SUMMER 2015

UT HEALTH SCIENCE CENTER

SAN ANTONIO

At long last: What if a drug could make us live longer, healthier lives?

"So many things happened. One moment and it's done forever. But the memories are still there." (1)

-Ramiro Guerra, 90, can still recall certain moments from his wartime youth. But other, more recent memories are fading away. (see cover story, Page 11.)



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It sounds like a magic pill—a drug that could help you live longer and healthier and could even sharpen your mind. But does it really work? After one round of clinical trials, Ramiro Guerra's children believe rapamycin just may have slowed their father's retreating memories.

Photos by Lester Rosebrock, Creative Media Services

## There's a tsunami approaching.

Every day, more than 1,000 people are diagnosed with Alzheimer's disease. These are our mothers, sisters, fathers, brothers and spouses. They are scientists, artists, teachers and policymakers.

As time goes on, even more of us will be affected, because the numbers are rising at a startling rate. Today, one in nine Americans aged 65 or older has the disease. In just one decade, the number of Alzheimer's patients is expected to reach 7.1 million, a 40 percent increase from today. In our state, the numbers are expected to nearly double.

San Antonio is facing an especially worrisome scenario. Age is the greatest risk factor for the disease. There is a high number of retirees who make their homes in this city and the surrounding region. As a result, we will see higher incidences of Alzheimer's than many other areas of the country. Compounding the problem is this: Hispanics are one and a half times more likely to have the disease and other forms of dementias. In South Texas, this statistic is significant since 60 percent of our population is Hispanic.

Doctors do what they can to manage the illness with therapies that are available, but there is no known cure for the disease, no way to prevent it and its progression cannot be stopped or even significantly decreased.

As the region's academic health science center, it is our duty to do everything we can to tackle and eventually annihilate this terrible disease. To that end, we are working to create South Texas' first comprehensive institute for Alzheimer's and neurodegenerative diseases. Through this endeavor, we envision offering all medical, dental, allied health and social services for Alzheimer's and dementia patients and their families under one roof, and aligning these interdisciplinary health services with our basic and translational aging research programs. We will address the enormous challenges of Alzheimer's from every pressure point—physical, emotional and financial.

We have a strong platform on which to build. The nationally recognized experts that make up our Health Science Center faculty have already made significant strides in age-related research, and we have a long tradition of excellence in neurological education and service to patients. You will see many of those accomplishments throughout this issue of *Mission*, including in our cover story.

We recognize that we do not accomplish these great feats alone. We are fortunate to have garnered the support of such impactful and dedicated friends as the J.M.R. Barker Foundation and The Robert J. Kleberg, Jr. and Helen C. Kleberg Foundation, as well as many other contributors who also feel compelled to help us in the fight against Alzheimer's (see story, Page 26).

We have much more work to do, and so much more to offer those suffering from this disease. Together, we will persist, committed to discovering better therapies and providing superb care to all our patients.

Triaml. Henrich, Mr.

William L. Henrich, M.D., MACP President and Professor of Medicine UT Health Science Center at San Antonio

## UNIVERSITY *in motion*

## First patient given novel brain tumor treatment

The idea: tiny radioactive fat particles, only 100 nanometers across, inserted by the thinnest of catheters directly into a tumor where they remain, radiating only a tiny distance, affecting only the tumor.

The target: glioblastoma, the deadliest of brain tumors.

On March 10, David Williams became the first human ever to have the new radiation treatment implanted in the center of his brain tumor.

The technology, developed by scientists from the UT Health Science Center's Cancer Therapy & Research Center, uses radioactive liposomes, or fat particles, and inserts them into a tumor. There they remain, radiating a tiny distance and affecting only the tumor, causing less damage to surrounding healthy tissue.

Conventional radiation therapy, considered the best treatment option to date, has not changed much in 40 years. It also has limitations. It must send its beams through healthy tissue to reach the tumor, and so must be limited in the amount of radiation it delivers.

Days after the procedure, Williams reported feeling well and had not experienced adverse side effects.

"This technology is unique," said Andrew Brenner, M.D., Ph.D., a neurooncologist who is leading the clinical trial. "Only we can load the liposomes to these very high radioactivity levels."

The concept was developed by nuclear medicine physician William T. Phillips, M.D., and biochemist Beth A. Goins, Ph.D., in the Department of Radiology; and Ande Bao, Ph.D., a medical physicist and pharmaceutical chemist formerly in the Department of Otolaryngology.

One of the challenges was getting the highly radioactive nanoliposomes into the brain and directly into the tumor. Past chemotherapy treatments using catheters had limitations because of the catheter design, said neurosurgeon John R.

### **Revolutionary** approach

David Williams was the first patient to receive a new radiation treatment implanted into the center of his brain tumor.

Doctors inserted radioactive liposomes, or fat particles, directly into the tumor (tan mass), using a tiny catheter (blue cylinder) inserted through a small hole drilled into the skull. The liposomes retain the radiation and keep it from spreading throughout the rest of the brain or blood stream, causing less damage to surrounding healthy tissue. The mass shown in teal was another tumor surgically removed.

Floyd II, M.D., who worked with Dr. Brenner to apply the first treatment to Williams at University Hospital.

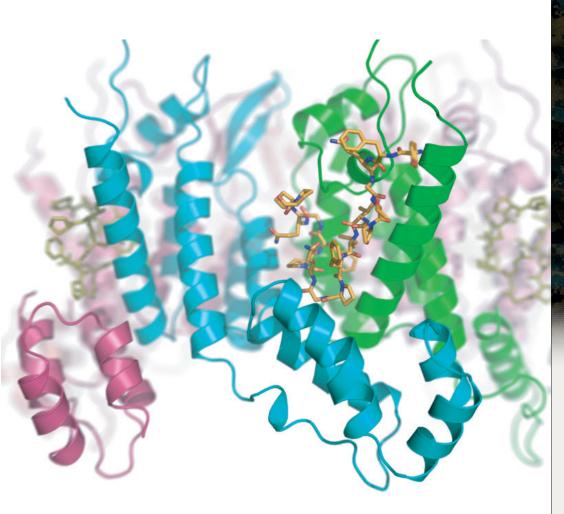
"To effectively deliver this novel therapy and improve our surgical targeting, [we knew] we would need a better catheter. The one we are using is a new design, enabling us to deliver small quantities in precise locations. We are very pleased already with delivery in our first case."

While not all brain tumors are malignant, the glioblastoma is especially deadly. Moreover, as the tumor advances, it affects the brain in unpredictable ways, often involving radical shifts in personality and behavior.

"It's a terrible thing for a family to lose a loved one to glioblastoma," Dr. Brenner said. "It's tough to lose them to any cancer, but with the brain tumor you see them change right before your eyes."

The nanotechnology is igniting hope that there will soon be a major step forward in treatment options for brain cancer, and there is potential that it also could be adapted for use in other cancers.

### UNIVERSITY in motion



## **Molecules in 3-D**

Imagine a suitcase on a bumpy ride. With enough jostling it opens, spilling clothes everywhere. Similarly awkward, the suitcase locks may jam and not open at the destination.

This analogy illustrates the importance of the protective capsule, called the capsid, which surrounds the HIV-1 genome. The capsid has to disassemble once the virus enters the cell, releasing its disease-causing cargo at precisely the right time and place.

"It's still a matter of debate at what point the capsid falls apart in HIV-1 infection of cells," said Dmitri Ivanov, Ph.D., assistant professor of biochemistry at the UT Health Science Center. Dr. Ivanov is a senior author on a study, published in *Proceedings of the National Academy of Sciences*, that offers clues about HIV-1 capsid disassembly. Akash Bhattacharya, Ph.D., was the first author on the study.

An HIV-1 inhibitor called PF74 and a host protein called CPSF6 bind to a

small pocket on the surface of the capsid and prevent it from disassembling. Using the analogy, the suitcase is locked. Viral information is kept inside.

"We think that this process can be targeted for therapeutic purposes in HIV-1 infections," Dr. Ivanov said.

In part of the study, researchers used X-ray crystallography at the Health Science Center to visualize the three-dimensional structure of the bound HIV-1 capsid.

"Seeing molecules in 3-D is illuminating; it tells us something about their function," Dr. Ivanov said. "We now know how PF74 and CPSF6 interact with the adjacent building blocks of the HIV-1 capsid, thus stabilizing the entire capsid structure. It tells us that these molecules bind to the capsid before disassembly, blocking viral replication."

Image by Akash Bhattacharya, Ph.D.

## 'Most hopeful' suicide research

Short-term cognitive behavioral therapy dramatically reduces suicide attempts among at-risk military personnel, according to findings from a research study that included UT Health Science Center investigators.

The two-year study, funded by the Army's Military Operational Medicine Research Program, was conducted at Fort Carson, Colorado. It involved 152 activeduty soldiers who had either attempted suicide or had been determined to be at high risk for suicide. The study evaluated the effectiveness of a brief cognitivebehavioral therapy in preventing future suicide attempts.

Soldiers receiving cognitive-behavioral therapy were 60 percent less likely to make a suicide attempt during the 24-month follow-up than those receiving standard treatment. The results were published by *The American Journal of Psychiatry*.

The findings are particularly encouraging given that rates of active-duty service members receiving psychiatric diagnoses increased by more than 60 percent during a decade of war in Iraq and Afghanistan. Rates of suicides and suicide attempts rose in comparable numbers.

"The significant increase in military suicides over the past decade is a national tragedy," said Alan Peterson, Ph.D., a co-investigator on the study who is a professor of psychiatry and director of the military-focused STRONG STAR Consortium. "The Department of Defense has responded by investing significant resources into military suicide research, and the findings from this study may be the most important and most hopeful to date."

## Drug cocktails increase risk of death

It's been seven years since actor Heath Ledger, 28, was found dead in his Manhattan apartment. The New York medical examiner ruled that Ledger died of "acute intoxication" from six kinds of painkillers, sleeping pills and anti-anxiety drugs.

Most drug overdoses are unintentional, said Barbara J. Turner, M.D., M.S.Ed., MACP, professor of medicine and director of the Center for Research to Advance Community Health. "People with chronic pain don't mean to end their lives," she said. "But they're taking a lot of drugs with substantial risks."

These painkillers include prescription opioids, such as hydrocodone, that are often prescribed along with sedative-hypnotics, such as alprazolam (Xanax) and zolpidem (Ambien). Many patients are prescribed antidepressants, as well, to treat their pain and mood disorders.

Two new studies authored by Dr. Turner and Yuanyuan Liang, Ph.D., also of the School of Medicine, found that a morphine equivalent dose of 100 milligrams or more daily significantly increased the risk of drug overdose, and even lower doses of 50 to 99 milligrams daily were dangerous over an extended time. Patients prescribed more than four to six weeks of moderate doses were at higher risk. The findings are in a recent issue of *The Journal of Pain*.

"If you take moderately high daily doses of opioids and exceed a total dose of about 1,800 milligrams, you are almost at the same risk of drug overdose as somebody who is taking a very high daily dose," Dr. Turner said.

Physicians should take into account how much opioid a person has been prescribed over a period of time, in addition to the daily dose, she said.

The doctors also examined the increase in

drug overdose risk for patients with mental health disorders who are taking opioids, hypnoticsedatives and antidepressants in combination—the type of cocktail that killed Ledger.

"We found that if a patient is taking benzodiazepines (one class of hypnoticsedative) on top of the narcotics, the risk is multiplicative," Dr. Turner said of a separate study published in *The Journal* of *General Internal Medicine*. "If you are at fourfold greater risk of overdose from higher-dose opioids, and then there is more than a twofold greater risk from being on benzodiazepines for 90 days or more, the risk of drug overdose using both together becomes eight times greater."

### Nobel laureate stresses the power of science

Peter Agre, M.D., Nobel laureate and director of the John Hopkins Malaria Research Institute, spoke about the power of science during the 2015 Presidential Distinguished Lecture March 26.

"We should never underestimate the power of science to open doors," he said.

Dr. Agre shared the 2003 Nobel Prize in Chemistry for the discovery of aquaporins, a family of water channel proteins found throughout nature. Referred to as "the plumbing system for cells," aquaporins are involved in numerous physiological processes in humans and are implicated in multiple clinical disorders including malaria.

Dr. Agre joined the Johns Hopkins School of Medicine faculty in 1981 and has served as director of the Johns Hopkins Malaria Research Institute at the Bloomberg



Nobel Laureate Peter Agre, M.D., was the featured speaker at the 2015 Presidential Distinguished Lecture. He shared the 2003 Nobel Prize in Chemistry.

School of Public Health since 2008. He oversees 20 faculty research groups as well as field activities in Zimbabwe and Zambia.

In a personal message to UT Health Science Center students and written in the Presidential Distinguished Lecture Series Commemorative Album, on permanent display in the Dolph Briscoe Jr. Library, Dr. Agre said his message was simple: Creative science that will shape the future is undertaken by young scientists.

"The experiences you are having right now may have profound impact," he wrote. "And importantly, you do not have to be perfect in order to do something important.

"Please take advantage of opportunities, keep the faith and never give up. The world is counting on you."

### UNIVERSITY in motion

## **Staying in balance** after stroke

Strokes affect nearly a million Americans each year, but an already-approved drug used for epilepsy could dramatically reduce their debilitating impact.

New research shows one dose of the anti-epilepsy drug retigabine given hours after a mouse experienced a stroke preserved brain tissue and prevented the loss of balance and motor coordination.

In the study, both treated mice and untreated mice were placed on a balance beam after a stroke. The untreated mice showed a marked loss of coordination with repeated slips and falls, while treated mice had no difficulty with balance, ambulation or turning around on the beam.

"You couldn't even tell they had a stroke," said Mark S. Shapiro, Ph.D., professor of physiology. "They ran across the balance beam like gymnasts."

Brain tissue of the treated mice showed significantly reduced damage to the tissue, compared to untreated mice. The protective effects of the medication were seen up to five days after the stroke, said Sonya Bierbower, Ph.D., postdoctoral fellow. The study was published in *The Journal of Neuroscience*.

Future studies will assess how long brain function can be protected after a

stroke, whether injury-related seizures can be prevented and if strokes can be prevented in high-risk animal models.

A drug called tissue plasminogen activator commonly treats strokes by dissolving blood clots to restore blood flow, but there are significant limitations. It is most effective in the first hours after a stroke, but its later use may do more damage than good.

Drugs such as retigabine work on a completely different system. Instead of thinning blood, they preserve cells by putting a brake on their electrical activity, Dr. Shapiro said.

"It's treating the first step in the sequence and stopping the more damaging secondary effects," Dr. Bierbower added. "These agents directly affect the nerve cells themselves."

Retigabine is approved by the Food and Drug Administration as an anticonvulsant, so physicians may use it off label in stroke patients. FDA approval for use as a stroke therapy will require a clinical trial to be conducted—something that a team of neurologists and neurosurgeons is already considering, Dr. Shapiro said.



### Dental implants for diabetics

Diabetics heal slowly and often face high infection rates. For some 20 years, these reasons have kept dentists from placing dental implants in patients with diabetes.

But a new study shows that with some accommodations, diabetic patients—even those with poorly controlled diabetes—had as high a success rate with implants after one year as patients with healthy sugar levels.

When a tooth is lost, a dental implant, usually made of metal or another material, can be permanently implanted in the jawbone to become the base for a false tooth.

"The most striking thing to me about the study is that we are not only able to see that dental implants can be successful for patients with diabetes, but that the patients are truly benefiting from them," said Thomas Oates, D.M.D., Ph.D., interim associate dean for research and assistant dean for clinical research in the School of Dentistry, who led the study published in the *Journal of the American Dental Association*.

The study evaluated 110 patients, including those without diabetes, and those with both controlled and poorly controlled diabetes. Each patient had two implants placed in the lower jaw followed later by a full set of dentures anchored to the implants. After the implants were placed, patients were followed for at least one year. Diabetics, like nondiabetic patients, had nearly 100 percent implant success rates.

"The study findings showed no significant differences between the nondiabetic and well-controlled diabetic groups. The group with poorly controlled diabetes required a longer time for the implant to heal before placing the dentures," Dr. Oates said. For this reason, there was a four-month healing time following implantation for all groups instead of the usual two months. All patients were prescribed antibiotics and a chlorhexidine gluconate mouth rise following implantation to guard against infection.

# Early detection

### First FDA-approved microarray testing rapidly diagnoses genetic conditions in babies

Having a baby is a joyous event but can be nerve-wracking, even when the baby is the picture of health.

Now imagine being the parent of an infant who has a congenital anomaly, a developmental delay or an autism spectrum disorder. Three months is the average wait time faced by parents to learn the nature of their child's health issue, the severity of it and the help the baby needs.

The clock is ticking, precious time is lost. Anxiety abounds.

Yet this time doesn't have to slip away. Parents now have the option of rapid-turnaround, Food and Drug Administration-approved microarray testing to diagnose genetic conditions, done at the UT Health Science Center. The Clinical and Molecular Cytogenetics Laboratory of South Texas Reference Laboratories, in the Department of Pathology, recently became certified to offer Affymetrix CytoScan® Dx Assay microarray testing.

"The sooner you identify the underlying cause of these children's medical conditions, the better the outcomes for the children in the long run," said Veronica Ortega, B.A.,



CG (ASCP)<sup>CM</sup>, manager of the laboratory. "We can confirm the common abnormalities within 24 hours, which is a relief for families because conditions are diagnosed sooner so that the parents can pursue better care options for their children."

Gopalrao Velagaleti, Ph.D., FACMG, professor of pathology, pediatrics and clinical laboratory sciences and director of the cytogenetics laboratory, said microarray testing is the first line of testing for children with these conditions. It is widely used already, he said, but the Health Science Center is the only institution offering an FDA-approved assay within a region including Texas, Oklahoma and Mississippi.

"It is a tremendous benefit to some of these families to know the underlying

cause of their child's condition, and what the typical outcome is for other babies with similar diagnoses," said Steven Seidner, M.D., professor of pediatrics at the Health Science Center and the medical director of the Neonatal Intensive Care Unit at University Hospital. "Occasionally this knowledge will also change our management of the baby, including the timing of needed surgeries."

Testing also tells families whether the child has a new mutation that likely will not recur, or whether there is a strong pattern of inheritance in the family.

"We can often learn whether this is something of major concern to parents in future pregnancies," Dr. Seidner said.

## **Broccoli for life**

The world's longest-lived rodents don't eat broccoli, but they have the protection of a protein that, in humans, is activated by consumption of steamed broccoli.

The protein is called Nrf2, and it was connected with the maximum life span in 10 rodent species tested by the UT Health Science Center's Barshop Institute for Longevity and Aging Studies. But its signaling is highest in the naked mole rat, which boasts a maximum life span of 32 years—eight to 10 times longer than the oldest mice of comparable size. Naked mole rats don't just live longer, however. They also don't develop cancer, and they remain healthy almost to the end of their extraordinarily long life span.

In the naked mole rat, Nrf2 is well regulated by several other proteins, which

work to degrade the protein. Unregulated gene expression of certain protective molecules leads to diminished signaling and shorter life span.

Graduate student Kaitlyn Lewis is the lead author on the study that suggests targeting negative regulators of Nrf2 could yield interesting results in longevity and life span-extending drugs.

So, do you want to live longer? Changing your diet and adding more broccoli, Brussels sprouts and cabbage can increase your Nrf2 activity, and just may provide some of the same protective mechanisms seen in healthy long-lived rodents.



### School of Nursing faculty and students collaborate with nurses from Mexico

By Rosanne Fohn

Teachers relish "aha! moments," when students understand a complex concept for the first time. These moments are coming from both sides of the border with a new educational program between nursing schools at the UT Health Science Center and Universidad Autonoma de Nuevo Leon in Monterrey, Mexico.

The Salud: Nuevas Fronteras program is bringing eight faculty members from UANL to the Health Science Center to learn teaching methods based on U.S. standards. They are enrolled in graduatelevel coursework in the School of Nursing three weeks each semester for four semesters. The program began in fall 2014.

The program allows them to better coordinate their clinical and educational programs, and integrate research into the process. But it's not a one-sided relationship, said Eileen T. Breslin, Ph.D., RN, FAAN, dean of the School of Nursing.

"This partnership is enriching both

Eight faculty members from the Universidad Autonoma de Nuevo Leon in Monterrey, Mexico, joined nursing faculty and students at the UT Health Science Center to learn teaching methods based on U.S. standards. It's part of the Salud: Nuevas Fronteras program that works to enrich nursing programs on both sides of the border.

of our educational programs," she said. "These are some of the best clinical faculty members at UANL. All of them have a master's degree and some have doctoral degrees or are pursuing a Ph.D. UANL is one of the best universities in Mexico," known for promoting graduate education and research.

At the Health Science Center, the Mexican faculty members have focused on palliative care, health assessments, clinical education and educational theory. This spring, the UANL nurses saw how Health Science Center faculty teach nursing students to interview patients and take medical histories, use simulation for clinical training and learn to care for patients in clinics and hospitals.

"We don't have the same level of simulation training [in Mexico]," said Dani Amaro Hinojosa, a Mexican faculty member. "It is much more intensive here. I definitely want to take this [knowledge] back to Mexico."

In the Center for Simulation Innovation, students practice caring for patients using computerized manikins programmed to exhibit various health issues, such as cardiac arrest, the birthing process and emergency blood transfusion.

During one simulation, the Mexican faculty members observed undergraduate nursing students as they assessed a manikin simulating respiratory failure, which led to inserting a breathing tube in the manikin. The Mexican nurses then participated in the exercise themselves, as if they were students. Finally, they took the helm as instructors, guiding the students as they would teach their own students in Mexico.

"Our students learn from their mistakes here before working with real patients," said Clinical Assistant Professor Lark Ford, M.A., M.S.N., RN. "And we link what our students are learning in theory to their clinical training. They teach these separately in Mexico, so this was a new concept for the Mexican faculty members."

Salud: Nuevas Fronteras is supported by \$600,000 from the Mexicans and Americans Thinking Together Foundation. The universities of Michigan and Pennsylvania are partners in the program.

# AT LONG LAST Drug could hold key to longer, healthier life

**By Will Sansom** 

Ramiro Guerra, 90, does yard work whenever the weather's good. Other times he is inside, often sleeping and sometimes agitated. The U.S. veteran began to forget things in 2006, the year his wife of 57 years, Elida, passed away.

"It seemed like my dad short-circuited," said his son, Robert Guerra.



Cindy Holmes and Robert Guerra have seen their 90-year-old father, Ramiro Guerra, slowly lose his memories as he ages. Their father recognized his own cognitive decline, so when he was offered the chance to join a research study of an intervention in human aging, he jumped at the chance. PHOTOS BY LESTER ROSEBROCK. CREATIVE MEDIA SERVICES

The elder Guerra served in Africa, Italy and France in World War II and helped liberate survivors of the Nazi concentration camp at Dachau. He was an Army platoon leader, performed reconnaissance missions and served in three infantry regiments.

In 1948, a year after the Air Force became its own military branch, Guerra enlisted again and served 28 more years, including duty in Korea and Vietnam.

"He did three wars," Robert Guerra said, and for this Guerra earned Purple Heart and Bronze Star medals.

But it's a time that his father sometimes struggles to remember.

Described as having a Type A personality, Ramiro Guerra can no longer "connect the dots" cognitively, his son said. "He can see his decline, and it bothers him."

When asked to join a study of an experimental intervention in human aging involving rapamycin, Guerra "almost insisted he wanted to do it," his son said.

Rapamycin is the first pharmaceutical intervention shown to extend the life span of middle-aged mice, a finding reported by researchers from the UT Health Science Center's Barshop Institute for Longevity and Aging Studies and two collaborating institutions in *Nature* in 2009. *Science, Nature* and *TIME* magazine each extolled the finding as one of that year's top discoveries.

Rapamycin was first proposed as an intervention for aging at the Health Science Center and has been extensively

studied in cells and animals at the Health Science Center ever since.

A naturally occurring bacterial product first isolated from soil taken from Easter Island, the base drug rapamycin has long been federally approved to suppress organ rejection in transplant patients.

"We thought, goodness gracious, this is an approved drug. We should be able to do this [trial] fairly quickly," said Dean L. Kellogg Jr., M.D., Ph.D., professor of medicine and the principal investigator of the rapamycin study.

"But how can researchers study life span in humans? A lot of times, the subjects will live longer than the researchers. So we are looking at proxies for life span."

The first clinical trial was conducted in 2013 at the Audie L. Murphy Memorial

VA Hospital by researchers from the Barshop Institute.

Ramiro Guerra and seven other male veterans, aged 80 to 95 years old and in relatively good health, were immunized for hepatitis B—chosen as a marker to determine an improvement in immune systems. Then the veterans were split into two groups. One group, including Guerra, received rapamycin; the second group received an inactive placebo. The trial lasted four months.

Researchers recorded any changes in the veterans' physical functions, such as walking speed and hand-grip strength. They also documented changes in their cognitive functions such as decision making, learning and memory. They continue to study antibody responses to see if they were more robust during treatment with rapamycin.

"If we can demonstrate an effect on an age-related process, such as rejuvenating immune function or improving physical or cognitive function, then that will suggest rapamycin has a life-span function, as well," Dr. Kellogg said.

Rapamycin was approved for use as an immunosuppressant in transplant patients in 1999. For years its value was debated—many scientists thought rapamycin might do as much harm in people as good.

"Rapamycin has been used in transplant patients who are very ill and receive many medications. I have found there is a clinical bias against it, that it causes diabetes or raises lipids [fats in blood]. This is based on studies from transplant patients," Dr. Kellogg said.

"Very few studies have done work with rapamycin as a single agent in relatively healthy persons," he said. "We've found it to be a well-tolerated drug, and there were no changes in the blood sugars and only a mild increase in triglyceride [lipid] levels, but this change was the same as in the placebo group."

If clinical trials demonstrate rapamycin's value as an intervention to improve health span, the drug would then need to gain Food and Drug Administration approval for use in healthy people. Health span refers to the years of good health a person enjoys across the life span.

For Guerra's family, the rapamycin did make a difference, although it was small.

During the trial, he could again follow plots of TV shows and was more interactive, according to family members. Sadly, the family noticed after the study that the effects went away, although it is not known why, said Dr. Kellogg. That is one of the mysteries Dr. Kellogg hopes to solve as clinical trials continue. He and his team are applying for additional funding to continue the human research.

"It wasn't a magic pill, but we did see some improvement in his cognitive abilities," Robert Guerra said. He offered an analogy to describe his father's daily life:

"When we get up in the morning and start our day, and we begin creating all these memories, we are writing a run-on sentence on a chalkboard all day long, and we can refer back to things," he said. "In the case of my father, he is writing that sentence with his right hand, but with his left hand he is erasing it as he goes. If he tries to refer back to what he did 10 minutes ago, it's gone.

"We believe rapamycin might have slowed down his eraser."



To prove that aging interventions, such as rapamycin, actually work in humans, researchers must first move the science of healthy aging from the idea stage to preclinical and animal studies.

Human clinical trials are at the end of a multi-year, sometimes arduous process. The Barshop Institute for Longevity and Aging Studies, which opened in 2005 after many years of aging research had been conducted at the UT Health Science Center, is one of the few places in the country that can both investigate the aging process and move the findings into the clinic. As a recipient of the Claude D. Pepper Older American Independence Center grant from the National Institute of Aging (NIA), the Barshop Institute is now comprehensive, said Barshop Institute Director Nicolas Musi, M.D., a physician-scientist in the areas of aging and metabolic disease.

The Pepper Center designation, expected to bring as much as \$3.5 million over five years, enables translation of research into practical applications in the lives of older Americans. Another NIA award could arrive soon, Dr. Musi said. The Health Science Center received a perfect score on its renewal application for the Nathan Shock Center of Excellence in the Biology of Aging, and is likely to be refunded for an expected \$3.5 million over five years. This will provide core services and support for aging research and education.

These new grants ensure that the research geared toward improving how people age will continue and expand over the next several years, Dr. Musi said.

"We will be unique in the country in our capacity to investigate the aging process and move our findings into the clinic," he said.

The Barshop Institute became one of a handful of centers in the country to have a Shock Center in 1995, and has maintained the designation ever since, receiving more than \$18 million in funding.

"A very small number of these centers are able to secure the NIA Shock Center funding," Dr. Musi said. "It is the equivalent of a National Cancer Institute designated cancer center in terms of stature in the world of aging research."

The Barshop Institute is also one of only three centers in the NIA Interventions Testing Program and last year received funding of \$7.5 million through 2019. With the renewal of the Geriatric Research, Education and Clinical Center designation within the South Texas Veterans Health Care System, also received last year, the Barshop Institute has all four sought-after designations.

# **Pursuing concussion's cure**

By Will Sansom

eronica Carrillo, 17, and her mother, Paula, waited in the emergency department at University Hospital for the doctor's diagnosis. The avid soccer midfielder had gone up to head the ball in a game when, in midair, the side of her head collided with the forehead of another player. Skulls are hard; no ball could make that kind of impact.

"I felt dizzy but kept going," Veronica said. "I didn't stop until I tried to head the ball again; I headed it wrong, with the top of my head, and I had a period of time when I didn't know what was going on. They told me I blacked out.

"I thought I was going to get better, so I just went home and stayed there. I started getting really bad headaches, but I'm hardheaded and went and played again a couple of days later. After that game, I felt really bad. I had headaches and started throwing up. I've been throwing up since then [for three days]."

Concussions happen every day, everywhere, to anyone, and they happen in so many ways:

Your toddler, who's interested in everything, reaches for the unanchored TV set, which falls and slams into her head. You're filled with fear as you agonize about her developing brain.

Your son, the high school football jock, takes a helmet-to-helmet hit. The players climb off the pile, and you realize that the one who lies limp and immobile on the field is your son. The world stops as you see him carried off the field.

Your mother, 85, who still insists on doing things for herself, falls on loose floor tiles. You see closed eyes and a trickle of blood, and you realize she has hit her head. You frantically call 911, wondering what this will mean for the weeks and months ahead.

"I see head injuries every day in the emergency department, and the age range varies from small infants to 90-year-old people who trip and fall," said Christopher Gelabert, M.D., assistant professor in the Department of Emergency Medicine and physician with UT Medicine San Antonio. "The most common is probably a slip and fall from a standing height."

A concussion is a type of brain injury that temporarily stops the brain's functions. It is commonly described as "getting your bell rung" and "seeing stars." These casual terms may make the condition sound minor, but concussions are serious. Symptoms can range from a nagging headache to seizures, bleeding in and around the brain, and death.

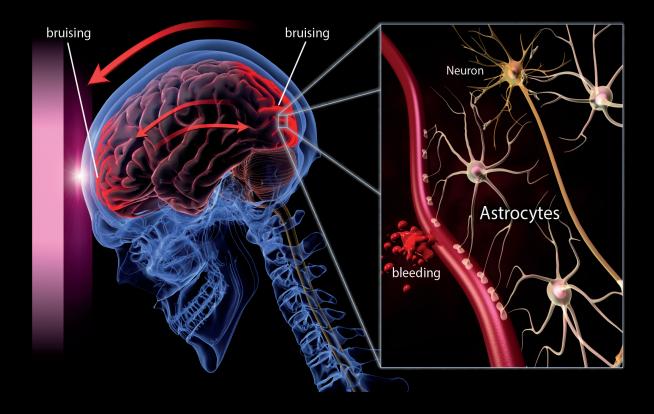
"What we've done in sports medicine is to try to separate the word 'mild' from 'severe' in a concussion diagnosis," said Rudy R. Navarro, M.D., assistant professor in the Department of Family and Community Medicine and family physician with UT Medicine. "This is because all concussions are treated the same way, currently, and secondly we don't have a way to really determine what's mild or severe or chronic until after the fact."

Unlike cuts, there is no way to treat a concussion with a Band-Aid. The injury is within the skull, and it isn't healed readily. Rest and observation are the recommended

A concussion is a type of brain injury that temporarily stops the brain's functions. It is commonly described as "getting your bell rung" and "seeing stars." These casual terms may make the condition sound minor, but concussions are serious, and can even be deadly.

When a concussion occurs, the brain is temporarily and violently shifted. **Swelling creates** pressure in the confined area and can lead to the death of neurons. Researchers have found that stimulating astrocytes, the so-called caretaker cells, with agonist compounds could kickstart a reduction in swelling.

Illustration by Sam Newman, Creative Media Services



ways to treat a concussion today, but with an injury like this, they may not be enough.

"Any concussion has the potential to be a serious concussion," Dr. Navarro said. "A person can develop myriad symptoms, including headaches, dizziness, fatigue, lightheadedness and loss of balance, as well as cognitive issues such as short-term memory impairment, increased time to learn new concepts, and difficulty retaining information. These effects may be developed over days, weeks and even months."

Over the long term, repeated injuries could be associated with the early onset of degenerative brain diseases, as the public is learning through stories of former National Football League players such as Hall of Fame running back Tony Dorsett of the Dallas Cowboys, who was diagnosed with chronic traumatic encephalopathy. The disease is associated with memory loss and confusion, as well as problems with impulse control, aggression and depression. Eventually, it leads to dementia.

"During football season, we see more head injuries in young people," Dr. Gelabert said. "Parents are very concerned, with all the things you see on TV with the NFL."

#### A potential answer

But what if the brain, the seat of reasoning, memory and emotion, could be stimulated to heal itself? Researchers in the School of Medicine have discovered a possible avenue to do just that, and it lies—appropriately—within the brain's so-called "caretaker" cells, called astrocytes.

The skull is a confined space, and the brain rests inside

it in a bath of cerebrospinal fluid. When a concussion occurs, the brain is temporarily and violently shifted. Swelling from fluid retained in the brain tissues, called edema, creates pressure in the confined area. This can lead to the death of neurons—cells that signal nerves throughout the central nervous system to do all of life's functions.

The research centers on a class of compounds called purinergic receptor agonists.

James D. Lechleiter, Ph.D., professor in the Department of Cellular and Structural Biology, has found that treating the astrocytes with the agonist compounds can stimulate the caretaker cells to be more active—essentially giving them a kick-start to minimize the swelling.

The effects are significant. In the brains of live mice, treatment of the astrocytes with the compounds consistently and dramatically reduced neuron death. The results also held true in the first trial on human brain tissue, obtained from patients who underwent surgery for epilepsy.

"We hope to limit and even reverse the effects of concussions," Dr. Lechleiter said. "Essentially, we think we can enhance the brain's ability to heal itself."

Dr. Lechleiter received a U.S. patent for the discovery of the compounds' benefits at the close of 2013.

He endured a lengthy process—seven years—replete with rejections and arguments. The UT Health Science Center technology commercialization team helped him in this effort.

"You get three strikes and you're supposed to be out," he said. "In this case we had at least four strikes but prevailed. When you're developing something, you have to believe in it. We're very excited about the clinical impact of our findings and hope this success leads to new drug therapies for people with multiple types of brain injuries."

According to the Centers for Disease Control and Prevention, an estimated 1.7 million people sustain a traumatic brain injury annually. About 75 percent of these are concussions or other milder forms of brain injury. Children 4 and younger, adolescents 15 to 19, and adults 65 and older are at greatest risk, CDC statistics show. Head injuries result in more than 1 million emergency department visits per year.

"A concussion can happen at any age," Dr. Navarro said. "The symptoms can be very subtle and can be masked by other disease processes. Also, if a patient has a significant traumatic injury or fracture and is on pain medicine, what may be completely missed, not even considered, is that the patient had a concussion."

In toddlers and older developing children under the age of 12, the symptoms can be subtle and unusual, and are commonly missed. These symptoms can include irritability, excessive crying, a change in eating or sleeping patterns, loss of balance and appearing dazed or listless.

"That is a difficult group in which to make the diagnosis, because their symptoms are very different from what we see in teenagers and adults," Dr. Navarro said. An added complication is younger children often can't articulate what they're feeling.

The elderly are susceptible to falls and, by extension, concussions.

"We worry in this group about hemorrhages, stroke, fracture and vitamin D deficiency, but sometimes we forget. We don't step back and say this might be a concussion," Dr. Navarro said. "There are so many confounding factors that it is difficult to treat."

Medical science has miles to go in learning how to treat concussions. Rest is usually advised, along with ceasing sports and other activities that increase the risk of a second injury and refraining from activities such as schoolwork and computer use that require thinking and concentration.

In each age group, when a concussion is suspected, a medication based on stimulation of the caretaker astrocyte cells could be a true breakthrough, Dr. Navarro said.

"A treatment that could help prevent immediate or longterm complications, especially the cognitive issues, would be tremendous," Dr. Navarro said. "We would have to show it makes a significant difference in patients' lives, more than what we are doing now. We need to truly define the effects of concussion down the road. If we find that these injuries cause dementia or psychiatric issues long term, then any kind of treatment that is an adjunct to current care would absolutely be novel and groundbreaking."

#### **Promising beginning**

The earliest preclinical testing of the therapy is complete, and Dr. Lechleiter, the Health Science Center and his new start-up company, Astrocyte Pharmaceuticals Inc., seek to move the program into different animal models, and ultimately to Food and Drug Administration trials in humans.

"We are at a stage where we know we have a molecule that works," Dr. Lechleiter said. "The plan is to make small modifications to see what works the best. Once we have the molecule we want, we will enter a subcontract to test it in small animals."

It is difficult to predict how many years it might be before this therapy could be widely available to the public.

"Right now the delivery method is uncertain," Dr. Lechleiter said. "Clinical trials may test intravenous injections. It could later be sublingual, and melt in your mouth. We don't know at this time."

Animal studies and then human clinical research must show that the benefits of receiving an astrocyte stimulator for a concussion greatly outweigh any possible risks.

Things often move slowly in drug development. But if it takes 10 years or 20 years, it will be worth it, Dr. Lechleiter said, because the applications are enormous—from a toddler's accident to the battlefield in Iraq.

And, of course, to the sports field.

The day of Veronica Carrillo's visit to the hospital, nothing was more important than learning the extent of her head injury and what could be done. It was a minor concussion; rest and cessation of activities were prescribed. But what if a safe, effective infusion of astrocyte therapy had been available for a nurse or physician to administer?

"I feel like if I had taken a pill or something, it would have healed me sooner, and I could have played again sooner," she said a week later.

Her future rides on her getting back on the field. The South San Antonio High School graduate has a scholarship to play for the Larks women's soccer team at Hesston College, located about 35 miles north of Wichita, Kansas.

Will she do headers during games? "Oh yes," she said without hesitation. "I am going to play like I've always played—strong—I'm still going to do headers and everything."

She could be just one game away from her next concussion, but that's a risk she's willing to take, she said.

In the future, if Dr. Lechleiter's astrocyte therapy proves successful and is available to emergency responders, someone at such a game could call 911, and the player could either receive the medication at the field or after arriving at a local hospital.

This is the future of medicine Dr. Lechleiter envisions.

"We don't want to get ahead of where we are with the science," he said, "but no other options are available to treat concussions at the moment, so any novel effective therapy is going to be a blockbuster. It would be used in emergency rooms and ambulances, in primary care and in any place with trained medical personnel. With professional supervision of this very powerful medicine, we could relieve not only the immediate effects of concussions but prevent many of the long-term effects, too."

## NO ORDINARY LESSON School of Dentistry students face

School of Dentistry students face the realities of homelessness

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Fourth-year dental students, including Adam Pfeifer (right), are required to complete a rotation at San Antonio Christian Dental Clinic, which provides free dental care to homeless and underserved adults.

PHOTOS BY JOEL SPRING

### **By Lety Laurel**

• hey treated victims of abuse and people who had lost everything after some unforeseen, devastating crisis. They treated prostitutes and drug users who measure time by the number of days since their last fix. They treated people living on the streets who used every last cent they had on a meal, not a toothbrush.

They were at times met with anger and impatience, were sometimes yelled at and cursed, but were also blessed and thanked.

They treated, they listened. They nervously confronted their own stereotypes. And now, they say, they feel ready to become dentists.

All fourth-year dental students must complete more than 31 days of clinical rotations in San Antonio and South Texas before graduating. Yet there's one clinic that is met with both dread and anticipation. The mandatory rotation is at San Antonio Christian Dental Clinic at Haven for Hope, which provides free dental care for homeless and underserved adults and gives the students a unique patient pool with challenges rarely experienced by students, said Vidal Balderas, D.D.S., M.P.H., assistant professor of comprehensive dentistry at the UT Health Science Center.

"Most students have never had the opportunity to be a part of cases where they're exposed to [post-traumatic stress disorder], addiction, bipolar disorders sometimes all in the same patient," he said. "Our primary goal of the experience at San Antonio Christian Dental Clinic is to expose our students to patients whose lives have been compromised. It's almost assured that at least one of those experiences with the patients we deal with there will be heart-wrenching. You can't help it. When you're homeless, something devastating put you on the streets."

Haven for Hope has served more than 6,870 residents since it opened in 2010. In that time, residents have accounted for 2,800 visits to the dental clinic.

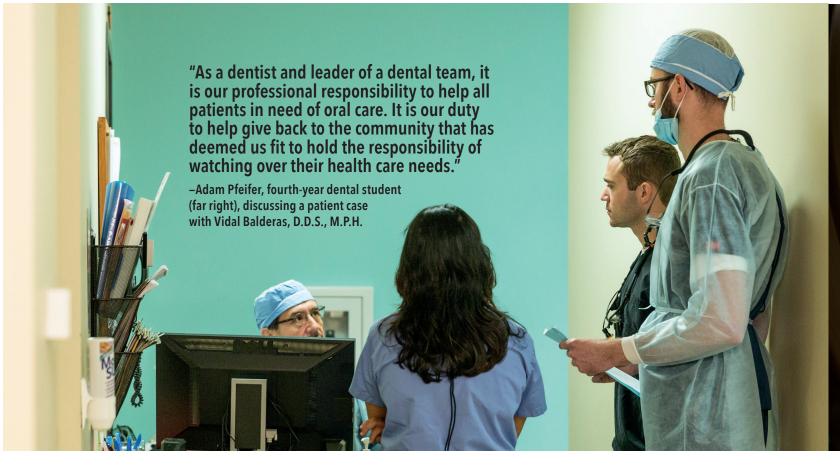
"For many, the nature of poverty and homelessness becomes tangible at San Antonio Christian Dental Clinic," said Gloria Canseco, executive director of the clinic. "Students come face-to-face with profound cases of patients who have suffered from domestic violence, substance abuse, mental [illness], abandonment and other severe obstacles to healthy lives. At the same time, students are also dealing with people who have made a commitment to recovery, demonstrating courage and resolve in the face of daunting circumstances."

It's not your average rotation, Dr. Balderas said, so School of Dentistry faculty don't treat it as one. Before students begin at the clinic, they are prepped about situations they may face. They're shown the panic buttons affixed to hallway walls. They're told to watch out for signs of "meth mouth," the so-called calling card of the methamphetamine user, who often has decay in every tooth. They're trained to look for the signs of a detoxing addict, whose behavior can swing radically from mellow to aggressive like a flip of a switch.

And they're told they must not pre-judge their patients.

"It doesn't matter what they look like, how they talk, what their language is. You treat them with respect. Members experiencing homelessness at Haven for Hope come from all walks of life," Dr. Balderas said. "You've got people with master's degrees and Ph.D.'s who were living on the streets."

When the rotation is over, the students meet around a lunch table and reflect on the experience, led by Moshtagh Farokhi, D.D.S., M.P.H., FAGD, clinical assistant professor in comprehensive dentistry, who also works with the students at the clinic.



What would they have done differently? How did they treat their most compromised patients? What was the hardest situation they faced?

Then they tour the Haven for Hope campus to get a glimpse at the lives their patients lead.

In essays, they write about their experience.

#### In her own words

"I assumed that the patients would be out of control and I would fear for my safety. Honestly, I am embarrassed that I felt nervous or scared about the idea of working on these patients. This impression completely changed over the course of the rotation. Many patients...did not appear to be any different from me. This experience reminded me to look at patients as a whole and unique individual rather than letting the homelessness define the individual." –Mary Grace Camp, student

Mary Grace Camp, a fourth-year dental student, readily admits she has thin skin. She was nervous about the rotation at the clinic, and expected the worst.

Two days into her rotation, while trying to get the medical history of a male patient, he began yelling, frustrated about the amount of time he had been waiting.

"I got a little upset, but I tried to stay professional and said, 'I would appreciate it if you don't use that language with me," she said. She and Dr. Balderas calmed the patient and he got through the appointment. But strangely for Camp, she said, she felt encouraged by the experience, not overwhelmed. She realized she was not helpless, but that many of her patients feel that they are. It gave her a better understanding of where they were coming from.

"Some of my patients were really thankful to be there and thankful to have someone take care of them," she said. "I feel like every patient was just ecstatic to have treatment done."

In most cases, they've never been taken care of before, said Dr. Farokhi. The Department of Housing and Urban Development reported that in 2014, San Antonio's homeless population cited dental care as its highest need. Only 14 percent reported receiving the dental care they needed.

"They don't have money. They don't live in a warm house or apartment like you. They've been on the streets," Dr. Farokhi said. "So when you give them attention and you're polite and professional toward them, you are likely the first who has done so. Then you do all this work. You take them out of pain, you remove their source of infection and you are courteous to them. That's why they are so appreciative. You make a difference in their lives."

Five years ago, the School of Dentistry faculty asked their pre-doctorate students if they would be interested in volunteering a half day once a week at the clinic. Their jobs would be similar to what is done routinely in the School of Dentistry's eight clinics—exams, fillings and extractions. The response was overwhelming and unexpected. More than half of the fourth-year dental students signed up. The one critique faculty repeatedly received: One half-day a week wasn't enough.

Eventually, the volunteer opportunity became a required weeklong rotation, funded through annual support from Methodist Healthcare Ministries of South Texas, Inc. After "I learned that it is not only about dentistry but also about spiritual care of the patients. At the end, it is humanity that we have in common."

–Jina George, fouth-year dental student (seated at right).

collecting three years of reflection papers, Dr. Balderas said, it's now obvious students want even more time at the clinic. Faculty are considering extending the pre-doctorate rotation to two weeks.

In the meantime, the school has expanded its services at San Antonio Christian Dental Clinic by adding residents in the advanced education in general dentistry program. Twice a week, they do more extensive dental work, such as root canals and surgical extractions. Dental hygiene students also have joined the rotation, providing cleanings and oral disease prevention education. Last year, 223 students, residents and faculty provided more than half of all dental services at the clinic.

"I see this as an opportunity for them in a tough environment to learn how to treat the most difficult behaviors in a positive manner," Dr. Balderas said. "It's a learning experience. Some of them go through a week without any major things, but they get to at least hear a story. They get the chance to validate someone's life."

#### Learning from experience

The rotation at San Antonio Christian Dental Clinic revealed a few surprises for Camp. One of them was how deeply she was touched by the stories she heard from her patients. They didn't just give her a renewed appreciation for what she has, but they also reminded her that, as a dentist, she'll have a duty to help others who can't help themselves.

"No one is immune to emergencies and disasters we can't control that drain us of resources, financially and emotionally," she said.

According to the clinic, an estimated 130 million

people lack dental insurance in the U.S. Locally, less than half—41 percent—of Bexar County residents reported seeing a dentist in the past year. Compounding the problem, Bexar County and surrounding counties in the region are considered "dental deserts," where the dentistto-patient ratio is lower than the national average.

The patient load is higher for the students at San Antonio Christian Dental Clinic than at the clinics offered at the School of Dentistry. A typical day there can have up to five patients scheduled per dental student, plus emergencies. This is about two to three times higher than a typical day at the university's on-campus clinics.

"For our part, the partnership [with the Health Science Center] extends our capacity for direct patient care, nearly doubling the numbers of underserved patients we treat," Canseco said. The clinic has no paid dentists on staff, beyond its director of dental services. "The partnership guarantees a minimum threshold for capacity and assures a level of excellence on par with that of an academic health science center. And at a higher level, working with underserved patients contributes to the development of a social conscience for the students."

These are lessons that can't be fully taught in the classroom, said Dr. Farokhi. Life lessons. At San Antonio Christian Dental Clinic, it's as real as it gets.

"I see more aha! moments in these rotations than I ever do in the classroom," she said. "But everything that is learned [at San Antonio Christian Dental Clinic] is true about all patients. Every patient has their own unique story. One shoe does not fit all."

## Heartening journey

The art of medicine pushes the boundaries of science and extends a life

**By Catherine Duncan** 

# Andres Castillo Jr. was born with a hole in his heart.

At age 2, he underwent his first major heart surgery to repair the hole—an atrial septal defect. Seven years later, his first pacemaker was implanted—a box the size of an old VHS tape, visible under his shirt.

He tried to live a normal life, though his teenage years and young adulthood were marked with repeated hospital stays and countless heart procedures.

"Every year, my doctors wrote notes to the school saying I couldn't do anything physical," he said. "I really wanted to play dodgeball and do what the other kids did. The doctors were scared my pacemaker would get hit."

Castillo was 35 when his tricuspid valve, the door that lets blood enter the heart from the body, narrowed. It took yet another open heart surgery for the tricuspid valve to be replaced with a bovine pericardial valve: a manufactured valve made from the sack that surrounds a cow heart.

It didn't last.

By his 43rd birthday, his bovine valve was failing and creating a deadly domino effect on his other organs. With a seventh pacemaker and four decades of surgeries, his options were limited.

UT Medicine San Antonio doctors, including cardiologist Marc Feldman, M.D., and A.J. Carpenter, M.D., Ph.D., the cardiothoracic surgeon who had performed his valve surgery, considered what to do next. They consulted with Steven R. Bailey, M.D., interventional cardiologist.

They all agreed: He wouldn't survive another invasive heart valve surgery.

"We knew we had to do something. If we didn't, he would be dead within six months," said Dr. Bailey, chief of the Janey and Dolph Briscoe Division of Cardiology at the UT Health Science Center.

Pacemakers had damaged Castillo's tricuspid valve, he said. When the right tricuspid valve doesn't work, the liver starts filling with blood and fluid. This condition results in cardiac cirrhosis of the liver. Once one organ shuts down, others can follow.

Castillo's immediate future looked grim.

"He would have endured extended stays in the hospital; he would have had no quality of life," Dr. Bailey said. "That is no way to live."

Members of the Heart and Vascular Institute, a collaboration of cardiologists and cardiothoracic surgeons from UT Medicine and the University Health System, considered a heart transplant, "but we learned that was not an option," Dr. Bailey said.

A heart transplant is performed when there is failure of the left ventricle. Castillo's case was unique because the failure was on the right. This unusual condition required a novel remedy.

They turned to a relatively new device called the Edwards SAPIEN XT Transcatheter Heart Valve, first introduced in the U.S. in 2011. The Edwards valve consists of an expandable metal mesh cage with bovine tissue within it that expands and contracts like the heart's natural valve. It is approved by the Food and Drug Administration for aortic or left valve use, but "there are so few patients with Andres' right valve problem that research has not been done on use of the Edwards valve on it," Dr. Bailey said. "This is where the art of medicine can extend the science."

It wasn't a guaranteed fix and did include some risk. But Castillo, a single father of 11-year-old son Andres Castillo III, said he prayed about it and decided the chance to spend more time with his son was worth the risk.

"Since he was 5 years old, I have been raising him by myself," Castillo said of his son. "I cherish every day I have with my son. He has made me a better father."

On Jan. 8, a team of 22 health care professionals at University Hospital inserted the valve into Castillo's existing bovine valve. The noninvasive procedure used a catheter to push the crimped valve into an expanded balloon.

"You get the equivalent of a new valve without having surgery," Dr. Bailey said.

Dr. Bailey is cautiously optimistic about Castillo's prognosis. Before the valve procedure, Castillo's liver had already begun to fail and other organs were following suit. Dr. Bailey said he is hopeful that treating the right valve will improve his overall health.

"In all reality, we don't know. In patients who have had similar problems with their tricuspid valve, this returns them to normal status. The only thing wrong with him was that right valve," he said.

Castillo still struggles to climb the stairs to his secondfloor apartment. Coughing fits interrupt his speech. A collection of prescription pill bottles lines his tabletops. This is his daily life.

Yet his body is getting stronger. Slowly. And his spirituality remains intact—evidenced by the crosses hanging on the wall in his apartment.

"I take life day by day. I take things slow," he said.

Dr. Carpenter has helped to save Castillo's life twice in seven years. She's seen him fight through prolonged hospital stays and multiple health crises. She is confident that with Castillo's right tricuspid valve repaired, he will be a candidate in the future for a heart transplant.

"Andres told me once that his dream was to see his son graduate from high school," she said. "I would like him to think bigger than that. I think we can help him be here for even more of his son's life."

Castillo has struggled with heart failure his entire life. He knows the struggles aren't over, but neither is his journey.

He has much to be thankful for, he said, including his family that continues to support him and his doctors who haven't given up on him.

"Thanks to all of them and to God, I am doing better," he said. "I believe God wants me to be here. I have been through so much, but, at a time when others may have said I had no options, these doctors worked together to help me. They saved my life."

Andres Castillo Jr. with his son, Andres Castillo III.

On Jan. 8, a team of 22 health care professionals including interventional cardiologists Steven R. Bailey, M.D. and Marvin H. Eng, M.D., and cardiothoracic surgeons A.J. Carpenter, M.D., Ph.D., and Edward Sako, M.D., Ph.D.,—turned to a relatively new device to extend Castillo's life.

Photos by Lester Rosebrock, Creative Media Services Elementary students express their struggles with asthma through artwork

**By Joe Michael Feist** 

yren Lopez just can't tolerate cats. "Cats and dust," he said in a polite whisper. In the second grade, Zyren recalled, "I started getting really sick. My chest was hurting and it was hard to breathe, so I went to the nurse and she called my mom. And they wanted to take me to the doctor. They wanted to rush me to the hospital."

Zyren was soon diagnosed with asthma, a chronic lung disease that inflames and narrows the airways, making it hard to breathe. Asthma affects one in 10 people, including an estimated 7 million children in the United States.

Now 11 and soon to be a fifth grader at Driggers Elementary on San Antonio's northwest side, Zyren considers himself a normal kid, albeit one who must be aware of symptoms and triggers, and who takes daily longterm asthma control medications.

Zyren and his family are exactly the kind of people who Mary Kay Hart, M.S., wants to help through the Asthma2Art program she developed, first in Dallas at Baylor University Medical Center, and now at the UT Health Science Center, for school-aged children with asthma.

"I am a registered respiratory therapist certified in asthma education and I'm an artist. I believe Asthma2Art is a great way for children to express what it feels like to live with asthma," said Hart, assistant professor and director of clinical education in the Department of Respiratory Care in the School of Health Professions.

The program for children who have already been diagnosed with asthma has two components, Hart explained: education and artistic expression. First, she and a respiratory care team go to a school and provide asthma management education to the students with asthma. The students rotate through three stations, each focused on a different subject.

"The 'What is Asthma?' station teaches the students

how the lungs work and signs and symptoms of asthma," Hart said. "Another station is focused on asthma triggers. Students identify their own asthma triggers, how these triggers make their asthma worse and which triggers can cause them to have an asthma attack."

Common triggers include allergens such as pollen, dust mites, cockroach droppings and mold, she said. Frequently, triggers are in the schools themselves, where carpeted libraries and stacks of books can gather dust mites, and water leaks in the ceiling or beneath sinks can accumulate mold.

The final station is about asthma medications and the difference between controller and quick-relief medications. While some children require a daily dose of medicine, others have intermittent asthma and require a quick-relief inhaler to prevent or treat an attack.

After the stations comes the art.

"Some kids choose to draw pictures of what triggers their asthma," Hart said. "Others draw pictures of being totally isolated indoors and unable to go outside with friends, because that's the way they've lived. The pictures I most enjoy seeing are the ones they create of them participating in the fun activities they enjoy when their asthma is controlled."

Kathryn Cruz, B.S.N., RN, is the school nurse at Driggers Elementary and an alumna of the Health Science Center's School of Nursing. About 100 of Driggers' 640 students have been diagnosed with asthma, and most participated in the Asthma2Art program in January, she said. Cruz called the artwork the students created meaningful and amazing.

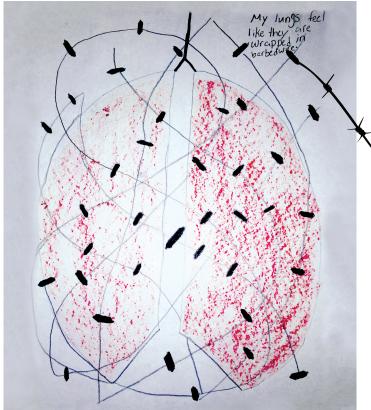
"One child [expressed] that during an asthma attack it felt like barbed wire, just very tight and painful on his chest," Cruz said. "Another little girl who was a second grader drew a very nice picture of her and her dad there in a house, and the dad was smoking, and she said, 'Dad, please stop smoking. I can't breathe.' And I was just very taken aback by that."

Tobacco smoke is especially bad for kids who have asthma, Hart said.

"It's very important for adults to know that just being around someone after they have smoked a cigarette can trigger an asthma attack. Even emotions such as crying hard or laughing can trigger asthma," she said.

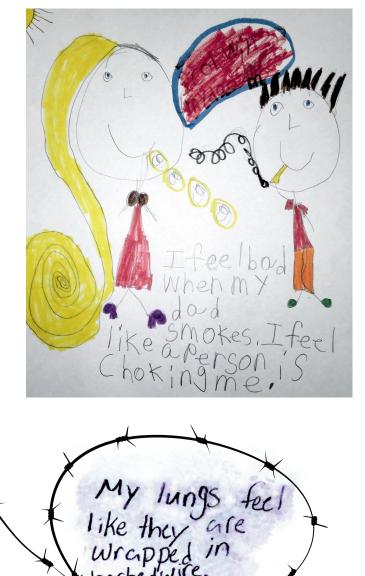
Since children spend most of their days in school, Hart and her team survey the physical condition of the school and identify potential asthma triggers. They recommend ways to maintain asthma-friendly classrooms and train teachers and staff to recognize signs and symptoms of asthma and respond properly to a child having an asthma attack.

"During the cold and flu season, lots of children come to class coughing and with runny noses, both classic warning signs of asthma," she said. "Knowing in advance which



children in the classroom have asthma may reduce the risk of an emergency situation. Otherwise, it may be missed.

"There are tragic instances where a child has died at school from an asthma attack. It was either not recognized as an emergency or the school did not have the medication readily available to treat the child soon enough," Hart said. "Having asthma action plans in place for the school to follow for each child and having school staff trained in asthma emergency management is key to preventing this from ever happening here in our schools."



Asthma2Art allows students like Zyren to articulate their fears and frustrations about the disease. Indeed, art therapy has proven to decrease anxiety and increase quality of life for children with persistent asthma, according to a study from National Jewish Health. To date, six San Antonio schools have participated in Asthma2Art aided by a grant from the Environmental Protection Agency.

Zyren, who wants to be an artist, said he enjoyed drawing a dreaded cat in the Asthma2Art program "because I could tell what's going on with my asthma."

All artwork is judged by local artists and the winning artwork is published in a calendar.

"We've seen incredible pictures that speak louder than words, very emotional pieces describing what it feels like to live with asthma," Hart said. "We are hoping through Asthma2Art to raise asthma awareness and offer tips to others about managing their asthma better."

## Alzheimer's disease research

Alzheimer's disease is the sixthleading cause of death in the U.S. There is no cure.

By 2025, the number of Americans age 65 and older with Alzheimer's is projected to grow by 40 percent. Texas is expected to see an increase of nearly 50 percent in that same time.

"One in nine of us over the age of 65 is going to develop this disease," said William L. Henrich, M.D., MACP, president of the UT Health Science Center. "The costs are incalculable."

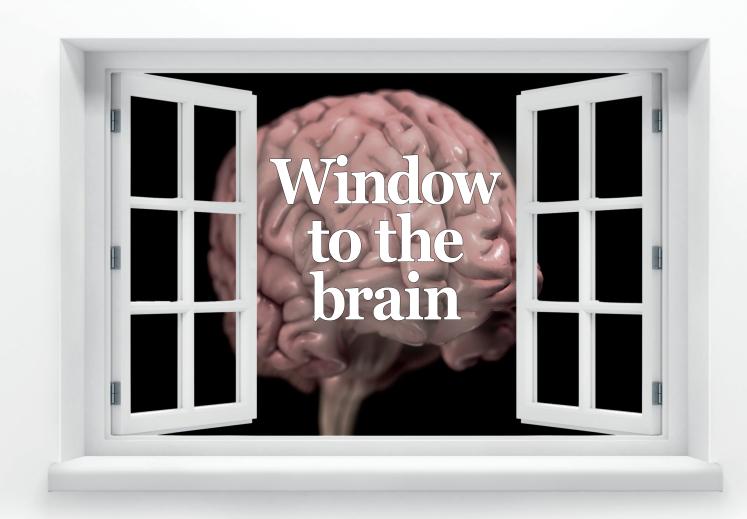
To help address the need, the Health Science Center is working to establish a comprehensive Alzheimer's and neurodegenerative disease institute to offer patient care and support for caregivers while simultaneously developing effective therapies for early prediction, prevention and cures, Dr. Henrich said.

"We have a responsibility to lead the effort in providing a comprehensive, compassionate network of care for Alzheimer's patients and their families," he said. "We also must lead medical research to relentlessly search for new, muchneeded therapies, including clinical trials, that will advance the field and offer promise for improved patient care, now and for the future."

In less than a year, the university has raised nearly \$30 million toward the creation of the institute. This vision was spurred by a \$5 million gift from the J.M.R. Barker Foundation and a challenge to match the gift with additional community philanthropy and other external support for the institute.

"The Health Science Center has stepped forward to address a growing and serious health problem that is devastating to patients, and their families and loved ones, in this region and across the country," said Ben Barker, board member of the Barker Foundation and member of the Health Science Center Development Board. "Our foundation is committed to investing in this vision for families. It touches all of us.

"If there is any area of science that needs a breakthrough, it is Alzheimer's."



## gets multi-million dollar boost

The vision for the institute is to adopt the approach of a patientcentered medical home, grounded in comprehensive and continuous care for patients with Alzheimer's, dementia, Parkinson's disease and other neurodegenerative diseases. It will also offer social, psychological and other support programs for caregivers to continue providing care while also maintaining their own health and well-being.

Neuroscience research already makes up one-third of the science at the Health Science Center, Dr. Henrich said, and the institute would build upon that and add educational programs to provide more health care workers specializing in the care of patients with neurodegenerative diseases.

"Establishing the Alzheimer's institute is of the highest importance to our university," Dr. Henrich said. "We see a tremendous public health need on the horizon, and we recognize that we are positioned to address it in a substantive way."

Texas is ranked third in the country in the estimated number of Alzheimer's disease cases and second in the number of related deaths.

And as the Hispanic population continues to increase—Texas is projected to become a majority Hispanic state between 2025 and 2035—so too will the number of Alzheimer's patients. Hispanics are about one and a half times more likely to have Alzheimer's disease and other dementias than non-Hispanic whites.

"Texas and San Antonio are right in the sights of this disease," Dr. Henrich said. "This gift from the Barker Foundation, and the many others we have received for this critical endeavor, will allow us to provide the research and compassionate and expert care to address the critical need for the growing number of families and patients who are facing this serious and challenging condition."

#### By Will Sansom

n a flap of skull the size of a pinhead, Martin Paukert, M.D., mounts and seals a thin window onto an anesthetized mouse.

This window will allow Dr. Paukert and his team to monitor, in real time, effects of stimuli to the brain of a conscious mouse while it walks on a tiny treadmill. That's something that's not often done, Dr. Paukert said, but that can yield important data.

Dr. Paukert is the principal investigator of a five-year, \$2 million grant from The Robert J. Kleberg, Jr. and Helen C. Kleberg Foundation to study brain activity that may take place long before Alzheimer's disease symptoms are observed.

"The unraveling of the mystery of this terrible illness will emanate from discoveries along the lines of what Dr. Paukert and his colleagues are doing," said UT Health Science Center President William L. Henrich, M.D., MACP. "You can't develop a drug, you can't develop an antibody, you can't develop something to prevent this unless you know what lies at the very center of the problem. That's why this work is so important. The consequences of having a neurodegenerative disease are deeply felt by everybody."

One of the earliest sites of noticeable neurodegeneration is a brain stem structure called the locus coeruleus. This structure has a major influence on the entire central nervous system because it delivers norepinephrine, a neurotransmitter associated with attention or arousal. Initial triggers of Alzheimer's disease may include less norepinephrine release, and fewer norepinephrine-dependent calcium spikes in cells called astrocytes. While astrocytes are the major support cells for neurons, in Alzheimer's this relationship appears to be somehow affected, causing the death of neurons.

Using Dr. Paukert's system, the scientists measure spikes in calcium signaling in the astrocytes, which occur when the mouse walks on a treadmill or, more pronounced, when the mouse follows the movement of the motorized belt of the treadmill. During the measurements, the mouse is conscious and the window to its brain is immobilized under the microscope. Critically, its legs remain free to walk.

"This technique gives us a window into how brain cells engage in a cross-talk and how these communications are determined and interpreted by a certain behavior," said Dr. Paukert, assistant professor of physiology.

"The hope is that we can use these signals as a readout of what is necessary to normalize norepinephrine signaling, and to see whether this intervention slows the progression of Alzheimer's disease."

Only a handful of labs around the world are recording these spikes in real time, while the mice are awake, said Manzoor Bhat, Ph.D., professor and chairman of the Department of Physiology.

"The Paukert lab is in its early phases in San Antonio, and funding from The Robert J. Kleberg, Jr. and Helen C. Kleberg Foundation will have a major impact on how quickly they can get the animal models established to address the central questions related to the early onset and progression of Alzheimer's disease in real time," Dr. Bhat said. "In the future, this will allow exploration of new avenues for therapeutic intervention."



## Mays Family Foundation marks CTRC anniversary with \$5 million gift

#### By Elizabeth Allen and Joe Michael Feist

Since its founding more than 40 years ago, the Cancer Therapy & Research Center has grown in stature, scope, funding, patient care and research. But there's been at least one constant: the support of Lowry and Peggy Mays. The couple has long been involved in the effort to make the CTRC the premier cancer treatment and research center in South Texas.

In January, at the CTRC's 40th Anniversary Reunion Dinner, the Mays Family Foundation announced a gift of \$5 million to endow the Mays Family Foundation Distinguished University Presidential Chair for the director of the CTRC.

"We are delighted to honor the CTRC for its 40 years of life-changing work and support its aspirations for the future," said Lowry Mays, foundation founder.

CTRC director Ian M. Thompson Jr., M.D., said the family's support helps ensure the level of excellence that has become expected from the CTRC.

"This endowment is an extraordinary gift that will fuel opportunities for scientific breakthroughs and invest in the best and brightest minds in cancer research," he said.

In a time of diminishing funding for scientific research, the Mays chair will allow for investment in important programs such as pilot research, faculty recruitment and retention, clinical trials, new technology and cancer prevention, Dr. Thompson added.

"It is a remarkable testament to the family's continuing commitment to the community and to the important role the CTRC has played herein, that they are not only early supporters and the founders of the CTRC Cabinet, but now have committed to helping us reach ever-higher standards of excellence," Dr. Thompson said.

"They planted a seed that has grown into a full tree. Now they're planting again, and we're soon to have an orchard."

The CTRC opened in 1974 as a nonprofit corporation providing outpatient radiation therapy. It has evolved into one of only four academic cancer centers in the state to be named a National Cancer Institute designated cancer center. Its Institute for Drug Development conducts one of the largest oncology Phase I clinical drug programs in the world, and participates in the development of cancer drugs approved by the Food and Drug Administration.

David E. Green, managing director of the Mays Family Foundation, said the gift is recognition of the CTRC's elite status earned through four decades of hard work. It is also a way to support the center's future.

"We were impressed with the strategic plan and wanted to show our support to kick off the next 40 years of their work," he said, noting that the previous major gift of \$500,000 donated in 2013 established the Mays Family Foundation Rising Star Physician-Scientist Award.

Combined with the Clear Channel Foundation, the Mays Family Foundation has contributed more than \$55 million to various causes.

"Our mission is to support the communities in which we live, work and serve through causes that aid, empower, enrich and educate," Green said. "Investing in the CTRC easily delivers on those goals."

### Grant helps advance the education of nurses

More students will be entering the School of Nursing, thanks to a \$700,000 grant from Methodist Healthcare Ministries of South Texas, Inc.

The grant, which continues a three-year pilot program, will help advance the education of nurses to meet national guidelines and address the nursing shortage by providing more highly educated nurses.

"These grants have helped us partner with community colleges and universities to encourage students to enter into our bachelor's, master's and doctoral programs," said School of Nursing Dean Eileen T. Breslin, Ph.D., RN, FAAN. "We are committed to advancing nursing education at all levels."

One example of this is at San Antonio College, where office space has been reserved for the School of Nursing faculty to regularly advise prospective students on prerequisites needed to enter UT Health Science Center nursing programs.

As a result, 52.3 percent of the students entering the School of Nursing's Bachelor of Science in Nursing program in fall 2014 completed their prerequisites at SAC, Dr. Breslin said.

The grant also provides funds for three scholarships each for the Doctor of Nursing Practice and Doctor of Philosophy degree programs.



The program supports the Institute of Medicine's recommendation that 80 percent of nurses have at least a bachelor's degree by 2020. Only 54 percent of nurses in Texas and 55 percent in Bexar County hold a B.S.N. or a more advanced degree.

# **Professor emeritus continues life's work through endowment**

Rajam Ramamurthy, M.D., may have been born and raised in India, but she's grown fond of a particular American idiom.

"I believe you should put your money where your mouth is," she says flatly.

Dr. Ramamurthy, professor emeritus in pediatrics, has a long history of giving back financially to the UT Health Science Center, where she has worked since 1977. Her latest gift of \$100,000 established the Dr. Rajam Ramamurthy Endowment in Neonatology.

The endowment will be used to educate those in the region about the importance of specialized care for premature infants. To that end, a portion of it was used to host the university's first Rajam Ramamurthy Lectureship in

Premature Infant Development in February,

which featured Tonse Raju, M.D., medical officer of the National Institute of Child Health and Human Development in the National Institutes of Health.

The Ramamurthy family began giving to the university in 1996. Their donations have surpassed \$154,000, and have supported student scholarships and endowments



Rajam Ramamurthy, M.D.

for research and education. In 2013, the family created the Dr. Somayaji Ramamurthy Professorship Fund in Pain Management, named for Dr. Rajam Ramamurthy's husband, Somayaji Ramamurthy, M.D., a professor of anesthesiology.

Gifts from faculty are a powerful example of philanthropy because of what they already contribute to the university, said William L. Henrich, M.D., MACP, president of the Health Science Center.

"Our faculty is the engine that drives the missions of our university, and giving fuels the engine," he said. "Faculty see firsthand the impact of what is accomplished here, and they know the difference gifts can make."

Although retired, Dr. Rajam Ramamurthy plans to continue research in prematurity and stay involved at the Health Science Center. And she'll keep on giving.

"My experience is you need to support things you believe in," she said. "And it's very important to do these kinds of activities so that these efforts can be sustained."

## Salud!

A national online network to reduce obesity received a one-year, \$1.3 million grant from the Robert Wood Johnson Foundation.

Salud America! The RWJF Research Network to Prevent Obesity Among Latino Children, created in 2007, is a San Antonio-based network of 10,000 parents, leaders, academics and advocates seeking environmental and policy solutions to Latino obesity. The funding will allow the program to expand its membership and build new scientific evidence and policy recommendations to guide efforts to reduce obesity. "Latino childhood obesity remains a national health threat, but we believe our research and multimedia educational content will continue to motivate people to push for healthy changes in their areas," said Amelie Ramirez, Dr.P.H., professor and director of the Institute for Health Promotion Research at the UT Health Science Center and director of Salud America!

## **Four stars**

Four School of Medicine faculty were honored at the national meeting of the American College of Physicians:

- Marvin Forland, M.D., MACP, professor emeritus of medicine who helped launch the School of Medicine, received the Texas Chapter Centennial Award.
- Ralph DeFronzo, M.D., FACP, Dr. Forland professor of medicine and chief of diabetes, received the Samuel Eichold II Memorial Award for Contributions in Diabetes.
- Ruth Berggren, M.D., FACP, professor of medicine– infectious diseases and director of the Center for Medical Humanities & Ethics, received the Nicholas
  E. Davies Memorial Scholar Award for Scholarly Activities in the Humanities and History of Medicine.



Dr. DeFronzo

• George Crawford, M.D., MACP, professor of medicine and associate director of the Internal Medicine Residency Program, was installed as governor of the Southern Texas Region of the ACP.

**Dr. Crawford** 

### **Cancer-fighting boost**

Researchers at the Cancer Therapy & Research Center were awarded more than \$5 million in grants from the Cancer Prevention and Research Institute of Texas to help in projects ranging from examining the on/off switch of a cancer-fighting molecule to preventing liver cancer in a majority Hispanic South Texas population.

"I'm not surprised, but I'm delighted," said CTRC Director Ian M. Thompson Jr., M.D. "These grants demonstrate the breadth and depth of our researchers' talents at every level."

More than \$3 million will go toward a core facility grant for single cancer cell analysis. Tim Huang, Ph.D., professor and chairman of molecular medicine and deputy director of the CTRC, said the grant, announced in May, will allow the CTRC to acquire key pieces that will complete the services already offered by the core facility. Those services include isolating and studying single cancer cells from urine and saliva to develop noninvasive methods for detecting cancer.

"This will give cancer researchers from throughout the region and beyond access to the latest analytical tools operated by a highly qualified technical team, helping them to develop new ways to diagnose, monitor and treat cancer," he said.

Three CTRC researchers received \$1.9 million to support their work in liver and colon cancer prevention and harnessing the body's defenses to prevent recurrence of cancer.

The awards come on the heels of \$6.6 million in research and product development grants given to researchers by the state-funded agency in February. Those included \$4.6 million to support researchers' work ranging from reducing chemotherapy's painful side effects to unmasking resveratrol's potential in managing prostate cancer, and a \$2 million product development grant to support a new brain cancer therapy's transition from a research project to a viable treatment option.

The product development grant is for NanoTX Therapeutics, a company formed to accelerate clinical trials of a highly promising nanotechnology that inserts radioactive isotopes into tiny fat particles, allowing concentrated radiation treatment precisely in the tumor. The process allows doctors to give far higher doses of radiation than current technology while minimizing side effects to healthy tissue.

The grant will also help the young company develop a management infrastructure and tackle the regulatory process involved in commercializing a new technology.











### BANDANA CHATTERJEE, PH.D.,

professor in the Department of Molecular Medicine, is a new fellow of the American Association for the Advancement of Science.

#### ANDREA GIUFFRIDA,

**PH.D.,** was appointed vice president for research after serving as ad interim since May 2014. Dr. Giuffrida is an associate professor of pharmacology and served previously as the director of biomedical research development in the Office of the Vice President for Research. He joined the School of Medicine and Graduate School of Biomedical Sciences faculty in 2003.

### VIRGINIA

**KAKLAMANI, M.D.**, was named director of the breast cancer program at the Cancer Therapy & Research Center.

### DANIEL LODGE, PH.D.,

a psychiatric disorders researcher, received an early career investigator award this year from the American Society for Pharmacology and Experimental Therapeutics.

### JAN E. PATTERSON,

**M.D., M.S.,** has been appointed to serve on the Healthcare Infection Control Practices Advisory Committee of the Centers for Disease Control and Prevention. Health and Human Services Secretary Sylvia Burwell made the appointment. The committee provides guidance regarding infection control practices and strategies for surveillance and prevention of health care-associated infections, antimicrobial resistance and related events.

### **Kinetic Kids**

offers 106 programs year-round, including wheelchair basketball, music, gymnastics and competitive swimming. KINETIC 48

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# It started with a simple question: Why can't kids with disabilities play sports?

#### By Lety Laurel

n 2001, Tracey Fontenot and Kacey Wernli, physical therapists working at a local San Antonio hospital, wondered how they could get their young patients with physical and developmental disabilities to be active past their therapy sessions.

What if they formed a baseball team, using the UT Health Science Center's ball field? Would kids show up?

Ten did.

"Once we got out there, we saw the kids just come alive," said Fontenot, '96. "They felt so confident being part of a team. Their parents felt so happy to be able to watch their kids be able to do something active and to be able to be team parents."

The physical therapists decided to continue the experiment. Over the next two years, the baseball group grew by 40 more players. In 2003, their experiment became an official nonprofit called Kinetic Kids.

Today, there are 1,800 special-needs children participating in 106 sports and recreation programs offered year-round throughout San Antonio. Among the many programs offered are music, gymnastics, cheerleading, basketball, competitive swimming, flag football, golf and wheelchair tennis.

"It started with a question," Fontenot said. "We asked ourselves 'why not?' and we did something about it."

The majority of the staff, program directors and instructors are physical, occupational or recreational therapists. Of the 800 or so volunteers who help with classes each year, many are students from the Health Science Center's physical and occupational therapy programs.

Although the sports and rec program isn't considered traditional physical or occupational therapy, "we're always thinking like therapists and are constantly working on maximizing their potential," said Wernli, '94. "We feel like the benefits of Kinetic Kids go beyond the health benefits. As they are out there participating in sports, they are also building relationships with people. They are having to take their turn and wait in line and do the things that other kids are doing in recreational sports."

They're also building confidence, Fontenot said.



Health Science Center alumnae Tracey Fontenot, '96, and Kacey Wernli, '94, saw a need for sports and recreation programs for special-needs children in San Antonio. In 2003, they founded Kinetic Kids, a nonprofit that serves 1,800 children. PHOTOS COURTESY OF KINETIC KIDS

"We hope that we're building future community members," she said. "Nobody here is going to play in the NFL or the MLB, but we're building people who are confident and can be leaders because of the skills they have learned through their sports. Sports is just the mechanism by which they are learning all these different things."

Kinetic Kids has become a full-time job for the founders. And it's one they said they feel lucky to have.

"There is never a day where we're dreading work. You just think of the kids you're serving and the smiles on their faces and work is easy after that," Fontenot said.

Just as there was a clear need for Kinetic Kids in San Antonio, there is a similar need in communities throughout the country, they said. Fontenot and Wernli would like to create a playbook that other organizations can use to bring similar programs to their cities.

"As people grow up and get married and start having families, we hope that they remember their childhood dreams of playing sports," Wernli said. "I hope we inspire people to realize that every child has that dream [to play sports]. We can help make that dream come true."

## Matchmaking at Match Day 2015

With the ripping of envelopes, more than 200 School of Medicine students learned where they would spend the next three to seven years as residents before launching their medical careers. Match Day, held March 20 at John T. Floore Country Store in Helotes, is an annual rite of passage for medical students and is held in ceremonies across the country. The 2015 Match was the largest in the 63 year-history of the National Resident Matching Program, with 41,334 total registrants.



▲ Samrawit Tekle was matched to Creighton University affiliated hospitals in Omaha, Nebraska, where she will specialize in family medicine.

Emily Beck and Peter Fletcher are headed to Banner–University Medical Center Tucson, in Arizona, specializing in emergency medicine. The couple met a few days before beginning medical school at the UT Health Science Center and became engaged just hours before finding out they would be matched to the same program.



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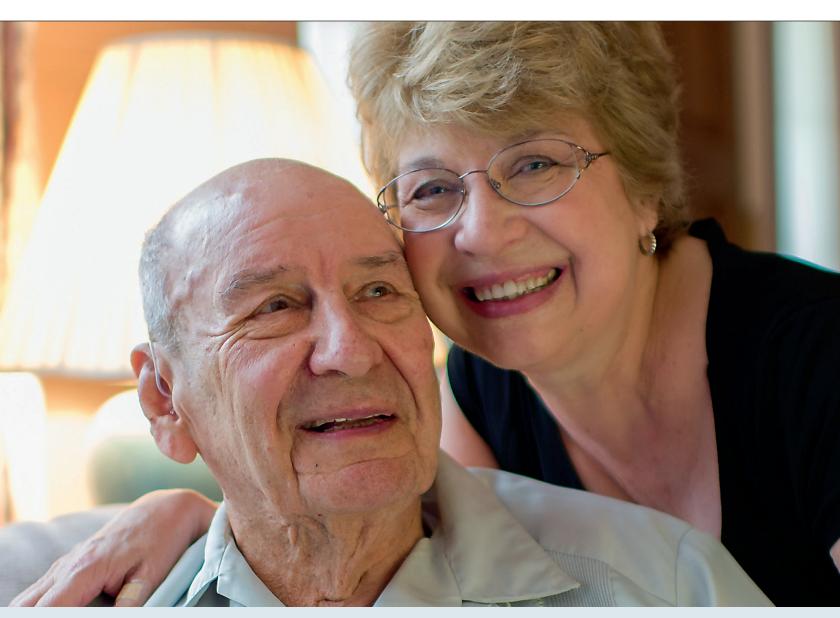
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