types of research and community resources and revolutionize the way we do primary care research in North Texas."

Through the formation of the Primary Care Research Institute, NorTex will expand its resources throughout North Texas through a new partnership with Parkland Health and Hospital System's Community-Oriented Primary Care clinics.

"Physicians in the Primary Care Research Institute will collaborate to conduct research in primary care and public health, including HIV/AIDS, preventive care research and so much more," said Kimberly Fulda, DrPH, and assistant director of NorTex and the Primary Care Research Institute. "This allows us to do research in partnership with the community, not just gathering information from members of the community without sharing what we've learned with them."

The goal of the CTSA award is to transform how basic, clinical and translational research is conducted to bring effective strategies and new treatments more quickly to health care workers and their patients. As a community engagement partner, NorTex will recruit research participants from the community and increase public trust in local research.

Cardarelli believes that primary care research helps lower hospital rates and health care costs.

"Most primary care is delivered in the outpatient setting, and it has the potential for the greatest impact on the public's health," he said. "During primary care visits, physicians can diagnose and treat health problems before they become chronic or turn into emergent situations.

"Primary care research also decreases health disparities — inequalities in the health status, access to health care and health risk factors among racial and ethnic minorities and the general population— and NorTex is one of the few practice-based research networks in the nation that focuses its research on health disparities.

"We have to understand disease processes and factors that impact the progression of disease in a population — in a primary care outpatient setting — in order to know how we can prevent, diagnose, and treat that population to the best of our abilities while taking into account their cultural beliefs and values," he said.

NorTex also conducts research in pediatrics, family medicine, epidemiology, health management and policy, and social and behavioral sciences as part of a new partnership with Cook Children's Physician Network. Its research focuses on primary care and public health issues in Tarrant County.

"NorTex is now growing into the Dallas region so it can fulfill its role for the CTSA," Fulda said. "That is, to collaborate with primary care and public health partners so that we can do research with whom it affects the most — the patients, the clinicians and the communities."

Dr. Roberto Cardarelli (right) brings his experience in treating individuals to the new Primary Care Research Institute.

Students appreciate mentors

Liz Davis, associate director of the Office of Outreach, recently received a letter from Barbara Novero, lead counselor at Paul Laurence Dunbar High School, one of the Health Science Center's Adopt-a-School partners, praising the program's effects on students' education.

"The students at Dunbar High School have accessed the services provided in the Go Center more than any high school in Fort Worth," Novero wrote. "They have completed college searches, applied for scholarships, registered for SAT/ACT, written magnificent essays, and attended presentations.

"It is this beautiful team work in motion that built to the grand finale at the end of last year with Dunbar students being awarded $3.5 million in merit-based scholarships! This achievement placed Dunbar at the top of FWISD again.

"These accomplishments are possible because of the team work and dedication of our Adopt-a-School partners. We are truly appreciative of our friends at UNT Health Science Center. They have … [given] … the best gift of all, opportunity!"

Health Science Center students serve as mentors in the Go Centers at Dunbar and North Side high schools, working at least two hours per month, in addition to their normal studies, and guide students through the process of college preparation. These centers focus on first-generation college students, especially African Americans and Hispanics.

Center *for* Community Health

In September 2007, the Health Science Center, in a unique partnership with the J. McDonald Williams Institute of Dallas, established the Center for Community Health to foster healthy, vibrant communities.

Under the direction of Dr. Kathryn Cardarelli, the Center's goal is to establish and enhance community relationships and collaborations, conduct research related to public health policy, prevent negative situations and improve the health of vulnerable populations in the Metroplex.

One of the first projects of the Center for Community Health, Youth HIV Outreach, Prevention and Education (Youth HOPE), involves reaching out and educating young people in vulnerable South Dallas neighborhoods about HIV and AIDS as a result of risky behavior. Working with local leaders from the community, UT Southwestern, Texas Health Resources, Youth Angle and many others, the task force hopes to educate children as young as eight and nine years old about AIDS and HIV risks. Intervention and prevention programs will follow in phase two.

Dallas County has some of the highest rates of sexually transmitted infections, including HIV and AIDS, in Texas. According to research by the University of Texas Southwestern Medical Center, 12 percent of newly reported HIV cases and seven percent of newly reported AIDS cases occur among youth 13 to 24 years old. Fifty-three percent of young people living with HIV/AIDS in the county are African American, and 22 percent are Hispanic/Latino.

Another of Cardarelli's efforts is the Aintie Tia Project, a partnership with the Fort Worth/Dallas Birthing Project under the Center for Health Disparities designed to combat infant mortality in Tarrant County, where the infant mortality rate is the highest in Texas. This project brings community women together in a doula model, training them in prenatal education, labor support, infant and childcare education, breastfeeding support/education and emotional support as a resource for pregnant young women in the community. The name "Aintie Tia" is coined from terms of affection for "aunt" in the African American and Hispanic communities. In local communities, these "ainties" or "tias" often help lead, support and develop young people.

Research in the first phase of the project will help determine whether or not social community-based support improves birthweight and increases breastfeeding in African American women. Another phase likely will include at-risk young Hispanic women.

"In December, we convened the first community advisory board meeting with representatives from both Dallas and Tarrant Counties," Cardarelli said. "We are conducting several of our studies in Dallas County instead of Tarrant County, because Dallas County has clear pockets of need and the worst health conditions. Tarrant County's demographics don't provide as clear a picture. Plus, the Williams Institute has a strong reciprocal relationship with Dallas County."

Additional projects may address pregnancy outcomes in both counties, HIV intervention and awareness in Tarrant County, and mental health issues across the DFW Metroplex.

Dr. Kathryn Cardarelli

Institutes

The University of North Texas Health Science Center is providing a healthier future for a changing world with new discoveries through research. Our internationally known faculty researchers are exploring new approaches to the treatment of disease through specialized institutes designed to research disease, treat patients with that disease and carry those findings to the marketplace.

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

Health Institutes of Texas (HIT)
HIT uses a bench-to-bedside attack against diseases that afflict Texans and rob them of their productivity, finances and quality of life, including infant mortality, aging and Alzheimer's disease, musculoskeletal disease, and ethnically disproportionate illness. Its mission is to solve problems through data analysis, laboratory research, clinical treatment and physician training.

Primary Care Research Institute (PCRI)
The PCRI is revolutionizing the approach to primary care research by developing collaborative partnerships within and outside the institution to improve the health and lives of the people of Texas through interdisciplinary and translational research and education.

Texas Center for Health Disparities (TCHD)
The TCHD, an NIH-designated (EXPORT) center, works to prevent, reduce and eliminate health disparities in our communities through research, education and community relations; and trains minority biomedical scientists in developing innovative programs specifically tailored to Texas minority populations.

Institute for Cancer and Blood Disorders (ICBD)
A unique university-community collaboration between the Health Science Center and the Center for Cancer and Blood Disorders, the (ICBD) provides leadership in all aspects of cancer research, education and training, along with highly experienced patient care capabilities.

Center for Community Health (CCH)
The CCH conducts policy-relevant health research and enhances community capacity for prevention; translates research into practice and policy; eliminates health disparities in the North Texas area; and creates replicable models of change to improve population health.

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.

Institute for Aging and Alzheimer's Disease Research (IAADR)
The IAADR focuses on early detection of Alzheimer's, estrogen's role in Alzheimer's and Parkinson's, stroke therapy and identification of oxidation processes to measure brain aging, with several treatment drugs in clinical trials.

Physical Medicine Institute (PMI)
The PMI promotes basic and clinical research, education, clinical practice and community outreach programs in the prevention, diagnosis, treatment and rehabilitation of neuromusculoskeletal disease for people of all ages.

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 Women's Health (Focused on Resources for her Health, Education and research - For HER)
For HER is a collaborative, multidisciplinary organization to address and meet the healthcare needs of women of all ages and ethnic groups.

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 vision disorders.

Classrooms without walls

James Flynn works with the Fort Worth Independent School District to bring students into the lab and beam himself into the classroom.

The Health Science Center recently turned research labs into distance learning television studios to bring science into public school classrooms across the state of Texas in a whole new way. These visual demonstrations brings public school students into the heart of the research lab.

In October 2007, Rusty Reeves, PhD and associate professor of cell biology and genetics, presented "How Systems Work in Your Body: The Human Heart and Lungs" to 54 Texas public schools from the gross anatomy lab on the UNT Health Science Center campus in Fort Worth's Cultural District. During the one-hour lesson, approximately 3,000 fourth- and fifth-graders saw human hearts and lungs, learned about the cardiopulmonary system, and compared a system in the body to other systems with which they are familiar, like Fort Worth's water supply system.

Reeves demonstrated how the heart and lungs work and explained how they interact to deliver oxygen to the body to students from the Texas Panhandle to the Gulf Coast, then gave students an opportunity to ask questions.

Reeves used the lesson to further the goal of the Health Science Center's outreach programs by bringing an interesting science lesson to students who might never get the chance to see or learn the subject, and present science as a "cool" career choice.

"Most of these students never see what a researcher really does," Reeves said. "These video conferences are the perfect way for us to bring students of all ages and from all over the state to the Health Science Center to see real labs and what it is researchers really do without them ever having to leave their classrooms. We're planning to improve on the technology and hold more of these in the near future."

A week later, PhD candidate James Flynn broadcast from his lab on campus into the SCORE (Schools' Cooperative Opportunities for Resources and Education program) classroom at Fort Worth's Carter Riverside High School at which he teaches every week. A new microscope camera was added, giving students watching the presentation an opportunity to see through the researcher's eye.

Outreach programs present science as a cool career choice.

SCORE, funded by the National Science Foundation's Graduate Teaching Fellows in K-12 program, was designed to form strong partnerships among Fort Worth Independent School District teachers and graduate students from the Health Science Center to improve science education in the district and foster interest in the sciences as a viable education and career opportunity for the students.

Flynn has been teaching his classes about his research at the Health Science Center — the possible effects of estrogen in preventing cataracts. Using video conferencing, he taught classes from his Health Science Center lab, letting students see him in his own environment.

After a quick tour of his lab, the students saw Flynn at work as he taught them how he grows cells from a pig's eyeball. The ninth- and tenth-graders completed lab worksheets during Flynn's lecture and demonstration.

"I've always had a strong interest in science, but it has been great to have a real scientist come into class and help," said Cody Floyd, a sophomore biology student in one of Flynn's SCORE classes. "I really didn't know how real experiments are actually performed, and these types of experiments are really interesting."

Teacher Adam James said that he has seen changes in his students' interest and abilities in science over the five years that he has been involved with SCORE.

"I see a lot more interest from the students," he said. "They always anticipate lab day and having Jim in class. I've also seen an increase in their state test scores in science."

James said that he has benefited from the SCORE program as much as his students have.

"It has increased the amount of technology I use in the classroom," he said. "Now, all of our laboratory experiments are inquiry based or true experimentation. I know I have become a better and more effective teacher since being involved with the program."

Plant workers' mortality

New research could help determine if mirco-organisms and prions in animals that we use for food cause cancer, and diseases of the cardiovascular and neurological systems in humans.

Relationship between animal viruses and human disease

For Eric Johnson, PhD, MD, MPH, DTPH and professor and chair of the epidemiology and environmental and occupational health departments in the Health Science Center's School of Public Health, the health and life cycle of some 30,000 workers in poultry slaughtering/processing plants may be an ominous predictor of the link between cancer-causing viruses in animals and cancer in humans.

Johnson and his team of researchers have just completed data collection from a three-year study of these workers. The team is analyzing the vast amount of data and preparing to publish their findings this year. This work will augment a two-year study begun in September 2007 that examines the mortality of workers in cattle, pig and sheep slaughtering/processing plants and in the meat departments of supermarkets.

"We also are conducting molecular studies aimed at finding out if pig endogenous retroviruses and avian leukosis/sarcoma viruses (ALSV) can be detected and integrated within the genome of cancer cells. These cells are derived from paraffin block biopsy tissue from workers who were exposed to these viruses, then died of cancers," Dr. Johnson said. "ALSV commonly infects and causes cancer in chickens. The detection of integration within the human genome will provide definitive proof that these viruses can not only cause cancer in animals but can also cause cancer in humans."

Johnson's research is based on a fundamental theory: animals used for food are infected with a wide variety of microorganisms and prions, which create in them chronic diseases including cancer, neurological diseases, cardiovascular diseases and more. Humans can be exposed to these same viruses when injected with measles and mumps vaccines, occupationally through contact with live animals, and through ingesting inadequately cooked meat or eggs or unpasteurized milk.

"Perhaps some chronic diseases like cancer occur in humans due to exposure to these agents," Johnson said. "The research has focused on meat workers because they have the highest human exposure to these transmissible agents. If these agents cause disease in humans, it can easily be manifested among these workers.

"I believe our research will contribute to one of the major breakthroughs in medical research. For more than 20 years, evidence has been obtained that a majority of cancers occurring in humans are related to diet, and not to occupational chemical exposures as was once widely thought. Using the retrovirus investigations being conducted in our lab, our research will provide evidence that many of the cancers and other chronic diseases occurring in the general population could result from our exposure to transmissible agents that are present in the animals that we use for food and in their meat, eggs and milk. Our findings have direct bearing on the health of workers in the meat and poultry industries. As we clearly detect sources of risk for these workers, steps will be taken to mitigate risks and protect workers."

Johnson proudly points to another achievement during his tenure at the Health Science Center. He and his team developed and tested a new set of mortality rates for approximately 135 non-cancer diseases such as multiple sclerosis, myasthenia gravis, anterior horn cell disease, Parkinson's disease and others, and incorporated the results into statistical software for analyzing occupational cohort mortality studies. This is the first time so many causes of death have been investigated in an occupational study.

"We have already tested these rates in old data and exciting new findings for certain diseases are beginning to emerge that have never been possible to investigate before," Dr. Johnson explained. The findings were reported in 2007 in two journals.

Where are they now?

A quest to block the ravages of stroke

A protein called an acid-sensing ion channel lives in the central nervous system, potentially playing a role in learning and memory, as well as in the sensations of pain and fear. Plus, it may hold the key to limiting damages from stroke.

Eric Gonzales, PhD, who received his doctorate from the Health Science Center in 2005, is determined to find out. Now working on his postdoctoral fellowship at Oregon Health and Science University's Vollum Institute in Portland, Gonzales' work was featured on the cover of and within a recent issue of *Nature*.

According to the study, acid-sensing ion channels are proton-activated receptors present in many human tissues and organs, but particularly abundant in the central and peripheral nervous system. They are part of a system that performs a range of functions in the body, including maintaining sodium levels and mechanosensation, the mechanism by which organs respond to mechanical stimuli.

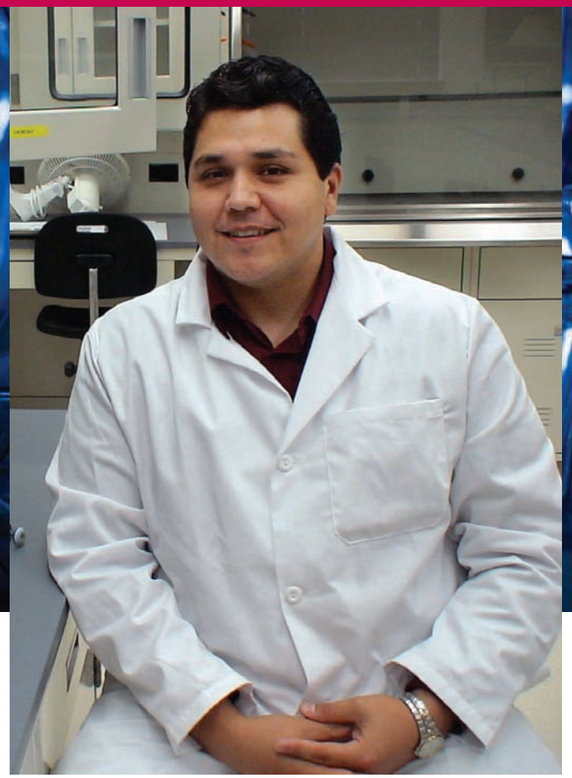
Until the report was published in *Nature*, the structure of this type of protein was unknown.

"We're using classic techniques to determine the structure of this protein," Gonzales said. "One day, we hope our findings will lead to the development of novel therapies that target this protein. If we can find molecules to block these channels, maybe we can limit damage from stroke."

Gonzales received his bachelor's degree from the University of Texas and was named Outstanding Graduate by the Health Science Center's Graduate School of Biomedical Sciences in 2005.

In 2004, while working on his doctorate at the Health Science Center, Gonzales was named a Grass Fellow by the prestigious Grass Foundation. The Grass Fellowship provides an opportunity each year for a small number of neuroscientists to conduct independent research at the Marine Biological Laboratory in Woods Hole, Mass.

Where are they now?



Are some of us destined to be fat?

More than 60 percent of American adults are overweight, according to the Centers for Disease Control and Prevention, and some races may be more prone to obesity than others.

That is the premise of a study that will launch this spring by Martin Farias III, a 2003 graduate of the UNT Health Science Center who now serves as assistant professor of physiology at the Irma Lerma Rangel College of Pharmacy at Texas A&M Health Science Center.

"Mexican Americans in South Texas have a higher percentage of obesity than Caucasians in the same region," Farias said. Working under a STAR Fellowship from the Health Science Center, Farias will collaborate with researchers at the University of Texas-Brownsville to study fat-derived hormones that are prevalent in various obese racial groups.

"If there are differences, it might explain why we're seeing greater rates of obesity among Latinos in South Texas," he said.

Farias' research focuses on understanding how hormones derived from fat affect blood flow to different parts of the body, and also concentrates on delineating the mechanisms of endothelial dysfunction and myocardial injury during obesity.

"We know that there are various hormone changes occurring during obesity," Dr. Farias said. "Yet nobody really knows how these hormones affect the blood flow to vital organs."

Farias received his bachelor's degree from Our Lady of the Lake University in San Antonio and his master's from the University of Texas at Brownsville. He received his doctorate from the Health Science Center in 2003.

Farias is a Health Disparities Scholar at National Institutes of Health and recently was appointed to the Council of Deans/Council of Faculties Task Force on Faculty Workforce for the American Association of Colleges of Pharmacy. He also was inducted into the Texas A&M Health Science Center Cardiovascular Research Institute in September 2007.

Brushing off plaque to improve brain function

Research has shown that more intracellular plaque in the brain leads to decreased brain cell function and increased brain cell death, which lead to cognitive and memory loss.

Certain proteins in the brain may be at the root of plaque formation, and Josh Gatson, PhD and a 2007 graduate of the Health Science Center, believes if he can learn how to decrease the activity of these proteins, Alzheimer's disease can be treated and perhaps even prevented.

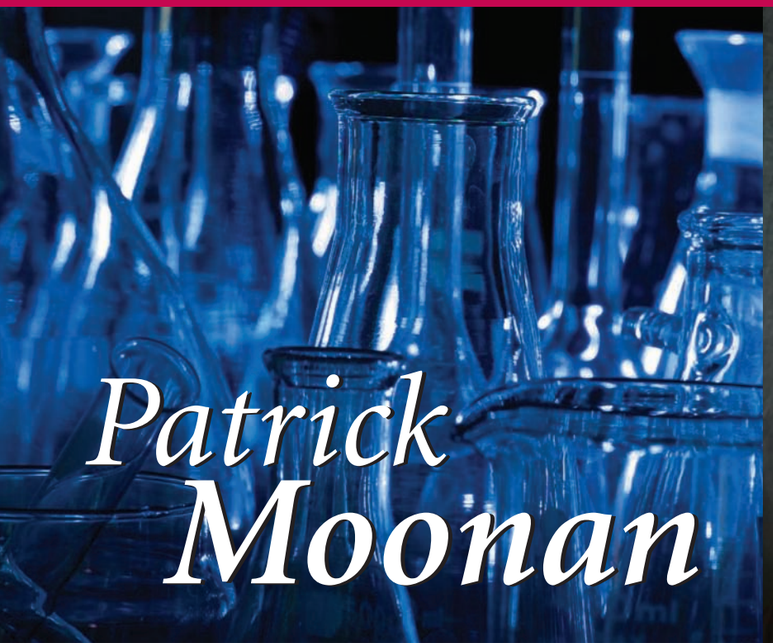
"My research studies the intracellular signaling pathways that govern plaque formation as seen in Alzheimer's disease," Gatson said. "I am developing a project to express mutated proteins in certain regions of the brain — the hippocampus and the cortex — to determine if these intracellular proteins are involved in Abeta — the main protein component of amyloid plaque — and plaque formation."

By injecting these proteins into the hippocampus and cortex of a mouse model with Alzheimer's disease, Gatson is studying the animal's subsequent behavior and plaque levels. If he can prove that a decrease in the activity levels of these proteins in the mice leads to lower plaque levels and preserved cognition, the results could lead to new drug therapies for Alzheimer's in humans.

"As a therapeutic strategy, use of drugs that counteract the actions of these signaling pathways could potentially decrease the incidence of Alzheimer's disease," he said.

Gatson earned his bachelor's degree from Texas Wesleyan University. His master's and doctorate degrees are from the Health Science Center. He is in his first year of a three-year postdoctoral fellowship in the department of neurology at Mount Sinai School of Medicine in New York.

While at the Health Science Center, Gatson had four scientific papers published, attended four national scientific meetings and received a Grass Fellowship while working on his doctorate — only the second student in the Graduate School of Biomedical Sciences to attain this prestigious achievement.



UNTHSC alumnus helps in national investigation of TB patient

Dr. Patrick Moonan, a 2005 graduate of the Health Science Center's School of Public Health, played a key role in the recent U.S. Centers for Disease Control and Prevention (CDC) investigation of Andrew Speaker, the Atlanta attorney who traveled from Atlanta to Europe and back again while infected with what was believed to be an extensively drug-resistant strain of tuberculosis (XDR TB). Speaker was ordered into involuntary medical isolation in May after he and his bride took the two transatlantic flights against doctors' orders, then drove across the U.S.-Canada border to return to Atlanta.

Moonan, a senior epidemiologist for the Division of Tuberculosis Elimination at the CDC, was the supervising investigator on the Speaker incident. His expertise in infectious diseases also garnered Moonan an interview for a report that aired on National Public Radio in June. The segment that aired on "All Things Considered" included an explanation of how TB genotyping is used locally.

In addition to his duties as part of the CDC's outbreak investigation team, Moonan co-ordinates the U.S. National Tuberculosis Genotyping Service. He has been with the CDC for two years.

What is the status of Speaker?

His diagnosis was reclassified as multi-drug resistant tuberculosis (MDR TB) in early July. He underwent surgery in mid-July to remove the infected lung tissue. Speaker was released from the hospital nine days after his surgery.

"Treatment for Mr. Speaker went very well, and we were able to release him more quickly than we originally anticipated," says Gwen Huitt, MD, in a National Jewish Medical and Research Center news release. "Although we believe there are still a few tuberculosis bacteria in his lungs, ongoing antibiotic therapy should kill those. We expect him to return to a full and active life."

Building the case for alternative healing

While people have been drawn to alternate healing methods for ages — often in search of cures not possible through conventional medicine — their popularity has exploded in recent years as the medical community has come to acknowledge their value as a complement to conventional medicine.

Still, the lack of scientific evidence leaves insurance companies wary, blocking access to many patients who might find these techniques beneficial.

Lisa Hodge, PhD and assistant professor, molecular biology and immunology, is helping build the body of scientific evidence to support one such method of healing.

"Wide use of antibiotics has substantially reduced the rate of death from infectious disease," Hodge said. "However, the prevalence of organisms resistant to antimicrobial therapy is growing. We need to re-examine the benefits of alternative medicinal procedures for the treatment and prevention of infectious disease."

Hodge said lymph stasis can result in edema and an accumulation of toxins and bacteria, leading to a variety of disorders. Manual therapies such as lymphatic pump techniques have been used by osteopathic practitioners to improve lymph flow, remove fibrotic tissue, and to prevent and eliminate infections.

Research in this area was pioneered at the Health Science Center by Fred Downey, PhD, professor and vice chairman of integrative physiology.

Hodge earned her bachelor's degree from the University of Texas at Arlington and her doctorate from the Health Science Center in 2000. She completed a postdoctoral fellowship at the University of Pittsburgh Medical Center.

She was named the first Heritage Basic Science Research Chair for the national Osteopathic Research Center (ORC) in January 2007, where she works with ORC researchers to explore osteopathic manipulative medicine. The ORC is located at the Health Science Center.

Where are they now?

Study probes role of stress in chronic disease

Psychological stress — a condition considered rampant and on the rise in the U.S. — has been blamed for a host of physiological maladies including hypertension, stroke and heart attack.

Now, it appears stress may play a role in the progression of such chronic diseases as cancer, asthma and bacterial pneumonia, as well.

Harlan Jones, PhD and assistant professor of molecular biology and immunology, is leading research on the effects of stressful situations. When lab subjects are unable to free themselves of the stress, their disease worsens. Conversely, where they are able to control their environment, the effect of the disease lessens.

"We think there's a relationship between the immune system and the stress-response system," Jones said. "Our goal is to understand how everyday life events translate into the health status of persons with chronic diseases — how quality of life may be dictating outcomes for the disease."

Jones' research has shown that in cancer, for example, the body's natural defense against tumor growth is blocked when stress is introduced. And, in asthma, cells that contribute to bronchial inflammation are not as active when the subject can control its stress level.

"The question we are asking," Dr. Jones said, "is 'If we understand the quality of life context of the patient, can we develop therapeutic models that maintain a balanced immune system to combat disease?'"

Jones received his bachelor's degree from Louisiana State University and his master's from Southern University. He received his doctorate from the UNT Health Science Center in 2001.

Sudden alcohol withdrawal can be hard on mind and body

Long-term heavy drinking can take a toll on the body. But, for heavy drinkers, suddenly quitting may create even more physiological and psychological stress, according to Dr. Marianna Jung, PhD and research associate professor in pharmacology and neuroscience at the Health Science Center.

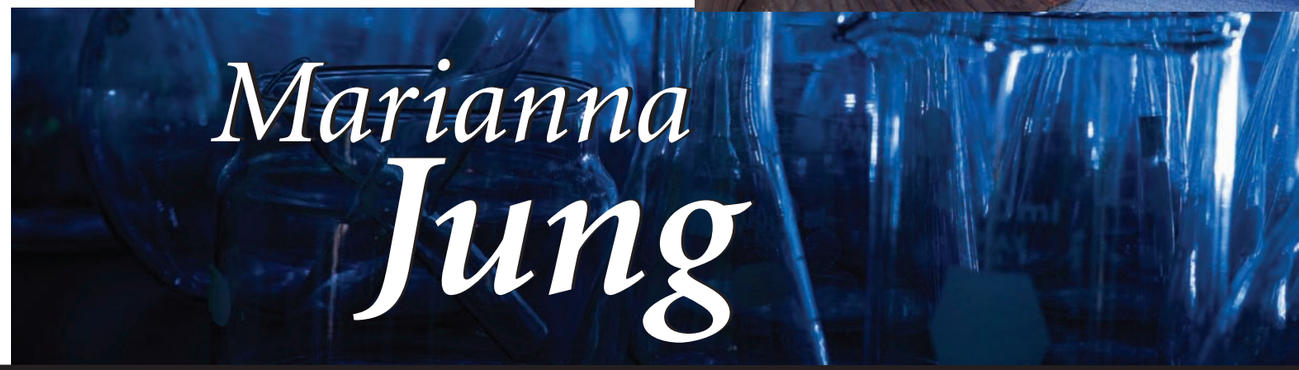
Jung is studying the effects of sudden alcohol withdrawal on the brain, and how women's brains react to the stress of sudden alcohol elimination. The study is part of a grant from the National Institutes of Health to study alcohol abuse and alcoholism.

"The brain struggles to adjust to the lack of alcohol because it's not ready for the sudden cessation," Dr. Jung explained. "This can cause additional stress, both physical and psychological."

Jung is also studying the effects of alcohol withdrawal on hormones, particularly estrogen, in conjunction with Dr. James Simpkins' hormone research.

"Alcohol withdrawal has an effect on hormones, and estrogen disturbance makes the brain more vulnerable to stress," Jung said. She also is studying how the quick withdrawal from alcohol makes older females more vulnerable to mitochondrial damage and diseases such as Alzheimer's.

Jung received her PhD from the Health Science Center in 1998, then took a year to visit her family in Korea before returning in 1999 to study with Simpkins and other researchers. Her next proposal involves the positive effects of hypoxia or lack of oxygen, which can provide defensive energy and prepare the body for a large hypoxia attack, if the body is given gradual exposure.



Where are they now?

Understanding the brain's role in breathing and blood pressure

Clearly, cardiovascular and respiratory disease affect the circulatory and respiratory systems. However, during the past decade the medical community began to evaluate the vital role that the brain plays in the effect of these diseases.

Jeffrey Potts, PhD and associate professor of integrative physiology, is a pioneer in the study of how brain functions actually participate in advances of circulatory and respiratory diseases, offering promise of new treatments for a host of conditions ranging from heart disease to sleep apnea and sudden infant death syndrome.

In contrast with traditional cellular research that has focused on tissue slices or single cells in isolation, Potts' research uses a variety of imaging techniques to examine brainstem responses to sensory input from the heart, lungs, bones, muscles and other organs.

"The focus of our work is to better understand how sensory feedback to the brainstem modifies breathing rhythms; how quickly the heart beats; and how blood vessels behave," Potts said. "We're looking at the causal relationship between cellular and molecular processes in the brain and integrating these findings with systems-level functions."

Potts received his bachelor's degree from the University of New Brunswick and his master's from Indiana State University. He received his doctorate from the Health Science Center in 1993. He completed post-doctoral fellowships at Johns Hopkins University and at the University of Texas Southwestern Medical Center at Dallas.

Prior to returning to the Health Science Center in October, Potts served as associate professor at the University of Missouri and assistant professor at Wayne State University School of Medicine.

Halting the devastating effects of autoimmune response

Perhaps the most insidious diseases are those where the body's own infection-fighting mechanism, the immune system, attacks normal cells — often causing permanent impairment or even death.

Little is known today about the causes of or cures for these disorders. But that is changing.

Research underway by Martha Stokely, PhD, has shown that the presence of tiny proteins called endothelins can starve the optic nerve of energy and blood flow, which causes blindness in glaucoma victims. More recent work has identified specific pathologic sequences that develop as a result of autoimmune response. If these sequences can be blocked, improved therapies can be developed for such diseases as multiple sclerosis.

"In my lab, we study mechanisms that regulate antero-grade axonal transport's pivotal role in controlling the balance of degenerative-regenerative events within the nervous system," Stokely said. "We focus on diseases or conditions where there is a cargo-selective axonal transport dysfunction such as multiple sclerosis, optic neuritis, glaucoma, stroke, Alzheimer's disease, Parkinson's disease, and epilepsy."

"The real goal of our work is to return people, whole, to their loved ones; to give people a chance at happiness," Stokely said.

Stokely received her bachelor's degree at the University of Texas at Arlington and her master's degree from Texas Christian University. She received her doctorate from the Health Science Center in 2002. Before joining the Health Science Center, Dr. Stokely served as post-doctoral fellow at the University of Florida at Gainesville.

Where are they now?

Study offers hope for stroke victims

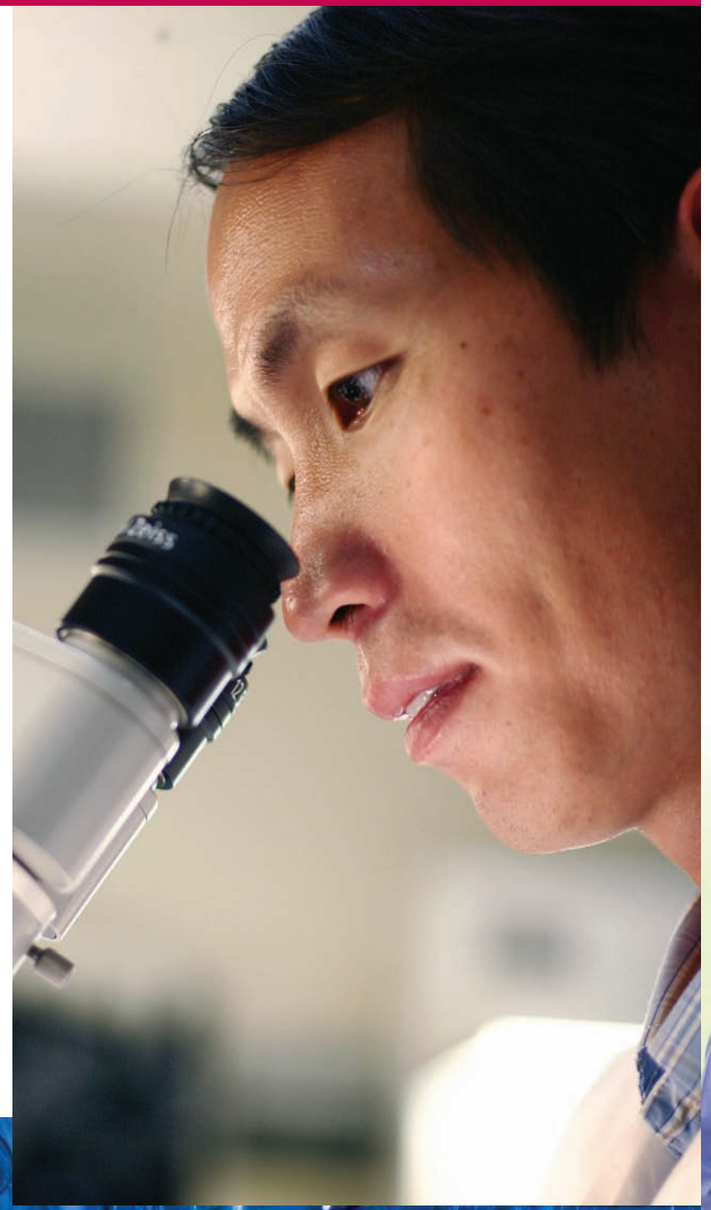
Someone in the United States suffers a stroke every 45 seconds. For them, time means everything.

A stroke or head injury causes a sudden interruption in the blood supply to the brain, which causes brain cells to die. The sooner a victim is treated, the greater the chance that damage can be minimized and the risk reduced for diseases such as Alzheimer's and vascular dementia.

ShaoHua Yang, MD, PhD and assistant professor of pharmacology and neuroscience, is leading the only research of its type to understand what happens in the brain following trauma caused by head injury or stroke, with promising discoveries in how to retard the damage they cause, thereby increasing the treatment window for victims.

"Epidemiological studies have suggested a progressive course of dementia following stroke," Yang said. "We are examining the long-term effects on sensory and cognitive functions of the brain to better understand the underlying mechanisms of vascular cognitive impairment. We also are testing the neuroprotective effects of estrogen, combined with an anti-clotting treatment, that could delay irreversible cell damage."

A native of the Peoples' Republic of China, Yang received his doctor of medicine degree from Peking University, and his doctorate from the Health Science Center in 2004. Prior to joining the Health Science Center, Yang served as attending neurosurgeon at Beijing Neurosurgical Institute.



ShaoHua Yang

Translational Research

The Office of Technology Transfer at the Health Science Center helps bring together those who discover the healthcare finds of tomorrow and the business owners who can most quickly get those discoveries into production.

Robert McClain, PhD and associate vice president of technology transfer and commercialization at the Health Science Center, helps researchers and small businesses apply for the Small Business Innovation Research (SBIR) and the Small Business Technology Transfer (STTR) program grants. These two competitive programs ensure that the nation's small, high-tech, innovative businesses are a significant part of the federal government's research and development efforts.

"These grants help bridge that gap between grants for research and investments to sell discoveries from the lab in the marketplace," McClain said.

Wolfram Siede, PhD, and UHV Technologies recently received SBIR and STTR monies to develop Siede's discovery of a screening method for anti-cancer compounds into an automated drug screening process. UHV Technologies has helped Dr. Siede develop custom equipment for the project.

"Essentially, we apply these compounds to genetically modified baker's yeast and look for changes in the colonies," Siede said. The compounds that he discovered are not yet ready for testing on human cells, but the yeast testing process can indicate if the assays would affect human cells and prevent cancer growth.

Nalin Kumar, PhD and president of UHV Technologies, and Manuel Garcia, UHV engineer, have mechanized Dr. Siede's work using a robot to distribute the agar and anti-cancer compounds to 96-well slides automatically. They then use a camera and a custom-programmed computer to visually analyze the slide. The software can recognize changes in the yeast colonies on the slide — a process Dr. Siede formerly did manually.

Kumar plans to add more elements to the machine which would allow for thousands of compounds to be similarly tested at once, as well as creating and storing the slides until the lab conducts analyses.

The grants will fund the growth of Siede's discovery until the technology garners interest from biomedical companies seeking an automated process.

From left, Dr. Nalin Kumar, Manuel Garcia, Dr. Robert McClain and Dr. Wolfram Siede work with the machinery developed by UHV Technologies that automates Dr. Siede's anti-cancer drug screening. The team recently was awarded a federal grant to fund the transition.

DNA in the news

Dr. Arthur Eisenberg was filmed by "America's Most Wanted" for the lab's work identifying charred remains found in Fort Myers, Fla. The segment aired on January 19, 2008.

The DNA lab at University of North Texas Health Science Center has conducted DNA analysis for national missing persons cases for more than eight years, and national media are taking notice.

From *USA Today* to truTV's "The Investigators," the lab has been featured in DNA analyses of missing persons and highlighted in high-profile cases that the lab has helped solve.

- The UNT Center for Human Identification was featured on page 2A of USA Today where Arthur Eisenberg, PhD and director of the lab, explained DNA analysis and the importance of family reference samples in identifying missing persons.
- The lab was featured on several news Web sites for its role in identifying Mississippi victims of Hurricane Katrina in 2005.
- Several business journals ran the Department of Justice's announcement that the DNA lab would receive $1.4 million to continue offering its services for free to law enforcement entities and families of missing persons across the U.S.
- In late September, the lab was noted in several national articles about the identification of Raj Narain and her 14-month-old baby, whose remains were found in three separate rivers in 1987. DNA samples from all over the world, including Narain's brother in Sydney, Australia, were used for identification.
- Another story that piqued the nation's interest pertained to the identification of bodies found along the Texas-Mexico border using DNA analysis. The story featured a mortician on the border who sends blood samples from unidentified remains to the DNA lab before they are buried.
- The lab's identification of a child-sized skull found in Washington received national attention in November. The skull appears to be from a person who lived about 700 years ago.
- The Houston Police Department used the DNA lab in its pursuit of the killer of seven prostitutes whose bodies were discovered near churches.
- Print media from across the nation and TV stations in Fort Meyers, Fla., featured the DNA lab in the case of the bodies of eight unidentified men, all found in the same location and without any identifying clothing or personal items.
- The tragic discovery of Baby Grace, a two-year-old whose body was discovered in a plastic storage bin in Galveston Bay, brought nationwide media attention that ultimately led to the identification of Riley Sawyers. DNA tests conducted at the Health Science Center confirmed the baby's identity.
- truTV filmed a segment of the series, "The Investigators," at the DNA Lab explaining its work on the case of Clayton Daniels, who faked his own death in order to cash in on a life insurance policy. The DNA lab analyzed a badly burned body found in Daniels' car to determine its identity.

Stephanie Zavala, Wyrene Medina and Phillip Herrera, Summer 2007 McNair Scholars, attended Senator Leticia Van de Putte's (second from right) Distinguished Speaker presentation on June 21.

HSC hosts distinguished speakers on campus

The UNT Health Science Center began its Distinguished Speaker Series in 2007 to promote intellectual and educational exchange with faculty and the community. This ongoing series of presentations features internationally renowned scientists who deliver keynote lectures followed by question-and-answer sessions. Panelists during these sessions include the keynote speaker and local experts, UNTHSC faculty and relevant community members.

David Fishman, MD, was the first keynote speaker in the series in early February. Fishman presented "The Detection of Early Stage Ovarian Cancer," concentrating on improving detection rates, early treatment and limiting long-term effects in patients with the disease.

Fishman is director of gynecologic oncology and the Cancer Detection and Screening Program at the New York University School of Medicine and Cancer Institute.

Senator Leticia Van de Putte, RPh, was the second distinguished speaker on June 21. Her presentation, "Genes, Culture and Medicines: Bridging the Gaps in Treatment for Hispanic Americans," focused on the complex relationships among culture, environment, population genetics, drug metabolism and drug response; identified ethnic differences in clinical response to drugs, drug metabolism and response; defined strategies to increase greater diversity in health professions and improve cross-culture communication; and educated primary care physicians about the various health disparities facing the Hispanic American population in the 21st century.

Van de Putte has been a pharmacist for more than 26 years and has served in the Texas Legislature since 1990. She was a Kellogg Fellow at Harvard University's John F. Kennedy School of Government in 1993, and she earned her Bachelor of Science from the University of Texas at Austin, College of Pharmacy.

Steven T. DeKosky, MD, discussed advances in Alzheimer's disease research and treatment at the third Distinguished Speaker event in October. Dr. DeKosky is professor and chair of the Department of Neurology and director of the Alzheimer's Disease Research Center at the University of Pittsburgh.

DeKosky's clinical research includes differential diagnosis, neuroimaging and genetic risks for Alzheimer's disease, and trials of new medications. His basic research centers on structural and neurochemical changes in human brains in normal aging and dementia.

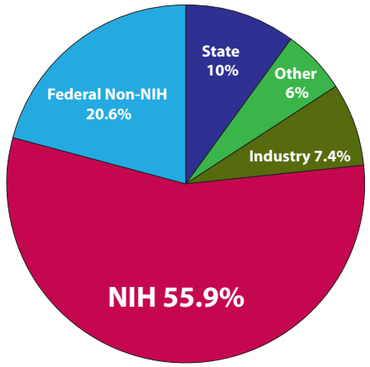
Upcoming distinguished speakers will focus on women's health issues; physical and osteopathic manipulative medicine; and health equities.

Research 2007

Research expenditures at the Health Science Center grew to an all-time high in 2007, to more than $26 million. Since 2002, our research expenditures have increased by 100 percent, the largest growth rate of any health science center in Texas. In each of the past two years, our faculty submitted grant proposals totaling more than $150 million. This momentum combined with the Research Advisory Council's strategic plan should continue to fuel our exceptional research growth.

We will continue to expand and invest in technology and equipment such as our new $750,000 confocal microscope to enable researchers to excel.

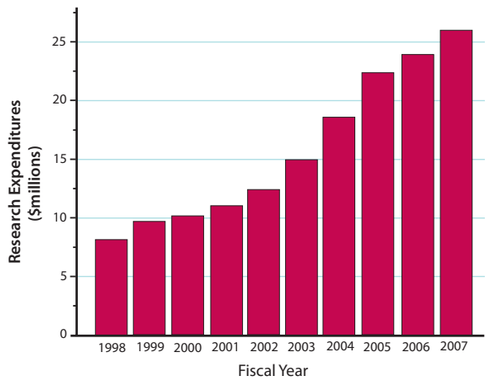
This past year, more than 75 percent of our funding was from the federal government, with the majority of that coming from the National Institutes of Health (NIH). In fact, in the face of flat levels of research funding at NIH, our faculty have continued to secure funding for their research.



Funding By Source

We continue to expand our collaborations with partners in industry. For instance, this past year we applied for and received more NIH-funded small business innovation research awards than at any time in our history.

The Health Science Center's commitment to supporting and expanding research in aging and Alzheimer's disease, cancer, health disparities and other key areas is unwavering. In addition, our approach to translating our scientists' bench discoveries into real solutions for clinical and public health problems is proving to be remarkably successful. Our faculty's research discoveries will continue to help improve the health and lives of our citizens.



Grants Awarded

Collaboration and Synergy

You may notice a theme in our research at the UNT Health Science Center. Collaboration and synergy among teams and even family members strengthen our research efforts and give them depth and breadth that single efforts simply can't provide.

Whether it's the father-and-son Team Awasthi, the Brothers Gryczinski, or the husband-and-wife Cardarelli Duo, the Health Science Center is at the forefront of cutting-edge research, analysis and treatment.

The Awasthis' life-long pursuit of a cancer cure is an important component for our new Institute for Cancer and Blood Disorders in partnership with the Center for Cancer and Blood Disorders at Fort Worth. Our expert and talented researchers will work to bring innovative medical treatments to cancer patients. It's this ability to relate highly technical research, collaborative analysis and knowledgeable patient care that forge the most positive aspects of research and medicine to help people.

The Gryczinskis have brought space-age fluorescence testing and research to a commercial application that better detects and diagnoses diseases, supports national security surveillance and aids in thwarting bioterrorism threats.

The Cardarellis, alumni of the Health Science Center, each have launched new institutes that stress primary health care for families and at-risk populations – the Primary Research Care Institute and the Center for Community Health both debuted last summer to help address research and healthcare needs in North Texas.

These fascinating professionals are bringing the results of tremendous amounts of knowledge to people across North Texas. Plus, you've seen a plethora of alumni who are using the fine education that they received at the Health Science Center to build synergies and discover new frontiers throughout the nation.

In fact, our renewed emphasis on research led me to name Dr. Thomas Yorio executive vice president for research. Dr. Yorio's long-standing commitment to this organization and his drive to be an international leader in research are building a strong and powerful base for our research and translation work.

Scott B. Ransom, DO, MBA, MPH
President
University of North Texas Health Science Center
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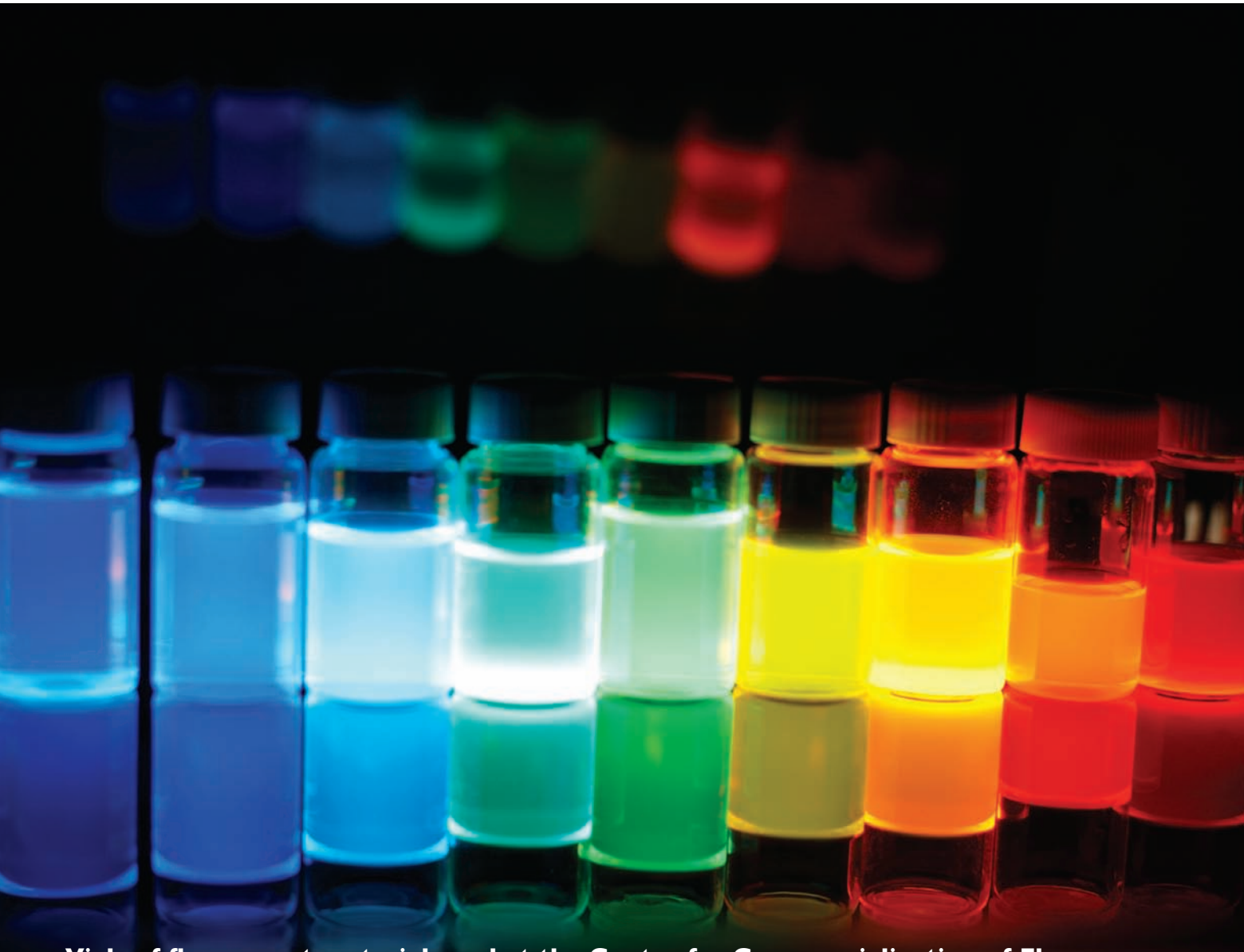

Vials of fluorescent material used at the Center for Commercialization of Fluorescence Technology. (See story on page 11).