

Welcome



Welcome to the fourth edition of the University of North Texas Health Science Center's annual research publication, Synergy. It has been another exceptional for the Health year Science Center. We have been fortunate to be able continue attracting exceptional scientists. Their addition to our existing talent is accelerating the pace of discovery and leading to

new approaches combating a spectrum of medical diseases, conditions and major public health problems. In this issue, you'll find a number of innovative researchers and research teams featured.

The Institute of Forensic and Investigative Genetics has hired additional experts in microbial and biosecurity forensics and bioinformatics. They solidify a unique team of national leaders in the research and development of new tools in forensic investigation, biosecurity and human identification.

The state of Texas has taken on the fight against cancer by creating the Cancer Prevention and Research Institute of Texas (CPRIT). CPRIT will fund ground-breaking research that could result in new treatments for this dread disease. In this issue, you will read about an innovative cancer research program designed to treat cancer in adolescents and young adults. This program, developed with our partners at Cook Children's Health Care System, will be unlike any other. The Health Science Center's cancer researchers are developing new drug delivery approaches and assessing novel targets for improved therapeutics.

The Health Science Center is also stepping up research efforts to combat cardiovascular disease, and has recruited cardiovascular scientists to provide new insight into the pathophysiological mechanisms of hypertension and heart

disease. These faculty will contribute to the ongoing work toward our Cardiovascular Research Institute's goal of promoting basic and clinical research, clinical advancement and community outreach programs in the prevention, diagnosis, treatment and rehabilitation of cardiovascular disease.

Clinical and translational research continue to progress. One example is a study assessing a novel treatment for traumatic brain injury, which is being conducted in partnership with the UT-Southwestern Medical Center. Our investigator's research efforts will be further enhanced following establishment of our Phase I clinical research unit and a GLP (Good Laboratory Practice)-capable pre-clinical research unit. These capabilities are essential to advancing potential new medicines and treatments. These facilities will also be available to local biotechnology researchers.

We've also recruited excellent scientists in the areas of wound healing, human movement analysis and rehabilitation, health economics, and vision. All of these researchers will expand our existing expertise in these fields, as well as in Alzheimer's disease, biotechnology and public health.

UNTHSC has always fostered collaborative, inter-disciplinary research, and top scientists continue to cite this as one reason for joining our team, adding that they appreciate Fort Worth's quality of life.

Our scientists and their teams will continue to advance the knowledge critical to solving the pressing biomedical and public health problems facing Texas and our nation. If you would like to learn more about our programs, please contact me.

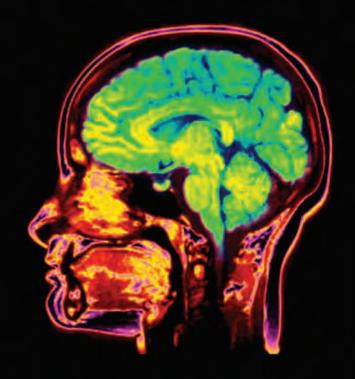
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Cover Photo: Chandra Bathina, Yong Park, Molsaurol Spencer, Thekkethis Negungadi, Dr. Steven Mifflin, Dr. Thomas Cunningham and Melissa Vitela prepare telemetry implants.



Welcome to the fourth 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 for the betterment of all people.

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in Integrative Physiology department attracts top talent

The University of North Texas Health Science Center has big plans for its Department of Integrative Physiology. In fact, the vision to grow the department to world-class status convinced Steve Mifflin, PhD, chair of Integrative Physiology, and Tom Cunningham, PhD, professor of Integrative Physiology, to relocate to Fort Worth from their previous positions at the University of Texas Health Science Center at San Antonio.

Both researchers agree that the Health Science Center's tremendous growth in education and research, coupled with its record for excellence, convinced them to make the move. In addition, the supportive environment that fosters interdisciplinary research was an added benefit.

Mifflin's lab researches the ways that neurons in the brain adapt to pathophysiological conditions and contribute to the cardiovascular complications observed in these conditions.

"We study these adaptive processes in incidents of high blood pressure and exposure to reduced oxygen as occurs in heart failure and sleep apnea," Mifflin explained. "Our research has garnered a great deal of interest because it mimics many of the problems observed in sleep apnea patients — high blood pressure, insulin resistance, etc. It also is a good example of what is meant by integrative physiology — which is research that integrates information obtained from molecular to cellular to organ to human levels — to achieve a much more complete picture of pathology than one obtains using information obtained from a single level of analysis."

Cunningham leads the Health Science Center's Cardiovascular Research Institute. "In my lab, we study the role of the brain in controlling the cardiovascular system, and water and electrolyte balance," Cunningham said. "Some research focuses on determining how the brain participates in the normal regulation of blood pressure and

fluid balance, a process called homeostasis. Other studies explore how changes in central nervous system function contribute to chronic diseases like hypertension, and water or salt retention that can be associated with heart disease or liver failure."

The researchers share a common vision when it comes to their hopes that their research will lead to identifying new ways to treat these afflictions and improve the quality of people's lives. They also hope their research will provide a better understanding of the ways that the brain regulates physiological processes that are necessary for a normal, healthy life.

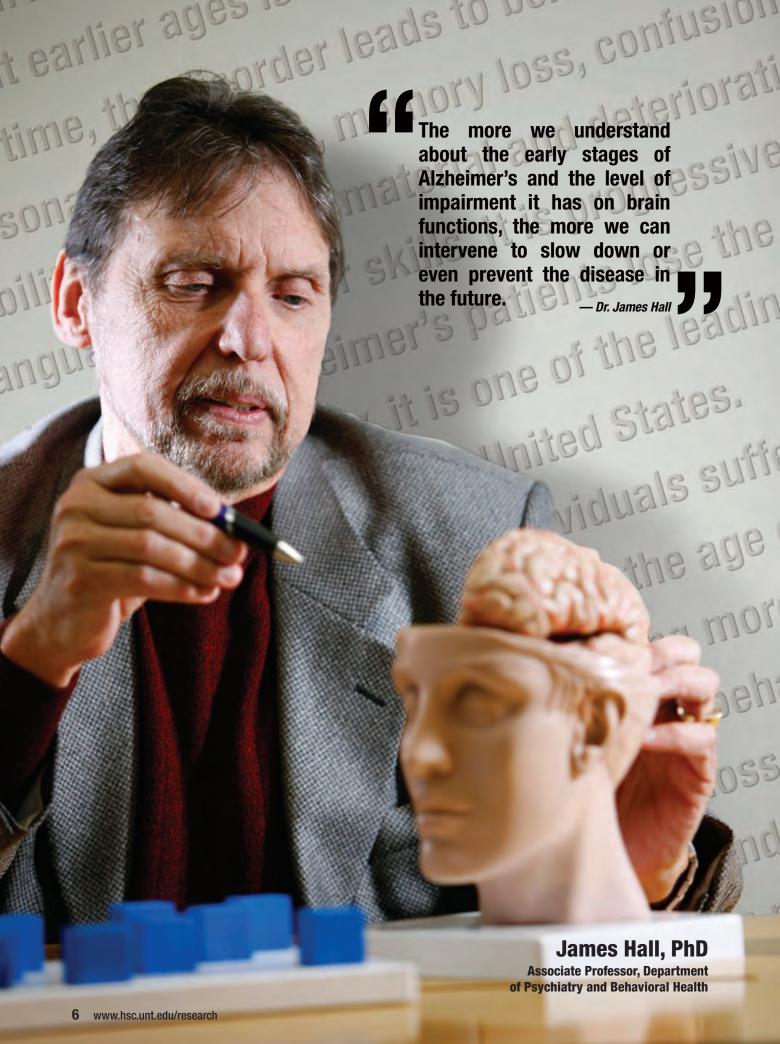
"Relocating to UNTHSC will help us achieve these goals through new collaborative relationships," Cunningham continued.

"We are working with investigators in the department to determine if any of the changes we have reported in our animal models of disease are present in humans who suffer from high blood pressure or sleep apnea. If so, our work could provide insights into novel therapeutic targets for treatment," Mifflin said. "In terms of opportunities for collaboration, the Cardiovascular Research Institute is a wonderful example. The institute will facilitate interactions and collaborations between investigators studying the cardiovascular complications of high blood pressure, diabetes, obesity, heart failure, stress and other conditions prevalent in Texas and the United States."

Mifflin and Cunningham are impressed with the friendly, supportive environment that has welcomed them to Fort Worth and the Health Science Center.

"Resources provided by the institution have allowed us to expand the scope of our work, creating new opportunities to compete for external funding and provide training for students from the Graduate School of Biomedical Sciences and Texas College of Osteopathic Medicine," Cunningham concluded.





Teaming Up to Explore Warning Signs of Alzheimer's

As the U.S. population ages, Alzheimer's disease continues its insidious infiltration of the minds and families across our country. Although the vast majority of individuals suffering from Alzheimer's are over the age of 65, onset at earlier ages is becoming more common. Over time, the disorder leads to behavioral and personality changes, memory loss, confusion, inability to learn new material and deterioration in language and motor skills. It is progressive, and, in later stages, Alzheimer's patients lose the ability to communicate. Today, it is one of the leading causes of death in the United States.

In collaboration with the state-funded Texas Alzheimer's Research Consortium (TARC), James Hall, PhD, participates in group and individual research to improve early diagnosis, treatment and prevention of the disease afflicting more than 5 million Americans. TARC consists of five of the state's leading medical research institutions. Baylor College of Medicine, University of Texas Southwestern Medical Center, Texas Tech Health Science Center, UNT Health Science Center and University of Texas Health Science Center at San Antonio hope to identify the genes and biomarkers associated with the onset and progression of Alzheimer's disease.

Hall serves on the TARC neuropsychology committee for the UNT Health Science Center, advising on protocols for neuropsychological testing and reviewing proposed research projects. Each institution within the consortium conducts research and contributes genetic and blood biomarker data on Alzheimer's patients and healthy control subjects to the shared Texas Alzheimer's DataBank.

"Our short-term goal is to gain a better understanding of the nature of the disease," Hall said. "Over time, we hope to establish further understanding of those factors that contribute to the onset on Alzheimer's and, from that, create methods to decelerate or prevent progression of the disease."

Hall specifically focuses on the relationship between depression and Alzheimer's disease in which certain clusters of depression symptoms seem to be related to the development of the disease. Individuals with a history of depression are at a greater risk for developing the disease.

The Health Science Center's Thomas Fairchild, PhD, vice president for the Office of Strategy and Measurement, and Janice Knebl, DO, endowed professor and recipient of a Reynolds Foundation grant for research in aging, are active in TARC's research efforts. Fairchild serves as the TARC principal investigator for the Health Science Center, and Knebl is clinical director.

The first state funding for Alzheimer's research in Texas history was approved in 2005 by the 79th Texas Legislature, which appropriated \$2 million to fund TARC's first two years of set-up, volunteer recruitment and data collection. In 2007, Texas lawmakers nearly doubled the state's investment in the consortium. Most recently, state lawmakers approved another \$6.8 million for TARC over the next two years to build on its early work, recruit more volunteers (including those with mild cognitive impairment) and launch a new research focus on the impact of Alzheimer's disease on Hispanics.

"The more we understand about the early stages of Alzheimer's and the level of impairment it has on brain functions, the more we can intervene to slow down or even prevent the disease in the future," Hall said.

This research complements the research being led by James Simpkins, PhD, into estrogen and Alzheimer's. (See story on Simpkins' research on the next page.)

Estrogen protects brain in trauma victims

In a groundbreaking study, researchers from the University of North Texas Health Science Center in Fort Worth and the University of Texas Southwestern Medical Center in Dallas are partnering to battle the effects of traumatic brain injury, shock and sudden cardiac arrest.

James Simpkins, PhD, chair of the Department of Pharmacology and Neuroscience and director of the Institute for Aging and Azheimer's Disease, has partnered with Jane Wigginton, MD, of the Emergency Medicine department at UT Southwestern, to study the protective effects that estrogens have on patients who need emergency resuscitation, specifically those with traumatic brain injury, shock and sudden cardiac arrest. These studies are critical because fewer than 5 percent of the 1,000 Americans who suffer sudden cardiac arrest survive.

"The hope is to devise an intervention so when emergency medical personnel show up and they deduce that someone has had traumatic brain injury, a stroke or sudden cardiac arrest, they can then, on site, administer something that can protect the brain," Simpkins said. "If we can administer these drugs to people very early, we can protect the brain and increase survival."

This new study has found that the rapid administration of a combined dose of estrogen, a strong anti-oxidant and an anti-inflammatory drug in sudden cardiac arrest cases increases brain cell survival by up to 65 percent. Additionally, it was found that the same combination of estrogen and other substances delivered intravenously post-injury may have similar effects in subjects suffering from traumatic brain injury.

Simpkins explained that right now, emergency medicine procedures are in place to immediately work to resuscitate patients who have suffered one of these traumas, but typically resuscitation efforts are designed to make a person's heart start beating

again, for example, or restart breathing. However, until now, no measures have been put into place to attempt to protect the brain's health in the case of a traumatic injury requiring resuscitation efforts.

"We have to act as soon as possible when emergency medical crews arrive on the scene," Simpkins said. He explained that by the time an emergency crew has performed resuscitation efforts, then transported a patient to a hospital, and the patient is stabilized enough to undergo the tests necessary to determine if there is brain injury, it is often too late.

"We know these substances can protect the brain and are safe to send out with emergency medicine personnel," he said. These compounds can be easily administered to a patient on-scene to provide the necessary protection to the brain. Importantly, the compounds have no dangerous effects on a patient if they do not have any sort of brain injury.

Simpkins said he is passionate about this study because he lost his father and grandfather to strokes — but there were no medical procedures in place to protect the men's lives. By the time the necessary help arrived and tests were run, it was too late, Simpkins said.

"There has to be a paradigm shift in that we need to administer these treatments as soon as possible, before it is too late," he said. "This can improve survival and reduce neurological deficits from shock. It is very much needed."

This study is part of the Resuscitation Outcomes Consortium, a National Institutes of Health-funded program designed to study cardiac arrest and trauma events in patients, the outcomes of these events, and how treatment in the field immediately after these events affect patient survival rates.



New Faculty

Eric Gonzales, PhD Assistant Professor, Department

UNTHSC alum returns to lead research into protein structure

Eric Gonzales wants to know how proteins work — specifically their structure and how they interact with drugs — and is eager to get his research laboratory up and running. New to the Health Science Center faculty, he is back on familiar ground, having cut his teeth in the lab at UNTHSC while a graduate student in the Department of Pharmacology and Neuroscience from 2000 to 2005.

"I received my PhD under the mentorship of Dr. Glenn Dillon, where I learned how a protein's structure, specifically for ion channels, influences function," Gonzales said. "I knew that when I started my career in academia, I wanted to be a part of the collegiality that exists here between faculty and students. Thankfully, UNTHSC offered me a research position that brought me back to my alma mater and back to my family in Fort Worth."

Gonzales' research involves a technique called protein crystallography to refine a protein's structure to an atomic resolution level. He applies the technique to determine the membrane protein structure. (An image of his crystallography is featured on the back cover of this annual report.)

"Membrane proteins are more challenging than most proteins," said Gonzales. "To form protein crystals, we must first remove the protein from its native environment and identify conditions that maintain the protein's stability. The most exciting step is collecting the data. Each protein is exposed to X-rays. The protein crystal, in turn, diffracts these X-rays to make a 'spot' pattern. We analyze these 'spots' to solve the protein's structures. We need to be able to collect the largest amount of data in the shortest amount of time and are working with Advanced Light Source in Berkeley, Calif., and Advanced Photon Source in Chicago, because they offer X-ray beams that meet our specifications."

Gonzales hopes his research will answer fundamental questions about protein structure and drug interactions. He believes that protein crystallography will show how a single drug can distinctly interact with two related membrane proteins with differing affinity — known as drug sensitivity.

of Pharmacology and Neuroscience

Saving contact lens wearers' sight motivates researcher's efforts

Acanthamoeba keratitis may be a mouthful, but for contact wearers the cost of the devastating condition can be loss of sight. The condition is almost always associated with contact lens use and is caused by amoebae invading the eye's cornea, resulting in severe inflammation. Identifying causes for the condition and possible new treatments is the focus of research being conducted at the Health Science Center by Hassan Alizadeh, PhD, associate professor of Cell Biology and Anatomy.

"I was working as an assistant professor in the Department of Ophthalmology at the University of Texas Southwestern Medical Center, when I learned about UNTHSC's active program of research on the eye through the North Texas Eye Research Institute," Alizadeh said. "The institution's exciting research activities and commitment to the Eye Research Institute convinced me to continue my research at UNTHSC."

Alizadeh researches several factors related to acanthamoeba keratitis — what predisposes the cornea to infection with this microorganism, how the immune system responds to the infection and which tissues of the cornea are involved in the infection process.

"I have been interested in infectious diseases, and the eye is an organ that has specific immune mechanisms that respond to pathogens," Alizadeh said. "The fundamental premise of our research is that no single therapeutic procedure is likely to be effective in the treatment of ongoing infection. However, we hope a carefully selected and evaluated combination of procedures that collectively or synergistically interfere with each step of the pathogenic cascade targeting pathogenic molecules will lead to the production of an 'anti-disease' vaccine."

Alizadeh hopes to collaborate with other researchers at the Health Science Center in his work.

Hassan Alizadeh, PhD
Associate Professor, Cell Biology and Anatomy



research places him at the center of today's perfect storm - health care reform.

"My research centers on what happens to health care access and quality in communities where there are large numbers of children and adults without health insurance coverage," explained Pagan. "My research shows that health insurance coverage not only improves access to a wide array of health care services, but it also strengthens local health care systems for the insured population. Widespread health insurance coverage increases the number of people who can pay for health care services and who can use local health care providers, which impacts everyone in these communities."

"I chose to come to UNTHSC because its mission and vision are consistent with mine," says Pagan. "The School of Public Health is an ideal setting to continue my work on health insurance, quality and access. It also is a great place to conduct collaborative work in health policy and health services research.

"My long-term vision is for my research to inform the health care reform debate by incorporating the intended and unintended effects of providing coverage to the uninsured population of society — individuals, local communities, states and the nation."

Unlocking the mechanics of skin inflammation could be the key to new diagnosis and treatment techniques

How do environmental and psychological factors regulate the body's immune system and what impact does this have on skin disorders? That's the primary focus of research in the laboratory of Mark Mummert, PhD, associate professor in **Psychiatry** and Behavioral Health. Mummert joined the Health Science Center faculty in June 2009 to research and assess the immune mediators and molecular pathways that initiate and augment skin inflammation in response to environmental (such as allergens) and psychological (such as chronic stress) factors. A second major research interest Mummert is pursuing is the development of technologies to enhance the detection of malignant skin lesions in skin cancer patients. "I joined UNTHSC after serving as faculty for several years at the University of Texas

"I joined UNTHSC after serving as faculty for several years at the University of Texas Southwestern Medical School in the Department of Dermatology," explained Mummert. "The open and collaborative research environment attracted me to UNTHSC. I also was excited about the prospects for career growth as the Mental Sciences Institute continues to expand, thus fostering opportunities for interdisciplinary research.

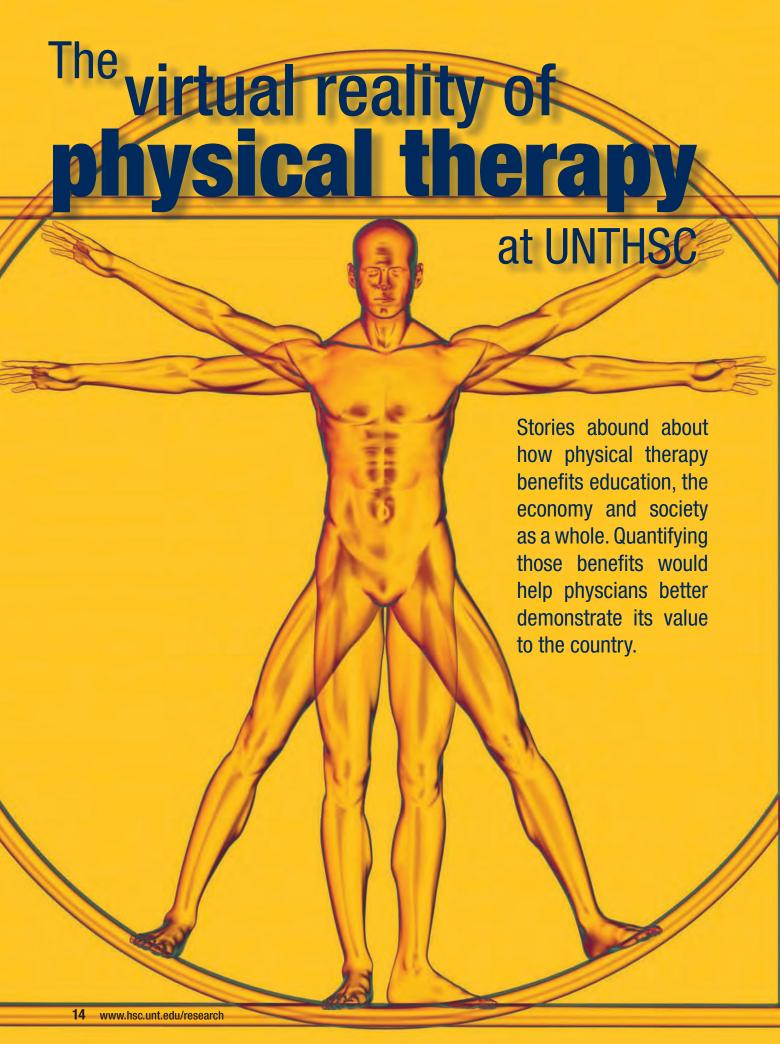
"Our research goal is to understand the mechanistic underpinnings of skin inflammation, which may ultimately prove useful in developing therapeutics for human disease," Mummert said. "We also are developing fluorescent molecular probes for the detection of malignant melanomas. These probes may allow physicians to more promptly initiate treatment before the cancer spreads to vital organs."

Associate Professor of Psychiatry and Behavioral Health

Mark Mümmert, PhD

Lishu Zhang

Research Associate Psychiatry and Behavioral Health



July, the UNT Health Science Center will welcome its first physical therapy students, expanding the School of Health Professions by 20 students and faculty by five. With the addition of the new doctoral degree program, the Health Science Center also increases its physical therapy research and collaboration among several of its schools. The new physical therapy faculty will be hands-on teachers and researchers.

As more doctors realize the integral role that physical therapy plays in both recovery and prevention of injuries — especially in an aging population — the more physical therapists will be needed to both treat and counsel patients.

"Physical therapists are experts in movement. Movement is normal, so we must get patients moving in order to recover and improve their health," said Clayton Holmes, PT, EdD, chair of the Physical Therapy department. This is the philosophy that has brought world-renowned researchers and administrators together at the Health Science Center to debut the new physical therapy program.

Joining Holmes are new researchers Nicoleta Bugnariu, PhD, PT, and Hau Liu, MD, PT, PhD. Both will conduct research into balance, gait and falls in a three-pronged approach melding research, treatment and teaching.

Bugnariu plans to use a three-dimensional system to analyze movement through virtual reality and will work closely with the Health Science Center's Physical Medicine Institute (PMI) lab and team of Alzheimer's disease experts. Her research into mechanisms of sensorimotor integration and resolution of sensory conflicts will be especially valuable to the new program.

By using a special helmet and equipment to simulate reality, she will study center of gravity, gait and sway in patients, especially the elderly, for whom falling is a constant concern. From her research, Bugnariu hopes to learn new neuro-scientific methods of preventing the falls that can create major health issues in older patients.

Using the virtual reality system, patients are supported and suspended as they walk so they won't be hurt in a fall. As a fall or other situation is simulated, Bugnariu records reactions and responses. In the future, this could help answer questions about the importance of vision and tactile perceptions. The entire virtual reality system is still in the planning stages and would be one of only a handful in the U.S.

Hau will contribute his expertise in preventing falls in geriatric patients, working with Dr. Janice Knebl, endowed Chair and recent Reyn-

olds Grant recipient for aging and Alzheimer's research, in studying the geriatric population, as well. He also will work closely with the PMI and the Osteopathic Manipulative Medicine department on campus.

Olga Dreeben, PT, PhD, brings her physical therapy experience in sports, spine and exercise research to the Health Science Center. Her knowledge of physical therapy related to stroke and acute care will be of particular importance to the team.

Michael Connors, PT, DPT, will manage the clinical orthopedic and sports medicine areas of the physical therapy program, focusing on shoulder injuries. He will oversee the physical therapy clinic's operations and has been instrumental in setting up equipment and programs on campus.

"Five years from now, anyone doing anything involving exercise will include physical therapy in their program," Holmes said. "Everything will involve interaction with physiology, oxygen intake and physical therapy. Motor control influences so many processes in the body, which makes OMM such a natural research fit with physical therapy research. And the neurological links to physical therapy are undeniable."

In addition to the research emphasis, quality teaching will be key. Holmes' goal of a 100-percent student pass rate on medical board reviews will be paramount. "If you don't put out a good physical therapist," Holmes said, "nothing else, including research, matters."

The PT students will share some facilities, including simulation models and labs, with the Texas College of Osteopathic Medicine, learning side by side with the medical and physician assistant students. It's just one more example of the collaborative research and learning that will take the Health Science Center into the next decade.



Clayton Holmes, Nicoleta Bugnariu, Olga Dreeben, Michael Connors



Adolescent and Young Adult Oncology Center

tolink cancer knowledge

Cancer at any age is tragic, but it's especially difficult for children.

But at what age are cancer patients no longer children? When should they be treated as "adult" cancer patients? Should a 17-year-old dealing with leukemia be treated as an adult on his 18th birthday? Or should he be given the same treatments as an eight-year-old with the same disease? And, perhaps as importantly, does leukemia behave the same way in a teen as in a child or a 38-year-old?

These are the questions that drive one of the Health Science Center's newest faculty members, Karen Albritton, MD, director of Adolescent and Young Adult (AYA) Oncology at the UNT Health Science Center. Albritton is a pioneer in the emerging specialty of AYA Oncology, recognized by the National Cancer Institute as the field focusing on the science and care of those diagnosed with cancer between age 15 and 40. The specialty had its start in the early part of the last decade, when reviews of clinical trial results in seven different countries, 64 percent of acute leukemia patients age 16-21 who were treated as pediatric patients experienced successful outcomes, versus 38 percent who were treated as adults. The fact that the same results were replicated seven times is astounding.

Albritton believes these findings indicate that cancers in young adults will not respond to treatment the same as cancer in children or older adults. She hopes to learn if the reasons relate to tumor biology differences, drug protocols, service delivery, support networks or other reasons. Because the answers are both about clinical care and basic science, Albritton will bring together researchers at the Health Science

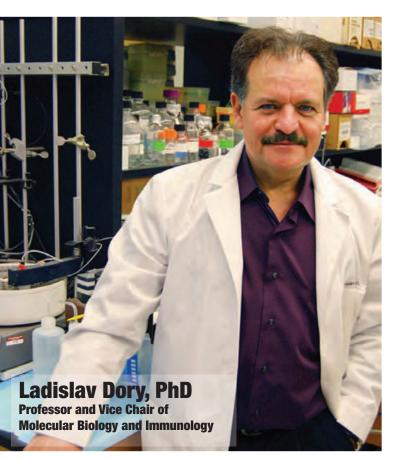
Center clinicians at Cook Children's Hospital Network and community cancer organizations throughout the North and West Texas regions to establish the North Texas AYA Oncology Center. As a resource for researchers, families and physicians caring for young people with cancer, the AYA Oncology Center will serve as both a repository of information, facilitator of research and brain trust for medical oncology groups serving the major health care providers in the region.

"I see this new center as a medical 'Switzerland,'" Albritton said. "It will be a valuable resource for everyone. We can use the knowledge from retrospective analysis of various outcomes, prospective clinical protocols and experiences and engage the Graduate School, Texas College of Osteopathic Medicine and School of Public Health researchers to establish best practices for treatment of adolescents and young adults.

"We can determine which patient parameters should be considered in the individualized treatment of young adults — age, weight, hormonal or puberty level, metabolic processing and delivery of health care. These may all affect the success rate in treating cancer, and they may differ depending on the type of cancer. I want to create a center that the health care community can turn to for consultations, clinical trials or even psychological insight related to cancer treatment for young adults.

"We shouldn't treat 18- and 19-year-olds like seven-year-olds," Albritton continued. "We have to take into account sexual activity, illicit drug use and independent status. But neither should they be treated as mature adults. Their emotional development, and even the way their bodies process and respond to treatment, often are more like a child, even if they look like an adult physically."

Seeking cancer answers



Could oxidative stress actually inhibit inflammatory colon and bowel diseases such as Crohn's disease? And could those effects ultimately treat colon cancer? These questions are challenging Ladislav Dory at the Health Science Center to research the long-term benefits of intermittent oxidative stress on cells and enzymes related to inflammatory bowel disease and possible effects of hyperbaric oxidative stress treatment on bowel and colon cancer.

"The common denominator in treating long-term, low-grade chronic bowel inflammation is oxidative stress," said Dory, PhD, Professor of Molecular Biology and Immunology.

Oxidative stress is induced by submitting cells to short periods of high doses of oxygen. This treatment has been shown to reduce cholesterol and arthrosclerosis. Treating chronic inflammation with oxidative stress through hyperbaric treatment reduces arthrosclerosis by protecting the extra cellular superoxide dismutase enzyme that protects the outside of the cell. By protecting it and holding it together, the probiotic factors are replenished and the body is stimulated to heal itself.

With the knowledge that is collected from research on oxidative stress and chronic bowel inflammation, Dory hopes to determine how colon cancer is related to bowel disease and how it would respond to oxidative stress treatment.

Cancer and Curcumin

Jamboor Vishwanatha, PhD and dean of the Graduate School of Biomedical Sciences, is in the early stages of developing a technology to encapsulate an anticancer compound called curcumin. This compound, similar to tumeric in curry, has the ability to kill cancer cells. Curcumin has been used in traditional medicine for many centuries in India and China.

Robert McClain, PhD and associate vice president of Technology Transfer and Commercialization, said Vishwanatha's new technology may offer cancer patients a new option for treatment.

"Dr. Vishwanatha and his team are working to create a means to deliver curcumin to the body in a packaged fashion," McClain said. "This process can be quite difficult because of the insolubility of the compound when administered orally."

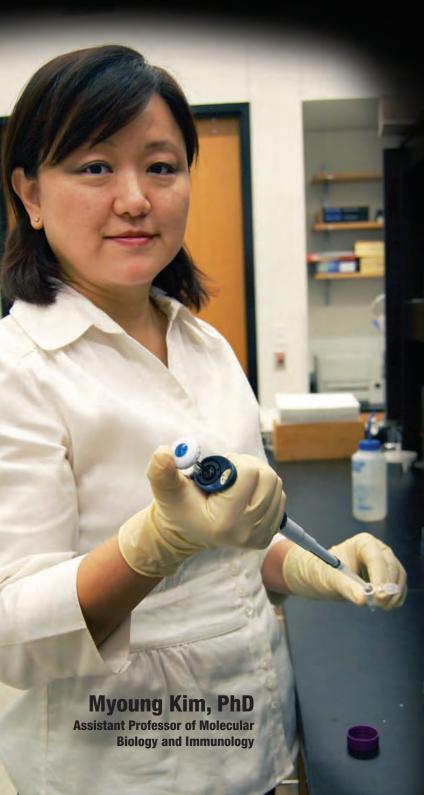
Vishwanatha and Anindita Mukerjee, post doctoral research associate, have investigated the efficiency of encapsulation of curcumin in polylacticco-glycolic acid (PLGA) nanospheres using solid/oil/water emulsion technique in order to develop a nanosystem for drug delivery. The challenge of the delivery is to prepare a carrier system that can encapsulate the curcumin within its structure and then deliver it to the cancerous tissue in its active form.

Previous investigations have established that curcumin can, with multiple molecular targets, affect the many processes in cancer formation. Curcumin has been associated with regression of pre-malignant lesions of the bladder, soft palate, gastrointestinal tract, cervix and the skin, with treatment responses in established malignancy. However, its poor solubility in water makes delivery of the substance tricky. Approximately 80 percent of curcumin received orally is wasted. PLGA nanospheres were chosen because they are biodegradable and biocompatible. Plus, they are approved by the U.S. Food and Drug Administration for use in humans.

During Vishwantha and Mukerjee's research, smooth, spherical curcumin-loaded PLGA nanospheres proved to be efficient in delivering high levels of the material to the target areas. Their study showed that curcumin was released over a prolonged period. Cells collected the curcumin, and cell viability studies revealed that the curcumin-loaded nanospheres were able to exert similar but more pronounced effects on prostate cancer cells as compared to free curcumin. This suggests its high potential for clinical application in prostate cancer.

Vishwanatha's research is being sponsored by Sign Path Pharma in Pennsylvania. Sign Path Pharma is working on commercializing this new technology as a form of cancer treatment. It currently has a license with the Health Science Center to test the technology at M.D. Anderson Cancer Center in Houston.

Proteins key to prostate cancer?



In 2009, more than 766,000 cancer cases were recorded in males in the U.S., and more than 192,000 of these were prostate cancer.

"With prostate cancer accounting for about 25 percent of cancer found in males, determining the source of the problem and how best to cure it is crucial," Myoung Kim, PhD and assistant professor of Molecular Biology and Immunology, said.

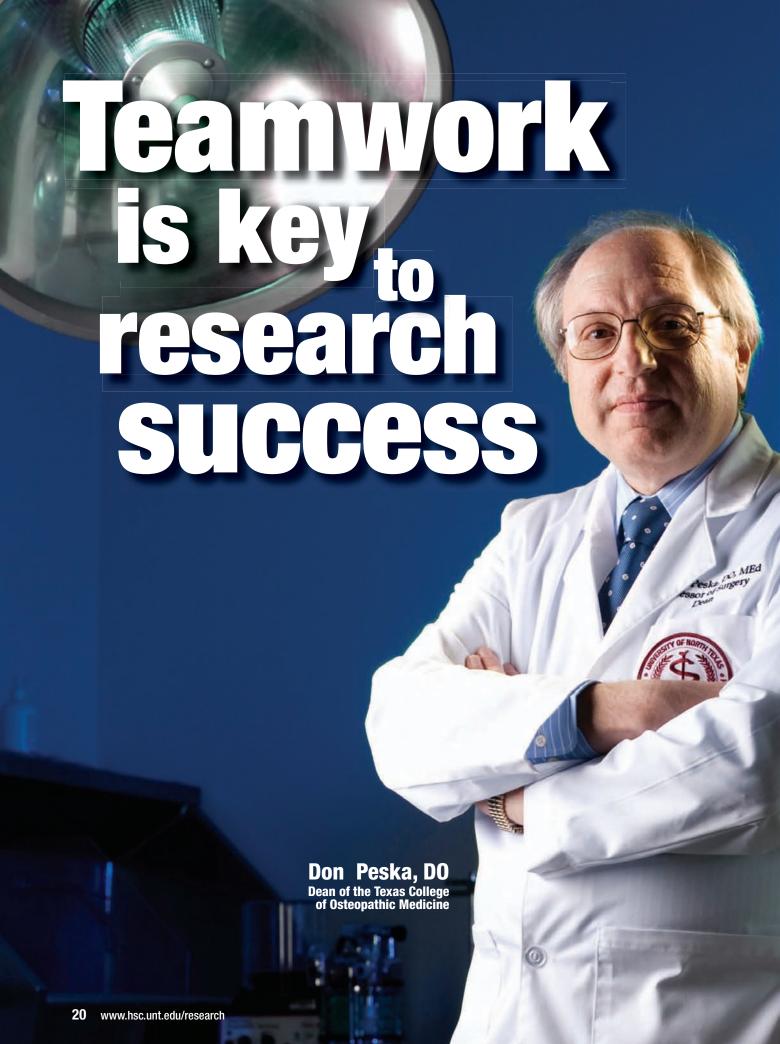
Kim recently was awarded a three-year research grant of \$886,693 from the Cancer Prevention and Research Institute of Texas (CPRIT) as a co-investigator into prostate cancer treatment. Along with principal investigator Jung-Mo Ahn, PhD and assistant professor of Organic and Medicinal Chemistry at the University of Texas at Dallas, and co-investigator Jer-Tsong Hsieh, PhD and professor of Urology at UT Southwestern Medical Center, Kim studies the development of small molecules mimicking pro-apoptotic proteins for treating cancer.

"It is really a three-step process," Kim said. "We each play a unique role."

First, Ahn designs small molecule inhibitors to mimic BH3 (pro-apoptotic) proteins. Once created, the compounds are given to Kim. She then performs an in vitro test to examine the effectiveness of the compound in killing cancer cells. The same test is performed on non-cancerous cells to ensure they are not damaged. Once Kim has discovered the most efficient compounds, they are passed on to Hsieh, who concludes with in vivo testing, assessing the effectiveness of the compounds on animals.

"I am very excited about this collaborative research among three great universities," Kim said. "It will bring three areas of expertise in cancer research together, and it is this synergistic effect that makes this research project so valuable."

While this research is in its early stages, Kim's expectations include, but are not limited to, identifying the most efficient compound to kill prostate cancer cells, expanding the research to find a compound that kills multiple types of cancer cells, and eventually making these compounds available through pharmaceutical companies as cancer-killing drugs.



The Beatles ... Watson and Crick ... the 1970s-era Steelers ... the litany of notable team collaborations is virtually endless, and for good reason: when people work together to achieve a common goal, the sky's the limit.

That belief in teamwork has been one of the career anchors of longstanding Health Science Center faculty member Don Peska, DO. Now, as the new dean of the Texas College of Osteopathic Medicine (TCOM), the no-nonsense lowan sees collaboration as key to building on the Health Science Center's successful research efforts.

"TCOM serves as an educational institution," Peska said. "But we look to the research needs of the Graduate School of Biomedical Sciences and the Health Science Center's 13 Health Institutes of Texas, and work collaboratively to strategically recruit resources in their respective clinical research areas of cancer, Alzheimer's or musculoskeletal disease, just as we do in clinical practice and education."

Peska also said that sharing clinical expertise to develop translational research that serves physicians, patients and students is key to accelerating research growth. "We've done a good job of removing barriers to multi-disciplinary collaboration so that researchers can better drive the advancement of applied science. And by demonstrating that research can be translated into beneficial, meaningful health outcomes, government and commercial funders gain the confidence to proceed with grants."

The community role of the Health Science Center is central to Peska's research vision for TCOM. "As the only medical school in this area, we should be a center of excellence in all aspects of health care, including educational opportunities, community health services and the pivotal role of research in terms of how we deal with issues. Through our graduates and hospital partnerships, we're well positioned to continue identifying opportunities to promote health care in the community, and that certainly includes research."

Noting that his vision for the role of TCOM as part of UNTHSC's ongoing research program is designed to evolve over time, Peska said, "TCOM is committed to moving 'from bench to bedside' — the idea that we're moving responsibly yet rapidly from laboratory experiments through clinical trials to actual point-of-care patient applications. Providing the highest quality primary and specialty care to the citizens of Texas is the name of the game."





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Eating less may influence life expectancy

New studies at the Health Science Center may change the way scientists study aging in mammals. Michael Forster, PhD, regents professor of Pharmacology and Neuroscience at the University of North Texas Health Science Center, and Raj Sohal, PhD, professor of the University of Southern California's School of Pharmacy, have discovered that eating less may not necessarily increase life span. The Forster-Sohal study found that lean mice that ate fewer calories did not lengthen their lifespan - a dietary factor which may be true for humans as well. Caloric restriction was beneficial to obese mice in the study, however.

"Although scientific views have held that limiting calories extends life span in all individuals, our research is showing that healthy individuals who are relatively lean may not benefit from calorie restriction," said Forster. "In fact, caloric restriction could be a detriment."

Although people respond differently, one study of middle-aged males indicated that caloric restriction may actually harm the health of the individual. While limiting calories may improve physical functions, it may not control the effects of aging on cognitive or thinking processes.

"It's definitely not OK to overeat," Forster continued. "We should maintain a neutral energy balance - approximately the same amount of energy coming in as being expended - especially as we age. Generally, people should eat a balanced and nutrient-rich diet throughout life and limit their calorie intake only when needed to maintain their weight at a healthy level."

"Our studies have concluded that limiting calorie intake and weight early in life may be beneficial, but by middle or old age, eating less may actually harm your health and mental abilities."

The study was funded by the National Institute on Aging, part of the National Institutes of Health. Results from the study were published in *The Journal of Nutrition*, *The FASEB Journal*, *Scientific American*, *Asian News International*, *Medical News Today*, *Science Daily* and *ScienceBlog.com*, among other publications.

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Omm Scientific

Resonant Sensors

Through a partnership with Omm Scientific, Ignacy Gryczynski, PhD, professor of Cell Biology and Anatomy, and Zygmunt "Karol" Gryczynski, PhD, professor of Molecular Biology and Immunology, are working to develop a fluorescence-based sensitive technique for detecting micro RNA.

Robert McClain, PhD, associate vice-president of Technology Transfer and Commercialization, helped establish the relationship between the Gryczynskis and Omm Scientific. Omm Scientific, a privately held bio-tech company, was awarded a Small Business Technology Transfer (STTR) program grant and chose to work with the UNT Health Science Center.

"This grant has allowed the Health Science Center to be a part of a hot research area," McClain said. "The research could help identify micro RNA as biomarkers of disease, leading to the detection of early stage cancer, among other diseases."

Encore Vision

Having sponsored past research projects with the Gryczynskis, Encore Vision is leasing laboratory space from the Health Science Center to develop methods of treating and preventing presbyopia, a condition affecting the eye's ability to focus on near objects.

"The research done at the Health Science Center facilities will support Encore Vision's efforts in submitting an Investigational New Drug application with the Food and Drug Administration (FDA)," McClain said.

Resonant Sensors

Resonant Sensors is leasing laboratory space from the Health Science Center to explore biological and molecular monitoring that does not require chemical tags or post-processing steps. This new optical sensor technology provides a faster and more accurate solution for analyzing biochemical reactions in real time.

Both John Schetz, PhD, associate professor of Pharmacology and Neuroscience, and Meharvan "Sonny" Singh, PhD, associate professor of Pharmacology and Neuroscience, have explored interactions with Resonant Sensors and their technology.

ZS Pharma

Health Science Center researchers are working with ZS Pharma to develop a drug to treat hyperkalemia, an electrolyte disturbance in which there is an abnormally elevated level of potassium ion in the blood. Through pre-clinical and clinical research at the Health Science Center, the treatment created ultimately could reduce the need for kidney dialysis in patients with hyperkalemia.

"Our pre-clinical capabilities will help ZS Pharma generate data in support of their Investigational New Drug submission with the FDA," McClain said. "ZS Pharma also intends to conduct clinical trials at the Health Science Center."

One pre-clinical project was completed by Sue Yi, PhD, research assistant professor of Pharmacology and Neuroscience, and James Simpkins, PhD and chair of Pharmacology and Neuroscience. Yi also served as principal investigator of the project. Other Health Science Center employees involved with this research include Jerry Simecka, PhD, chair of Molecular Biology and Immunology; Bill Weiss, director of pre-clinical services; and Egeenee Daniels, DVM, director of Laboratory Animal Medicine.

ZT Solar

Laboratory space at the Health Science Center has also been leased to ZT Solar, a company focused on commercializing innovative technologies for cost effective optical designs in solar cells, which convert the energy of sunlight directly into electricity. ZT Solar has the potential to develop disruptive and universal surface structuring technologies for all types of solar cells.

The surface structuring technology is solution based with low cost, high throughput and significant efficiency improvement. It easily can be integrated into current solar cell manufacturing processes.



On average, one person is diagnosed with Type 1 diabetes each hour. Often discovered before the age of 30, Type 1 diabetes takes a harsh toll on people. Not only must they eat a carefully calculated diet and check blood glucose levels several times each day, they are insulin-dependent for the rest of their lives. However, insulin is not a cure for the disease—it is simply life support.

Shinichi Matsumoto, MD, PhD, adjunct professor in the Department of Biomedical Sciences at the Health Science Center, works as part of the Baylor Islet Research Lab on a clinical research trial to isolate islet cells located in the pancreas and thereby allow diabetes patients to receive islet cell transplants. These islet cells, once injected through an IV into a portal vein in the liver of a patient with diabetes, will begin to create insulin. The Health Science Center laboratory is located at the Health Science Center.

The pancreas, an organ about the size of a hand, is located behind the lower part of the stomach and makes insulin and enzymes that help the body digest and use food. Throughout the pancreas are clusters of islet cells. Islets are made up of several types of cells, including beta cells that make insulin, which helps the body use glucose for energy.

"The challenge is isolating the islet cells from the pancreas," Matsumoto said. "Only one to five percent of the pancreas is made of islet cells, making them difficult to find and extract."

The first patient in the clinical research trial began treatment three years ago and has been monitored to identify how the islet cells work. Phases one and two of the research have proven that these islet cell transplant treatments are both safe and effective, following all Food and Drug Administration regulations. The first patient is still insulin independent,

although long-term insulin independence typically requires further treatments after one year.

Matsumoto said the ultimate goal of the study is to develop a long-term remedy to cure diabetes, before the disease causes serious damage to the body's organs, including the heart, nerves, kidneys and eyes.

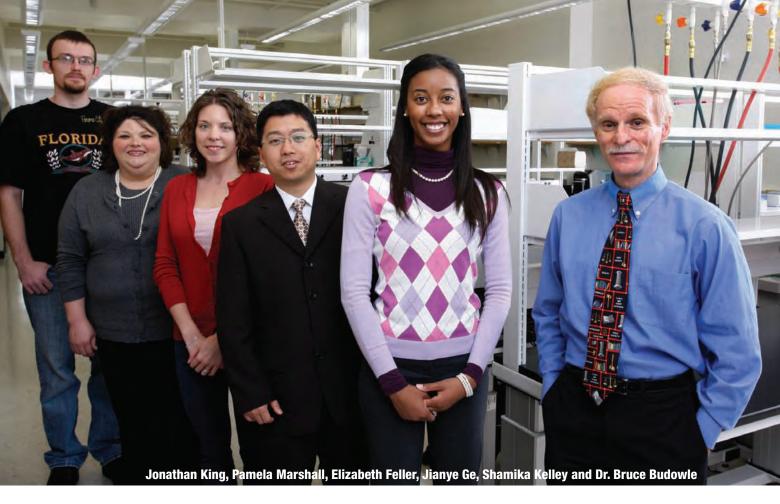
"This treatment is very important for patients with Type 1 diabetes, as they have no other option for permanent treatment," Matsumoto said. "This also concerns the 20 million Americans with Type 2 diabetes, as that type often becomes insulin dependent over time."

As they prepare for the third phase of the clinical trial, another challenge is the organ donor shortage. Almost one million Americans suffer from Type 1 diabetes, and more than 20 million suffer from Type 2. With only about 7,000 organ donors in the country, the possibility of many diabetes patients being able to receive the transplants is challenging. Diabetes is a disease that grows by generations, and this shortage is only expected to worsen.

The third phase of the clinical trial also will require many Type 1 diabetes patients as participants in order to prove that this can be the standard treatment for the disease.

"We have to start thinking about the next generation," Matsumoto said. "Many researchers have started looking into pig islet transplants because of the donor shortage. We also hope to expand the use of the islets from one donor pancreas to reach more than one patient.

"I am extremely happy to be a part of this research," he said. "Finding a cure for a disease that continues to affect more and more Americans will not only give them longer lives, but lives free of frequent finger sticks and daily insulin injections."



New Institute of Investigative Genetics brings FBI expert to UNTHSC

In 2009, the Institute of Investigative Genetics debuted at the UNT Health Science Center, bringing together several areas of molecular biology, forensic DNA expertise, health and bioinformatics. The institute comprises the world-renowned Center for Human Identification, the Center for Biological Safety and Security and the Center for Computational Genomics. Bruce Budowle, PhD, who formerly served as the Federal Bureau of Investigation's (FBI) senior scientist in its forensic laboratory, serves as executive director.

During his 26-year career at the FBI, Budowle helped develop and promote the use of DNA technology for forensic human identification and for microbial forensics, including detection of such agents as ricin and anthrax that have been involved in recent bio-terrorism threats. He sees tremendous opportunity to partner with other researchers and the Health Science Center's mass spectrometry capability to improve the world's understanding of a defense of biological weapons, threats and emerging diseases.

"The Health Science Center presented a better opportunity to broaden my research than I had with the

FBI," Budowle said. "It's a very collegial atmosphere here, and even the president talks with everyone. The university is tremendously supportive of what we do. The people in our group are enthusiastic and really want to do the best they can for crime victims, families and those wrongly accused of crime."

Budowle's first grant of approximately \$1 million involves investigating low-copy number DNA testing. By developing new and better technology, as well as an effective statistical interpretation, law enforcement will be able to present stronger, more compelling evidence that identifies suspects involved in crimes such as breaking-and-entering and other violent crimes, as well as identifying missing persons. In many criminal cases, the amount of DNA left by a perpetrator or missing person is so small — that it can not be typed with a high degree of confidence. Budowle hopes to refine and explore more defined methodology for recovering low-copy number DNA in a more efficient manner, increasing the confidence in currently questionable results.

"If we can catch and convict perpetrators of lowlevel crimes like breaking and entering, we can help reduce the possibility of these criminals escalating and committing far more serious violent crimes," Budowle related. "We can catch them early and include them in a database before they turn to more violent crimes."

Often, samples from human remains must be re-evaluated several times and exhaustive processes re-run to ensure the quality of the results. At the Health Science Center, researchers take the time to find answers and recover DNA that other labs may not have the resources to recover. But it's important to victims and their families to find answers to missing persons and criminal cases.

"It's part of our moral responsibility," Budowle said.

In addition, the institute will research tools to perform a molecular autopsy, in which genetic markers will be analyzed to detect the effects of drugs, health status and environmental insults. These results could lead to personalized genetic medicine, including drug therapy.

It also could help determine cause of death as determined by genetic determinants impacting the function of enzymes. Other determinants could be used to predict physical appearance and assist in identifying missing person's soft tissue facial characteristics. These genetic markers also could help determine if the perpetrator or missing person had blond hair, a broad nose or short stature, for example — details that may escape the notice of a traumatized witness or be distorted by disguises.

Other applications for the research include identification of assays for rapid detection of infectious agents such as H1N1 (swine flu), H5N1 (avian flu) and bacteria that cause sepsis. With faster identification of pathogens, proper and effective treatments can be applied expeditiously.

"All of this research may seem disparate, but it is all forensically related," Budowle continued. "They involve tracking down the biological basis for a crime or an epidemic. We use the same or similar technology whether we are tracking a possible bio-terrorist attack, a pandemic flu outbreak or low-copy DNA at a crime scene."

The new team at the Institute of Investigative Genetics is eager to tackle new research, and recently was awarded a new grant to begin its investigations.



DNA program helps reunite children with their families

By 2010, human trafficking is estimated to be one of the most significant categories of crimes worldwide. Of the 600,000-800,000 people abducted and transferred across international borders each year for purposes of prostitution, forced labor, militant activities or illegal adoptions, 50 percent are under the age of 18. Bruce Budowle and Arthur Eisenberg, professor and chairman of the Department of Forensic and Investigative Genetics and co-director of the Center for Human Identification at the UNT Health Science Center are on a mission to reduce this horrific practice.

Budowle and Eisenberg are collaborating with Jose Lorente, MD, PhD, associate professor of Legal and Forensic Medicine at the University of Granada-Spain, to help establish a worldwide DNA database to help reunite children with their parents and ultimately deter the trafficking of children. Through a \$500,000 grant from The Life Technologies Foundation, Eisenberg, Budowle and Lorente are developing the DNA-PROKIDS Program (Program for Kids Identification with DNA Systems). DNA-PROKIDS is an international humanitarian effort using DNA testing to reunite abducted children with their parents and to deter human trafficking of children. DNA-PROKIDS will initially help countries process their DNA samples and ultimately train them to perform this technology themselves. DNA-PROKIDS will provide kits for the collection of DNA samples from children suspected of being trafficked. Their DNA profiles will be stored in databases where these profiles can be searched against the DNA profiles provided by families whose children were kidnapped or lost.

Lorente was inspired to establish a record to help identify vulnerable children when he saw children wandering the streets in cities across the world. "Were their families looking for them? Without a way to identify them, it would be impossible to bring them home. Perhaps an international DNA database would help reunite these children with their families," he said.

In 2010, the experts were called in to help identify children from the Haiti earthquake prior to their leaving the country in case their families need to find them after the crisis subsides.

Research '09

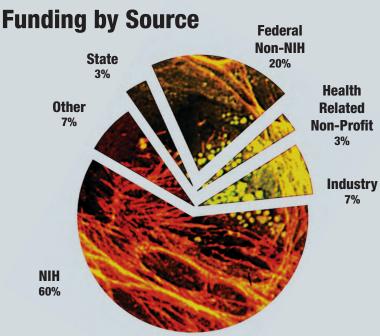
Research expenditures at the Health Science Center continue to grow, reaching an all-time high of more than \$34 million in 2009. Since 1999, our research expenditures have increased by more than 230 percent. Our faculty continue to aggressively pursue funding. Last year alone, faculty submitted proposals totaling nearly \$250 million. This activity should enable us to continue on our path of growth in biomedical and public health research.

Our scientists receive support for their research from a variety of funding sources. In 2009, 80 percent of the research awards were from the federal government. The majority of federal support was from the National Institutes of Health (NIH), considered the highest standard when judging quality of biomedical research. Although the federal stimulus bill infused drastically needed funding into the NIH research budget for 2009, overall funding has been relatively flat. Our growth in research funding from the NIH exceeds the overall national average. This is strong evidence of the exceptional, high-quality research being conducted by our faculty at UNTHSC.

At UNTHSC, we are committed to performing cutting-edge research in critical areas, including aging and Alzheimer's disease, cancer, cardiovascular disease and health disparities. Our faculty will continue to make the discoveries that lead to improved treatment, therapy and interventions that increase the health of our citizens.











Health Institutes

The UNT Health Science Center is providing a healthier future for a changing world with new discoveries through research. Its mission is to solve problems through data analysis, laboratory research, clinical treatment and physician training.

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 (OMM) through multicenter clinical trials, teaching research skills and promoting collaborative studies.

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.

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 Research (ICR)

A unique university-community collaboration between the Health Science Center and the Institute for Cancer Research provides leadership in all aspects of cancer research, education and training.

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 health care 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.

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.

The most noble pursuit

Socrates once said, "The only good is knowledge and the only evil is ignorance."

Since our world poses no end of mysteries, it's fitting that the more we learn, the more we discover what we don't know. And what separates mere curiosity from accumulated wisdom is understanding how to apply our hard-won knowledge to continue building on our discoveries.

This ability to harness our innate curiosity about nature's endless mysteries is at the heart of humanity's concept of "research." And harnessing that curiosity is all in a day's work for the talented researchers and scientists at the UNT Health Science Center, as they apply their accumulated wisdom and relentless curiosity to solving today's vexing medical problems.

From cancer and blood disorders to Alzheimer's disease and musculoskeletal disorders, we're pushing the boundaries of science to uncover innovative treatments. We're seeking to improve primary care clinical practices and provide real-world solutions through advanced forensic DNA analysis. And we're engaging in local and national partnerships to commercialize cutting-edge technologies that can translate into beneficial therapies.

Put simply, we're working to know the unknown and move our discoveries from the theoretical to the practical -- "from bench to bedside" - in as timely and efficient a way as possible. With apologies to Socrates, perhaps it's more accurate to say that "The only good is knowledge, and the only evil is leaving it unused."

Because isn't the pursuit of healing through the applied use of knowledge the most noble aspiration of all?

We hope you enjoy learning about our noble pursuit in this latest issue of *Synergy*.

Scott B. Ransom, DO, MBA, MPH

President

University of North Texas Health Science Center

Sword. Anon Do.



