

# CONQUEST

THE UNIVERSITY OF TEXAS

**MDAnderson  
Cancer Center**

Making Cancer History®

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**How a dog named  
Sadie is helping  
in the hunt for  
a brain cancer  
breakthrough**



## MISSION

The mission of The University of Texas MD Anderson Cancer Center is to eliminate cancer in Texas, the nation and the world through outstanding programs that integrate patient care, research and prevention, and through education for undergraduate and graduate students, trainees, professionals, employees and the public.

## VISION

We shall be the premier cancer center in the world, based on the excellence of our people, our research-driven patient care and our science.

We are Making Cancer History®.

## CORE VALUES

### Caring

By our words and actions, we create a caring environment for everyone.

### Integrity

We work together to merit the trust of our colleagues and those we serve.

### Discovery

We embrace creativity and seek new knowledge.



**On the cover: Physician-scientists from MD Anderson and Texas A&M University are teaming up to improve treatment for brain tumors known as gliomas in people and pets such as Sadie the French bulldog.**

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## LEUKEMIA DOCTOR CREATES A CLINICAL TRIAL FOR PATIENTS INELIGIBLE FOR CLINIC TRIALS

By Ron Gilmore

What if you or a loved one had cancer but were denied access to a research study testing a potentially beneficial treatment?

This scenario can be a frustrating reality for cancer patients who, because of health conditions or other reasons, aren't allowed to participate in clinical trials.

"Most cancer clinical studies exclude patients with co-morbidities, active or recent malignancies, organ dysfunction or poor performance status," says Guillermo Garcia-Manero, M.D., a professor of Leukemia. "How these criteria protect patients is unclear. Although some are based on clinical reasoning, it seems these criteria are actually in place to safeguard the drug or intervention being studied."

Garcia-Manero led a novel study of a combination of the chemotherapy drugs azacitidine (AZA) and vorinostat that revealed some acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) patients who typically couldn't be considered for clinical trials because of other illnesses or poor performance status—a measure of disease progression—responded well and were safely treated in the protocol setting.

Initially, 30 patients age 17 and older who hadn't been treated for either disease previously and who had poor performance, poor renal or hepatic function or any other active systemic disorder such as another cancer were enrolled in the study. Sixty-day survival was 83% with low-grade gastrointestinal side effects reported.

The study was expanded to include an additional 79 patients. Sixty-day survival for the second group was 79% with a median overall survival of 7.6 months. The average event-free survival was 4.5 months. Again, only low-grade gastrointestinal side effects were observed.

The study was designed with "stopping rules" that included monitoring of side effects and complete response rates. Patients were immediately placed on another therapy if their assigned therapy didn't indicate there would be a complete response within a 60-day period. To define the minimum expected

survival and response rates that would trigger the stopping rules, researchers relied on prior data of 181 patients previously treated at MD Anderson.

The study points to the need for further evaluation of standard exclusion criteria, which could increase the pool of patients likely to benefit from therapy, and lead to larger clinical trials in the future specifically treating patients with AML and MDS.

"Participation in clinical trials is fundamental for the development of new therapeutic interventions," says research team member Guillermo Montalban-Bravo, M.D., a fellow in Leukemia. "Despite this need, only 3 to 5% of patients with cancer treated in the U.S. currently are enrolled in clinical trials."



Guillermo Garcia-Manero, M.D. photo by F. Carter Smith

Read about the latest progress in Making Cancer History® at [cancerfrontline.org](http://cancerfrontline.org).



## UT GOES TOBACCO FREE TO COMBAT THE COST OF CANCER

By Clayton Boldt, Ph.D.

All 14 of The University of Texas System institutions will be tobacco-free by June 1, 2017, thanks to the Eliminate Tobacco Use initiative, designed to protect patients, employees and students from the detrimental effects of tobacco.

Eliminate Tobacco Use launched in February 2016 when representatives from each UT institution met in Houston to share resources and best practices for creating a tobacco-free culture.

The summit originated from a collaboration involving David Lakey, M.D., UT System’s chief medical officer and associate vice chancellor for population health, and leaders of MD Anderson’s EndTobacco program, a science-based initiative built on tobacco-control recommendations from the Centers for Disease Control and Prevention and the World Health Organization. EndTobacco is part of the cancer center’s prevention and control platform of the Moon Shots Program™.

This past April, tobacco control representatives from the 14 UT System institutions, partner organizations, state and local agencies, and other Texas universities and colleges gathered for the 2nd Annual Eliminate Tobacco Use Summit.

“Tobacco use is the single leading cause of preventable death in Texas,” says Lakey. “UT institutions have long been leaders in the area of tobacco and addiction research. Now we’re stepping forward as leaders in reducing the use of tobacco among our students, staff and faculty. The summit was an opportunity for us to assess our gains so far, two years into the initiative, and to push ourselves to keep going.”

MD Anderson has already implemented a number of tobacco control policies, including a tobacco-free hiring policy in 2015, and free, evidence-based tobacco-cessation services for patients, employees and their families, provided through the cancer center’s Tobacco Treatment Program. The MD Anderson campus has been tobacco free since 1989.

### Eliminate Tobacco Use affects :

- 14 UT System institutions
- >221,000 students
- 100,000 employees

### Tobacco’s effects in Texas

- 28,000 deaths annually
- >3.2 million people smoke
- \$8.9 billion in health care costs related to smoking each year

“As of June 1, UT System will have comprehensive tobacco-free policies in place on every campus, making it the largest single employer in Texas to prohibit tobacco use in the workplace,” says Ernest Hawk, M.D., vice president and head of the Division of Cancer Prevention and Population Sciences at MD Anderson. “Policies such as this are only a first step; translating policies into less tobacco use and better health is an ongoing challenge that requires us to assess our needs candidly, learn from each other and constantly strive to improve.”

Eliminate Tobacco Use prohibits the use of all tobacco products at UT System institutions. Those include cigarettes, cigars, pipes, water pipes, hookahs, electronic cigarettes, smokeless tobacco, snuff and chewing tobacco.

Ideally, the initiative will serve as a guide for other university systems within and beyond Texas interested in creating similar policies, Hawk says.

## AGREEMENT BRINGS ASPIRE’S CANCER-PREVENTION CURRICULUM TO HOUSTON STUDENTS

Teenagers know all too well how hard it is to find their place in the socially stratified halls of middle and high school. For many, there’s an ongoing battle between being themselves and trying hard to come across as cool, no matter the cost.

For years, smoking cigarettes was a shortcut to cool. It defined it. Fortunately, cigarettes no longer carry the cachet they once did. But other addictive products such as e-cigarettes and hookahs may be picking up where cigarettes left off.

“That makes educating students about the dangers of tobacco use and nicotine addiction all the more challenging,” says Alex Prokhorov, M.D., Ph.D., professor of Behavioral Science.

A longtime advocate of anti-tobacco education for kids, Prokhorov developed “A Smoking Prevention Interactive Experience (ASPIRE)” in 2001. The evidence-based, online tool uses a video game-like format, graphics, animations and streaming video to teach teens about the dangers of tobacco and nicotine, and encourages them to quit smoking or, better yet, never start.

“It promotes itself because it’s so incredibly engaging,” says Prokhorov. “It’s full of activities – it’s a fun way to learn and we’re not surprised that kids like it.”

ASPIRE is taught in various schools in 33 states and 66 countries. A new agreement between MD Anderson and the Houston Independent School District makes the program available to all 110,000 middle school and high school students in the district.



Alex Prokhorov, M.D., Ph.D. photo by Wyatt McSpadden

The curriculum is available in English and Spanish through HISD’s online learning platform. It also is taught in required health and physical education classes across 46 HISD high schools.

ASPIRE has a track record of success. A 2008 study revealed that students participating in the program were three times less likely to start smoking than those who only received anti-tobacco literature.

“Students are privileged to receive this specific education directly from our local, world-renowned experts,” says Annie Wolfe, HISD’s officer for secondary curriculum. “The inclusion of relevant facts, such as the negative effects of vaping, not only better informs our students, but also educates many adults who believe the myth that these more modern practices are not as harmful.”

# A legacy of growth and progress



Charles LeMaistre, M.D., John Mendelsohn, M.D., and Ronald DePinho, M.D. — three of the four full-time presidents to lead MD Anderson — were on hand for the 75th anniversary gala. *photo by F. Carter Smith*

**R**onald DePinho, M.D., who in 2011 became the fourth full-time president of MD Anderson, stepped down from that role on March 8. He'll continue his work to end cancer by focusing his attention full time to translational research as a professor of Cancer Biology – a dual appointment he held throughout his presidency. During his tenure, DePinho recruited world-class researchers; fast-tracked the development of novel, more effective therapeutics for patients; and forged new collaborations with other institutions and hospitals. He also mobilized faculty and staff to effect significant change in the way teams work, research is enabled, and ideas are converted to new treatments and digital solutions. Under his leadership, MD Anderson also showed how knowledge and expertise can inspire health policies that seek to reduce cancer risk for young people.

DePinho's signature achievement was the 2012 launch of MD Anderson's Moon Shots Program™, bolstered by new philanthropy, grants and alliance revenues approaching \$1 billion dollars. The comprehensive assault on cancer has expanded to 13 areas of focus, with 10 enabling platforms. The initiative has inspired the White House Cancer Moonshot Initiative

(renamed the Beau Biden Cancer Moonshot under the 21st Century Cures Act) led by former Vice President Joe Biden.

#### Additional highlights of DePinho's administration include:

- Top ranking in cancer care in U.S. News & World Report's annual "Best Hospitals" survey
- Close working relationships with key world leaders to advance public health
- Enhancing research competitiveness, including five-fold increase in national academy members and doubling the annual funding received from the Cancer Prevention and Research Institute of Texas (CPRIT)
- Dramatic expansion of MD Anderson's knowledge dissemination across the nation and in many countries to elevate the quality of care and science
- Transformation of strategic industry ventures to secure significant revenue and increase clinical trials options for patients
- More than \$1.2 billion in private philanthropy over five years, including a record \$294 million in fiscal year 2016

DePinho is internationally known for a number of groundbreaking discoveries, most notably for shedding light on the link between aging and cancer. He is a fellow of the American Academy of Arts and Sciences and a member of the National Academy of Science and the National Academy of Medicine. DePinho will continue conducting translational research to make a meaningful impact in the clinic and advocating for cancer research funding and effective health policy as vice chair of ACT for NIH: Advancing Cures Today, a nonpartisan effort to increase support for biomedical research and restore funding to the National Institutes of Health. In addition, he will coordinate a global multi-sector effort to advance cancer care, particularly for the impoverished.

"A true visionary who kept an eye on the horizon and worked hard to shape a better future beyond it, Dr. DePinho remains a tireless advocate for patients and for MD Anderson," says Marshall Hicks, M.D., the institution's *ad interim* vice president. "As president, he helped us redefine what was possible. Dr. DePinho's positive impact on our institution and our nation will be felt for years to come."



## With zebrafish photos, a scientist earns his stripes as a photographer

When Oscar Ruiz, Ph.D., entered the 2016 Nikon Small World photomicrography contest, he won both the grand prize and international recognition. The winning image – a zebrafish embryo he took while researching epithelial tissues – also was chosen as the November 2016 cover of *Nature Methods*, and a second photo won the 2016 BioArt competition, hosted by the Federation of American Societies for Experimental Biology.

Ruiz, a senior scientist in Genetics, is on the cutting edge of both science and photography. Most researchers working with zebrafish only study the skin cells on their tails, but in the lab of George Eisenhoffer, Ph.D., assistant professor of Genetics, Ruiz developed a novel means of stabilizing the zebrafish embryos using a clear agar gel that allows researchers to see the development of epithelial cells on the head and face.

This new angle for photography has opened doors for new research collaborations. In addition to the study of cancer cell development, Eisenhoffer's lab is working with scientists at The University of Texas Health Science Center at Houston to learn more about the development of facial deformities such as cleft lip.

"I love science and learning new things, and photography and images really speak to me," Ruiz says. "It's great to be able to combine the things I love at work."

– Gillian Kruse



# prescription for normal

By Clayton Boldt, Ph.D.

A cancer diagnosis can generate a great deal of uncertainty.  
 How do I tell my family and friends?  
 What treatments will I have?  
 Can I still live a normal life?

“When they tell you that you have cancer, you’re in shock,” says Tammy Pedersen, who was diagnosed with breast cancer in November of 2014. Pedersen’s care team skillfully guided her through treatment, and her breast-conserving surgery and radiation were completed by the following February.

“I had a lot of faith in my doctors,” she says. “Everyone was so positive, I never felt down. “However, uncertainty doesn’t always pass when treatment is over.

“The down part came afterward. When I got home, I was up for a little while and then all of a sudden, I was scared,” recalls Pedersen. “There’s nobody there now to watch over you, and tell you what to do.”

Being a survivor requires creating a new definition of “normal,” which can often produce just as many questions as the diagnosis. At home in Louisiana, Pedersen took a hormonal therapy that, over the next several months, caused terrible hip and joint pain. She tried a few exercise classes, only to be left exhausted for hours afterward.

“That scared me,” she says. “I thought, ‘What’s wrong with me?’ I was scared to do anything else.”

Research shows that exercise can improve survivors’ quality of life and decrease the risk that cancer will recur. However,

the physical stresses coupled with mental anxiety about the cause of her pains led Pedersen to stop exercising altogether.

Then she met Susan Gilchrist, M.D., a cardiologist and associate professor of Clinical Cancer Prevention. Gilchrist runs MD Anderson’s new Healthy Heart program, which helps patients monitor and maintain heart health during and after cancer treatment through personalized, evidence-based exercise prescriptions.

“One of the things we have found, especially with breast cancer patients, is the leading cause of death in these patients is actually heart disease – not breast cancer,” says Gilchrist.

The first step in the program is a consultation with Gilchrist and an exercise physiologist to discuss the patient’s concerns, goals and needs.

“A lot of my patients are worried about their health after cancer. They don’t know what they can and cannot do,” Gilchrist says. “And so as a cardiologist, I can provide in-depth discussions regarding their heart health and the right amount of exercise for them.”

Participants then complete a cardiopulmonary exercise test. It’s similar to what professional athletes might do to optimize their training, complete with heart and oxygen monitors. This allows Gilchrist to assess the health of a patient’s heart and lungs, and objectively determine their capacity for exercise.





**Susan Gilchrist, M.D., heads the Healthy Heart program at MD Anderson. photo by Adolfo Chavez III**

“I want each of my patients to feel like they are a professional athlete in my program,” she says.

Pedersen was afraid she wouldn’t be able to complete the test, but she was surprised at her own abilities and reassured by the results.

“I never broke a sweat. I wasn’t breathing heavily. It just really surprised me. My heart and lungs came out great.”

Every cancer patient undergoes different treatments, and every individual has a different fitness history. Therefore, Gilchrist analyzes each patient’s current status and his or her needs going forward in order to reduce any existing heart-risk factors.

“It’s reassuring to patients to have an exercise test, review their heart health, and come up with a strategy and exercise training regimen that’s right for them,” she says.

Gilchrist’s prescriptions are tailored to meet the individual needs of each patient, whether that means more focus on weight loss or rebuilding muscle mass. Each prescription lists detailed goals for both exercise volume and intensity, and is based on regimens proven to be successful in prior scientific studies.

Gilchrist, a former collegiate and professional tennis player, has always been committed to maintaining peak physical fitness. She carried this determination with her into medical school when her tennis career was ended by a torn rotator cuff.

“I always had inspirations to be a doctor after my tennis career,” says Gilchrist. “Cardiology is a great fit for me. I became interested in cancer patients mainly because there was no one thinking about how they might be at risk for heart disease. I feel like I’m one of the few cardiologists in the country really pounding the cancer community about the need to keep hearts healthy, especially for breast cancer patients.”

Pedersen now completes 160 minutes of moderate-intensity cardio each week, in addition to three days of conditioning such as yoga or swimming. She bought a treadmill, which she uses daily, and does water aerobics in her pool with friends. After meeting Gilchrist just a few months ago, her energy and outlook have markedly improved.

“I feel positive,” says Pedersen. “I don’t feel like I’m in limbo anymore. I’m heading forward and leaving all that behind. I’m normal. It’s like they told me, ‘Yes, you’re normal!’”

# Preaching better health

By Clayton Boldt, Ph.D.

Local churches may seem like odd places to perform cancer research, but for Lorna Haughton McNeill, Ph.D., the pairing is only natural.

McNeill's life in the church began at an early age – her mother was a reverend in an American Methodist Episcopal Zion Church in New York City – and she's spent her entire life involved with predominantly African-American churches. So she's well accustomed to the congregations' close-knit, community-centered culture.

Therefore, when designing a program to engage African-Americans in cancer prevention research, it made sense to the chair of Health Disparities Research to partner with churches. That collaboration became the foundation of Project CHURCH (Creating a Higher Understanding of Cancer Research and Community Health) in 2008.

"Project CHURCH started to address a need for MD Anderson to have a tangible focus on the African-American community here in Houston," says McNeill. "African-Americans are an important population because of their high cancer incidence and mortality rates, as well as their relative population size here."

In fact, according to the American Cancer Society, African-Americans have the highest death rate and shortest survival of any racial or ethnic group in the U.S. for most cancers.

Project CHURCH began as a large-scale research study involving 2,500 church members from three congregations. It was designed to understand the social, environmental and lifestyle factors driving cancer risk among African-Americans – factors such as tobacco use, obesity, physical activity, neighborhood environment and social relationships.

At the same time, McNeill wanted to provide church members with opportunities to take part in activities that promote healthy living and lower cancer risk.

## From a project to a partnership

The effort has been tremendously successful, leading to the publication of roughly 20 scientific articles on cancer risk in the African-American population. Today, the program hosts a variety of initiatives involving over 80 churches in the greater-Houston area.

"The CHURCH partnership," as McNeill now likes to call it, is less about individual projects and more about symbiotic relationships that continually engage African-Americans in new research and educational opportunities.

"What we're trying to do is make it easier for MD Anderson to service the African-American community through these relationships," McNeill says. "For participants, it gives them an opportunity to be a part of the innovative studies trying to help people improve their lives."

Those research efforts include testing new and unique approaches to improving diet and exercise in order to promote weight loss and prevent obesity, which is a major risk factor for African-Americans.

Through a research study named Project FRESH (Food Resources Encouraging Sustainable Health), MD Anderson is combating the health problems associated with living in Houston's food deserts – areas without much access to healthy foods such as fresh fruits and



**Brenda Clayton heads the health and wellness ministry at Fountain of Praise Church.** photo by Wyatt McSpadden





**To combat the limited access to healthy foods within the food deserts that exist in parts of Houston, Project FRESH provides 30 pounds of fresh fruit and vegetables each week for eight weeks to members of New Faith Church.** *photo by Adolfo Chavez III*

vegetables. Members of New Faith Church in Central Southwest Houston who enroll in Project FRESH receive two free, 15-pound bags of fresh produce each week for eight weeks, as well as recipes and health tips. Produce is provided by Brighter Bites, a nonprofit organization that makes nutrition education and fresh fruits and vegetables available at schools in Houston, Dallas and Austin. The feasibility of implementation in churches was tested as well. McNeill is studying how this intervention improves church members' diet and well being.

To increase physical activity, she developed a mind-body exercise similar to yoga or tai chi. Church members have embraced it, and she continues to investigate how the activity is changing their behavior. She also created Move to Quit, a study designed to help African-Americans quit smoking through exercise.

### Help for survivors

Project CHURCH also is working across Houston to implement Active Living after Cancer, an evidence-based program that teaches survivors to increase their physical activity through simple lifestyle changes.

When approached with this program, Brenda Clayton's answer is a testament to the strength of relationships between MD Anderson and partner churches.

"When I knew that MD Anderson was involved, I knew we could not do anything but accept it," says Clayton, a retired MD Anderson nurse who leads the health and wellness ministry at the Fountain of Praise Church in Southwest Houston.

Rhonda Haralson, a Fountain of Praise member, decided to participate after treatment for early-stage breast cancer left her fatigued. Interested in being more active and reducing her risk of recurrence, the opportunity came at just the right time.

"I've definitely been more active and purposeful as far as setting a goal and doing something every day," says Haralson. "I think I'm more informed about my lifestyle and cancer risk."

More than that, though, Haralson says the program offers an opportunity to bond with other cancer survivors at her church.

"I didn't know any of these ladies before the sessions, but we'll have a bond going forward thanks to the program," she says. "It's helpful to bring spiritual life and healthy life all together."

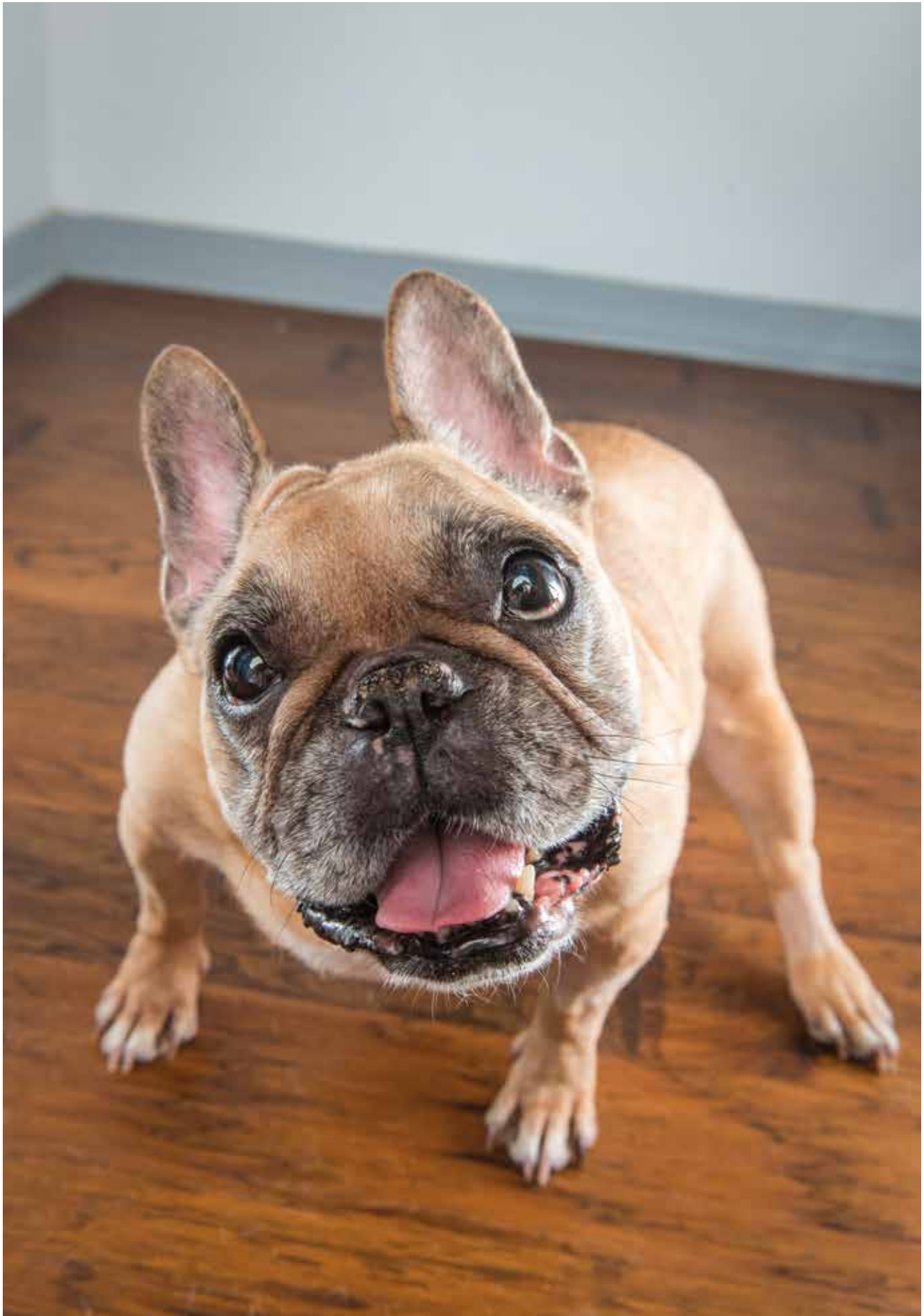
Clayton says there's an obvious role for church to play in members' spiritual and physical health.

"I think the church has to look beyond the spiritual needs," she says. "We have a lot of people with other concerns here, and they look to us for direction."

McNeill hopes to offer even more health-related programs to churches in the future. And, unlike most traditional health education efforts, these programs will be tested and proven to promote healthier lifestyles.

"Most people understand what they're supposed to do to improve their health, but they often don't know how to do it," says McNeill. "That's what we're doing through Project CHURCH. Trying to find innovative ways to help people do the things they want to do and reduce their risk of cancer."





# A dogged pursuit of aggressive brain cancer

**Dogs are helping researchers better understand the biology of brain tumors in hopes of developing better treatments for high-grade gliomas**

By Meagan Raeke  
Photos by Wyatt McSpadden

You probably wouldn't guess that Sadie Watson has much in common with anyone at MD Anderson. After all, Sadie is a 9-year-old French bulldog and beloved family pet.

But she's also facing the same diagnosis as many patients in the Brain and Spine Center: a brain tumor called a glioma.

It turns out that the same brain tumors that affect humans are found in dogs. Now, physician-scientists from MD Anderson and Texas A&M University are teaming up to help man and man's best friend.

## A common bond

Current therapies simply aren't very effective at treating extremely aggressive gliomas, such as grade IV glioblastoma, which spread quickly throughout the brain. And the survival rate is poor in both humans and dogs.

"We have the same struggles in that these gliomas in dogs are really hard to treat," says Jonathan Levine, D.V.M., professor and department head of Small Animal Clinical Sciences at Texas A&M College of Veterinary Medicine & Biomedical Sciences, where Sadie is a patient.

But scientists know tumors from both species look almost identical on MRI scans and under the microscope. And based on this, the National Cancer Institute (NCI) created a comparative brain tumor consortium in 2015 to evaluate canine brain cancer as a model for human disease.

"The big question is: 'Are human and canine high-grade gliomas genetically the same?'" says Amy Heimberger, M.D., professor of

Neurosurgery at MD Anderson and co-leader of the Glioblastoma Moon Shot™.

To find the answer, she's leading a multi-institutional NCI-funded study to characterize genetic alterations in canine glioma and identify immune responses in these tumors. Heimberger is also a dog lover, with a collie named Duke, a West Highland terrier named Winston and a long-haired dachshund named Millie.

Levine and brain tumor genomics expert Roeland Verhaak, Ph.D., professor and associate director of Computational Biology at The Jackson Laboratory in Connecticut, are co-investigators in the first-of-its-kind study. Levine has two dogs: Ramsey, a bloodhound; and Lucy, a border terrier. Verhaak has a Chihuahua named Lola.

Verhaak, a former associate professor of Bioinformatics and Computational Biology at MD Anderson, is currently analyzing data taken from whole-genome and RNA sequencing of 90 tissue samples from dogs with brain tumors. The long-term goal is to develop a safe and effective immunotherapy for both dogs and people with high-grade gliomas.

"These dogs, not only do they stand to benefit, but they represent an amazing opportunity to understand the biology of brain tumors, to understand how tumors evade drugs and to understand the immune response," Levine says.



**Kristin Patrick and her husband, Robert Watson, have two sons, but say Sadie was their “first baby.”**

### **A better model**

All new cancer drugs are tested for safety and effectiveness in the lab – often in engineered mouse models – before they are approved for clinical trials in humans or dogs.

“Pre-clinical studies can look fantastic in mice, but fall apart in humans,” Heimberger explains.

For a cancer like glioblastoma, which has a five-year survival rate of less than 10%, this is exceedingly frustrating.

“I want to reduce the cost and futility of clinical trials. When you have a patient facing something this dire, you want to offer them something with a good chance of success.”

The current model system is imperfect: Mice do not grow brain tumors on their own. Their tumors are small, sometimes microscopic. They live in a sterile environment. And their immune response is biased, making it difficult to accurately assess immunotherapies.

Dogs, on the other hand, spontaneously develop large brain tumors. They have a natural immune response to cancer. And they live in the homes of their human families.

### **A shared hope**

As Sadie’s owner Kristin Patrick says, “When you love a pet so much, they become part of your family.” Patrick and her

husband, Robert Watson, have two young sons, but Sadie was their “first baby.”

When Sadie was diagnosed in July 2016, Patrick and Watson decided she would undergo brain surgery to remove the tumor, donate the tissue for analysis and enroll in a clinical trial. Their perspective as parents and researchers (both are assistant professors in the Microbial Pathogenesis and Immunology department at Texas A&M Health Science Center College of Medicine) shaped the treatment decision.

“Participating in science is essential to move these therapies forward for families,” Patrick says. “If our actual baby had a brain tumor – I can’t even fathom that.”

As the researchers analyze tumor tissue samples from Sadie and other dogs, they will look for genetic mutations and immune responses known to occur in human brain tumors. If the results show that canine brain tumors are indeed a good model for human brain tumors, then clinical trials in man’s best friend could reveal which new immunotherapies have the best chance of success for humans.

“Cancer is horrible for anyone affected by it, whether that’s a dog or a person,” Levine says. “There’s a huge opportunity here to develop something that helps dogs and also helps people.”



# This puppeteer has a hand in answering questions, easing anxieties and preventing bullying

By Katrina Burton



**Pediatric education coordinator Kris Frost with a puppet that depicts neurofibromatosis.** photo by Nick de la Torre

**A**s new therapies offer better survival rates to children with cancer, some are returning to school in the midst of treatments.

They're sometimes met with stares, finger-pointing and blunt questions from classmates who have never seen chemotherapy-induced hair loss and other visible side effects of surgery and cancer-fighting drugs.

Kris Frost, a pediatric education coordinator at MD Anderson Children's Cancer Hospital, uses puppets to help ease cancer patients' return to school. Each mirrors a side effect of cancer, including hair loss, limb loss, or the need for a walker or wheelchair. With puppets in tow, Frost visits classrooms to help students understand cancer and accept their fellow classmate who looks different.

"Teasing and tormenting are usually caused by fear," Frost says. "Once we educate children and eliminate their fear, the teasing goes away."

The newest puppet depicts neurofibromatosis, an unpredictable, progressive disorder that causes tumors, sometimes disfiguring, to form anywhere in the body. Most of the tumors are benign, but about 7 to 10% become cancerous. MD Anderson's Neurofibromatosis Clinic treats children and adults who have the disease.

For help in drafting puppet show scripts that educate classmates, teachers and school administrators about pediatric cancers and related conditions like neurofibromatosis, MD Anderson enlisted drama students from Lamar High School in Houston. A question-and-answer period follows each production.

"Puppets are friendly and non-threatening, and a great way to get messages across to children," says Frost, one of two staff members who deliver the shows, which

are hosted by MD Anderson's Pediatric Education and Creative Arts Program. She also counsels about 50 patients and families each month, and meets with school administrators and teachers to pave the way for cancer patients' smooth re-entry into the classroom.

"Many of the kids I see are anxious about academics and relationships at school. Some have even been bullied," Frost says. "It's my mission to help each one resume a normal life with lots of love and support."

# Student counsel

Support group helps first-gen grad students who also were first-gen college students navigate the world of higher education

By Ronda Wendler *Photos by Wyatt McSpadden*

Jolie Schafer vividly remembers her close childhood friend battling cystic fibrosis, a genetic disease that clogs the lungs with mucus and damages other vital organs.

“He was in and out of the hospital a lot,” Schafer says. “His lungs collapsed several times, and he almost died.”

But in 2004, when Schafer was 13, her friend, Chase McGowen, became the first person in Texas to undergo a lifesaving double-lung and liver transplant. Today he lives in Austin and is doing well.

Schafer credits Chase’s story with piquing her interest in science and inspiring her to pursue a career in medical research.

“I want to contribute to finding cures for diseases that cut lives short and cause people to suffer,” she says.

This fall, Schafer will graduate with a Ph.D. from The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences. Jointly run by MD Anderson and The University of Texas Health Science Center, the school offers graduate-level degrees to those preparing for careers as biomedical scientists. Schafer is a student in the Immunology Program and specializes in “natural killer cells,” which destroy tumor cells while sparing healthy ones. (See more on Page 24.)

## Charting new territory

But attending college after high school wasn’t a “given,” Schafer says. Tuition was steep, and she worried about burdening her mother, a hairdresser, and father, an IT consultant for a state agency.

“My parents wanted the best for me and were very supportive of me going to college,” she says, “but I didn’t want to load them down with debt.”

An athletic scholarship to play volleyball at Houston Baptist University paid for her undergraduate education and lessened financial worries. But out-of-town games sometimes forced her to miss classes.

“I had to work twice as hard to teach myself the material I missed,” she says.

Several of Schafer’s professors were impressed by her dedication and encouraged her to apply to graduate school.

“They helped me realize my potential,” she says. “No one else in my family had attended college, so I was charting new territory, and that can be intimidating.”

Schafer excelled academically, and this year was awarded a public policy fellowship from the Archer Center, which serves as the Washington, D.C., campus of The University of Texas



**Jolie Schafer**

System. As a fellow, she’ll spend the summer learning how science and government work together to improve human health.

“Navigating the world of higher education hasn’t always been easy,” she says. “My parents couldn’t offer advice because college was unknown to them, but they always cheered me on.”

## Firsthand knowledge

Graduate School faculty member Melinda Yates, Ph.D., knows firsthand the obstacles first-generation students like Schafer face.

Yates and her identical twin sister are the first in their family to attend college. Growing up in rural Indiana surrounded by “lots of corn and cows and not much else,” Yates says, motivated the sisters to broaden their horizons. Both earned Ph.D.s and now work in academia. Yates is an assistant professor of Gynecologic Oncology and Reproductive Medicine at MD Anderson who conducts research to prevent and treat uterine and ovarian cancers. Her sister is an academic and career advisor for science students at a university in Oregon.

## Shared experiences

In undergraduate and graduate school, Yates noticed that the obstacles confronting first-generation students like herself were different from those encountered by more privileged peers.

Some “first-gens” as they are called, felt isolated and pulled between two worlds – the one in which they grew up, and the academic world in which they now resided. Many felt lost in school, where it seemed everyone but themselves knew the unwritten rules. A distinct feeling of “otherness” made them hesitant to ask for help and guidance – doing so would reveal they didn’t belong.

Further challenges awaited first-gens who pushed forward to grad school.

“Biomedical science Ph.D. students are tasked not only with the academic rigors of advanced coursework and scientific writing,” Yates says, “but also with social and cultural dilemmas like finding trusted mentors, learning the academic research language or even knowing how to dress while attending national scientific conferences.”

Some first-gens, Yates remembers from her student days, wrestled with “breakaway guilt,” worrying they’d abandoned their parents or siblings who counted on them. Most families didn’t comprehend the college experience, much less the intricacies of a Ph.D. program. Parents expressed pride that their children were excelling, even though they didn’t understand their field of study.

Perceived as different by family members at home and poles apart from classmates at school, some first-gens Yates knew weren’t sure where to turn for support. She wondered, “What would it take to change that?”

## Group support

The answer came four years ago when she formed the GSBS’s First Generation Student Group. The organization serves as a peer community where first-gens engage in frank discussions about the challenges they face, and together navigate the rigors of higher education.

“Being a first-generation student hasn’t always been easy, but the First Generation Student Group has given me the confidence and reassurance I need to succeed,” says Schafer, the group’s president.

Faculty members and biomedical science leaders from industry, government and academia often attend meetings to help students professionally network and explore career paths.

“It’s a ‘holistic advising’ approach,” Yates says, “where students learn to overcome academic obstacles, gain life-management skills like financial planning or stress management, celebrate their successes and embrace their first-gen identity.”

First-gens are not all the same, she says, but instead cut across all racial, ethnic and socioeconomic lines. All, however, benefit from mentoring and communing with others.

“They may not know which professional societies to join, how to present research at an academic conference, or even how

graduate school works in general,” Yates says. “Mentors can help them figure it out.”

The graduate school’s dean, Michelle Barton, Ph.D., is herself a first-generation student. She grew up on an Illinois farm, working outside and driving a tractor. When she first arrived at college, she felt like “a fish out of water.”

“There’s so much value in making connections with other first-gens and having a network of people who understand your struggles,” says Barton, a professor of Epigenetics and Molecular Carcinogenesis.



**Melinda Yates, Ph.D.**

## Flip side

Yates points out that first-gens aren’t less-than or lacking in any way. They’ve simply racked up a different set of life experiences than their non-first-gen counterparts.

“Those experiences,” she says, “are equally valuable and build character.”

With their backgrounds of hard work, financial discipline and fierce independence, first-gens are driven and determined.

“They’ve had to figure things out, do things for themselves, and help support their families,” Yates says. “That’s made them strong. They’ll stick it out when the going gets tough.”

That “grit” is exactly what employers and university admissions committees want to see. Casting adversity on one’s résumé as a skill-building asset is a new, upbeat take on the first-gen identity – one that highlights their resilience and adaptability.

“There’s a flip side to everything,” Yates says.



# First in their family



## **Benjamin Lopez**

*second-year Ph.D. student in Medical Physics*

**Benjamin Lopez was an intensely curious child who spent most of his time reading and learning. He excelled in primary school in Mexico.**

“My family congratulated me on every achievement,” he says, “so I was driven to succeed in school and make them proud.”

After his family moved to Louisiana, Lopez enrolled in the Louisiana School for Math, Science and the Arts, a charter school that Lopez says “had an amazing faculty and a breadth and depth of courses I’d only dreamed of.”

After graduating, he attended Rice University, where he earned a Bachelor of Science degree in bioengineering.

Lopez says he chose to work in the biomedical field because of its benefit to society, a “give-back” mentality shared by many first-gen students.

“I have been blessed with the opportunity to make a difference, and it would be irresponsible to not see it through.”

And he’s grateful to be a grad student.

“I’m getting paid a stipend to learn and explore and help others,” he says. “How amazing is that?”



## **Luisa Coronel**

*second-year Ph.D. student in Experimental Therapeutics*

**As a first-generation Mexican-American graduate student, Luisa Coronel is proud to be a role model.**

“I want to show people like me that they can reach their goals if they’re ambitious and persistent,” she says.

Coronel earned her bachelor’s degree in chemistry at the University of California, San Diego. While there, she participated in the Initiative for Maximizing Student Development Program, which helps students from disadvantaged economic and social backgrounds transition from undergraduate to Ph.D. programs in science.

“Without that program, I wouldn’t have known how to apply for graduate school or who to ask for help,” she says. “I wouldn’t have had the opportunity to work in a lab and gain the crucial experience needed for acceptance to graduate school.”

But when she arrived at grad school, Coronel quickly realized she’d taken an alternate route compared to most of her peers.

“I didn’t meet many people who shared my experiences,” she says. “The First Generation Student Group helped me know I wasn’t alone.”

Today Coronel is an officer in the Association for Minority Biomedical Researchers, “because it’s important to give back and support diversity in science,” she says. After graduation, she plans a career in higher education.



## **Cavan Bailey**

*third-year Ph.D. student in Experimental Therapeutics*

**Cavan Bailey was raised by a single mom in a working-class New Jersey neighborhood.**

“It was pretty rough,” he says. “We lived paycheck to paycheck. Sometimes we relied on welfare and unemployment benefits.”

Determined to create a different life after high school, Bailey enrolled in community college and later graduated from Rutgers University with a bachelor’s degree in neuroscience.

To pay for his education, he sought financial aid, won scholarships and did without “extras.”

“It was challenging,” he says, “but I made it.”

Now he’s pursuing a doctorate degree and, after graduation, plans to work for a pharmaceutical or biotechnology company researching new therapies for brain tumors.

Bailey remembers the learning curve he experienced as a new grad student. Today, he serves as a mentor for incoming students, helping them tackle the issues he’s already faced: financial struggles, “fitting in” with the academic research culture, becoming and remaining a successful student, and choosing a career path.

He also mentors undergraduate students who participate in the graduate school’s summer workshops and programs, and offers advice on how to apply to graduate school.

“I appreciate the people who’ve helped me along the way,” he says, “and I’m grateful I now can help others.”

# What I did on my summer vacation

Reaping the rewards of volunteering

By Lany Kimmons



**As part of his volunteer experience, Bovey Liu played piano for patients and visitors at MD Anderson.** *photo by Wyatt McSpadden*

**M**ost teens spend their summers by the pool, playing video games or working a summer job. At MD Anderson, 25 teens spent four weeks of their summer volunteering as part of the Teen Volunteer Leadership Program in Cancer Care.

MD Anderson always has a large number of volunteers assisting patients and caregivers. But during the summer, more young faces in blue jackets are seen, as teens between the ages of 14 and 18 from more than 15 Houston-area schools volunteer in various positions around the hospital.

“Becoming a volunteer at MD Anderson is one of the best experiences anyone can ever have,” says Bovey Liu, a 15-year-old student at Carnegie Vanguard High School. “Volunteering and helping others are one of the best ways to leave everyone smiling.”

The program requires a big commitment from the teens, who participate in one of two, four-week sessions in which they work eight-hour shifts in four volunteer positions. Their time is spent in the retail gift shops or Appearances, a specialty shop that serves the distinctive needs of cancer patients. Each teen is paired with an adult volunteer to work in a clinic. Other positions include patient navigator, coffee cart, hat cart, popcorn cart and the rose garden program.

While Liu enjoyed all his positions, his favorite was the rose garden program, where he would cut flowers from the cancer center’s rose gardens and deliver them to patients’ rooms. He found that the rose deliveries could bring a smile to any patient’s face. He also got the chance to use his 10 years of piano experience by playing for visitors.

Lydianne Juguilon, a 17-year-old student at Incarnate Word Academy, found the hat cart to be the most gratifying volunteer position. She enjoyed the meaningful conversations she had with patients and their families while handing out free hats, scarves and pillows.

“The stories they’ve told us about their lives are amazing,” Juguilon says. “Patients have opened up to us. Some have asked for a hug, others have asked for a prayer for their family. You get to connect with people on a very personal level.”

# A recurring nightmare

By Ronda Wendler  
*Photos by Wyatt McSpadden*



**Crystal Gully**





More than 30 years after she was declared cancer free, the disease came back. So she returned to MD Anderson where she beat the odds once before.

When 9-year-old Crystal Gully twisted her arm during school recess, the pain was intense.

“I thought the ache would subside,” says Gully, now 44, “but it got worse each day.”

Gully’s parents took her to the family doctor, who ordered X-rays. The result? No fractures. The third-grader’s arm was likely sprained, the doctor said, and would heal with time.

But her pain persisted, and Gully’s parents sought a second opinion. This time, the doctor ordered a blood test.

“He opened the results and his face just fell,” Gully recalls. “He told my parents, ‘This is not what we expected.’”

Gully was diagnosed with acute lymphoblastic leukemia, or ALL, the most common childhood cancer. The disease originates in the bone marrow where blood cells are made, and bone pain is a hallmark symptom.

The family was stunned. After leaving the doctor’s office, they stopped at a roadside diner for refreshments and to gather their thoughts.

“We decided MD Anderson was my best hope,” Gully says.

That evening, they boarded a plane and flew from her hometown of McAllen, at the southern-most tip of Texas, to Houston.

**Three little words**

At MD Anderson, more bad news followed. Gully’s disease had advanced. She wasn’t expected to live more than a few weeks.

But a young doctor named Lawrence Frankel offered a glimmer of hope. A new trial for pediatric leukemia patients was launching, and he invited Gully to participate.

Children who enrolled in the study would receive three powerful chemotherapy drugs injected directly into the spine, in addition to traditional chemo delivered through an arm vein.

Frankel offered no guarantees, but said it was worth a shot.

It worked. After two years of treatment, Gully was declared cancer free at age 11.

“I went home to south Texas, and picked up where I left off,” she says. “Life became normal again.”

Gully grew up, married, and gave birth to three healthy children, defying doctors’ predictions that harsh cancer treatments might leave her unable to conceive.

Life was good, and cancer was a distant memory until December 2015, when Gully, then 42, was awakened by excruciating chest pain at 2 a.m.

“I thought surely I was having a heart attack,” she recalls.

Doctors at her local hospital found that Gully hadn’t suffered a heart attack, but instead a pulmonary embolism — a potentially deadly condition that occurs when a blood clot becomes wedged inside an artery in the lungs. Blood flow is restricted, and the heart pumps harder and faster in a futile effort to get blood to the lungs. Sometimes a heart attack occurs.

The emergency room doctor recited a number of reasons pulmonary embolisms arise, including cancer.

“He explained that tumor cells increase clotting substances in blood,” Gully says, “so blood clots may signal cancer.”

To rule out the disease, the doctor ordered a blood test. A normal white blood cell count is 10,000. Gully’s was 48,000.

“I instantly knew what that meant,” Gully says. “I’d seen those numbers when I fought leukemia as a child.”

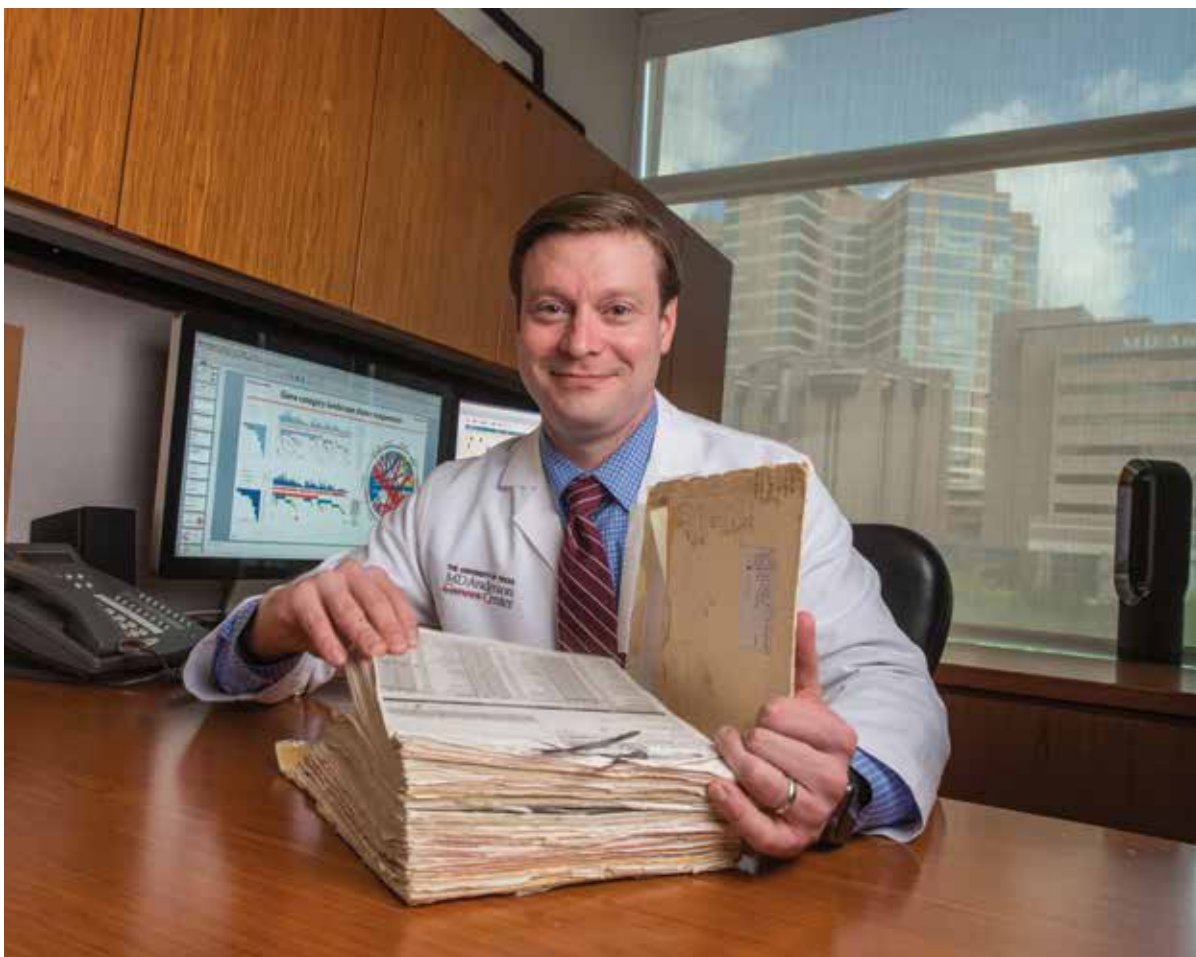
The doctor confirmed what Gully already knew.

“You have cancer,” he said.

“Those three little words are no less terrifying the second time around,” Gully says. “I was shocked. Fighting cancer again wasn’t in my plans.”

**Medical detective**

Remembering how she beat the odds 33 years ago, Gully headed back to MD Anderson, where a bone marrow test confirmed she had acute lymphoblastic leukemia, the same diagnosis as last time. Once



**Christopher Benton, M.D., who treats Crystal Gully, tracked down her 500-plus page medical file from 1982.**

again she was poised at the starting line of another cancer marathon.

“Wouldn’t it be nice if cancer were a one-time experience?” asks Christopher Benton, M.D., who became Gully’s leukemia specialist after she was admitted two years ago. “When your

Knowing the answer to this question would guide her treatment the second time around.

Like a medical detective, he ordered Gully’s 1982 medical file from an offsite facility where MD Anderson’s archived records are stored. The 500-plus page document was assembled long

before the days of computerized records. It contained hundreds of handwritten notes by teams of doctors who meticulously documented every detail of Gully’s pediatric treatment. Benton read the

well-worn chart cover to cover, seeking similarities that might prove Gully’s two cancers were related.

But the one piece of information he most hoped to find was missing. Benton wanted to know if Gully’s childhood cancer contained a genetic rearrangement called the Philadelphia chromosome, where parts of chromosomes 9 and 22 break off and switch places. The changed chromosome 22, named for the city where it was first discovered, is linked to a particularly aggressive form of ALL.

Benton already knew Gully’s adult cancer contained the Philadelphia chromosome. A test named FISH (fluorescence in situ hybridization), which detects chromosome rearrangements, confirmed its presence in her bone marrow.

**“When I was little, I was terrified of needles. This time, I was terrified I wouldn’t live to see my children grow up.”**

*– Crystal Gully*

treatment is finished, you can say you’d been there, done that and you’ll never do it again.”

Unfortunately, compared with someone who has never had cancer, a person who survives the disease once is more likely to get sick again, says Benton, an assistant professor of Leukemia.

Some people experience a recurrence of their original cancer when a rogue cancer cell escapes detection and re-emerges from hiding months, years or even decades later. Other survivors are dealt a second cancer down the road, unrelated to their first.

Benton’s challenge was to figure out if Gully’s second leukemia was a recurrence of her first, or a totally different cancer.

But the FISH test didn't exist when Gully first had cancer in 1982. A less-sophisticated technique was used to identify the Philadelphia chromosome back then, but in Gully's case, it didn't work.

"I wanted to perform the FISH test on her childhood tumor if we could locate her original biopsy slides," Benton says. "DNA is very robust. It doesn't easily degrade over time, so I had every reason to believe the test would work."

But where should Benton look for the 33-year-old, long-forgotten slides? Were they discarded years ago, or did they still exist? Benton searched the Internet for Dr. Frankel, Gully's pediatric oncologist. He found the now-retired doctor living in North Carolina, and called him.

Frankel clearly recalled that patients' slides were archived during his tenure at MD Anderson, but he couldn't remember where. Benton queried Leukemia Chair Hagop Kantarjian, M.D., who's worked at MD Anderson since 1983, along with other veteran faculty members. With their help, he tracked Gully's slides to a warehouse in west Houston where tumor samples from MD Anderson patients dating back to the 1950s are housed.

Historical slides aren't in demand, Benton says, so the warehouse has largely fallen from memory. He's delighted to know it exists.

"I feel like I've uncovered an archaeological treasure," he says.

### Lightning and lasers

With Gully's slides in hand, Benton consulted Carlos Bueso-Ramos, M.D., Ph.D., an MD Anderson professor who specializes in hematopathology – the branch of pathology that studies diseases of the blood and bone marrow.

Bueso-Ramos is an expert in using a laser to precisely cut cancer cells away from the slides on which they're mounted – a technique known as laser microdissection technology. The cells are then dropped into a collection tube for DNA sequencing, which can distinguish one type of cancer from another and identify cancers that are related. Before the development of this technology, there was no way to get cancer cells off slides, or to separate them from surrounding cells.

"Tumors are a complex mix of cancer cells and noncancerous ones. Laser capture microdissection uses a laser to cut out pure cancer cells from each tumor," Bueso-Ramos explains. "The technique also allows researchers to analyze each cancer cell in unprecedented detail, measuring the genetic changes that occur during the development of the disease."

Using this technique, MD Anderson scientists sequenced Gully's childhood tumor and her adult tumor to see if they were related. They were not. Benton will confirm the initial findings with another test, but says, "We now suspect Crystal Gully had two unrelated cancers. Lightning struck twice."

### God and good medicine

Gully's story is not uncommon. Of the 1.6 million people diagnosed with cancer this year in the United States, one in six will have already battled a different cancer, according to the National Cancer Institute.

It's a cruel encore, like surviving a hurricane, only to be swept away in a flash flood. It's also becoming more common. The odds of developing a new cancer are double what they were 25 years ago, Benton says. The blame is mostly pinned on better treatments keeping survivors alive longer to run the risk of getting cancer again. Not to mention that, in general, the older a person gets, the greater their risk of cancer.

"Most survivors will never get a second cancer," Benton says. "Research suggests that, in general, a survivor's risk of getting a new cancer diagnosis is 14 percent greater than the risk for someone who has never had cancer."

Today, Gully is in complete remission, with the aid of targeted therapy drugs like Gleevec, Sprycel and Iclusig, which block the growth of the aggressive cancer cells that are the hallmark of Philadelphia chromosome-positive leukemia.

Such drugs didn't exist when Gully fought cancer the first time.

"My survival is a miracle of God," she says, "and good medicine."

## Reunited, after 33 years

Amous Jones was working in MD Anderson's Laboratory Services Department when the phone rang.

"You may not remember me," said the voice on the other end of the line. "It's been a long time."

Instantly, Jones knew it was Crystal Gully.

The pair first met in 1982, when Jones was a young phlebotomist newly trained in the art of drawing blood, and Gully was a 9-year-old undergoing leukemia treatment.

The two formed an immediate bond, so strong that Gully would allow only Jones to draw her blood.

"We just clicked," Gully says. "Amous was always upbeat and happy, like a ray of sunshine."

Jones remembers Gully's dazzling smile and zeal for life.

"That precious child had such a sweet spirit and outgoing personality. She never complained, even when she wasn't feeling well."

After Gully beat cancer and was discharged, the two remained pen pals for years.

The pair reunited 33 years later when Gully called Jones from an upstairs hospital room after she was re-admitted with a second cancer diagnosis.

"I bolted out of my chair and ran upstairs to see her," says Jones, who now heads MD Anderson's phlebotomy training program. "What a reunion we had!"

They hugged and cried and reminisced, and vowed to never lose touch again.





*photo by Wyatt McSpadden*



# Rotationplasty turns an ankle into a knee

By Katrina Burton

Thanks to an innovative surgical procedure, a young bone cancer survivor can still ride a scooter and jump rope, and is looking forward to playing softball

When 10-year-old Elise Robinson felt pain in her right knee three years ago, her pediatrician thought it was growing pains.

But the pain persisted, so Elise and her parents visited an orthopedic surgeon. Scans revealed a tumor in her right tibia, the larger of the two bones between the knee and the ankle. A biopsy confirmed the tumor was an osteosarcoma – the most common type of bone cancer in children.

Elise and her family made their way to the MD Anderson Children's Cancer Hospital, where they met orthopedic oncologist Valerae Lewis, M.D. Lewis proposed a procedure called rotationplasty to remove Elise's cancer while preserving her mobility.

To perform the procedure, surgeons remove a portion of the upper leg, the knee and several inches below the knee to ensure all cancer cells are excised. Then they rotate the remaining portion of the lower leg 180 degrees and attach it to what's left of the upper leg. The rotated foot is now on the same plane where the knee used to be, with the toes pointing backward and the heel facing frontward.

"In this rotated position, the ankle acts like a new knee joint," says Lewis, chair of Orthopaedic Oncology.

The foot fits down into a prosthetic leg. Essentially it turns an above-the-knee amputation into a below-the-knee amputation and affords the patient better control, function and mobility.

"The aim of the surgery is to offer patients the best possible functionality," Lewis says. "Most patients eventually will be able to walk unaided and return to the sport of their choice."

Elise's mom, Jennifer, at first was hesitant to agree to rotationplasty.

"I was concerned about how people would react if they saw Elise without her prosthesis," says Jennifer. "I thought about the stares



Senior physical therapist Alexander Penny played a big part in Elise Robinson's recovery following rotationplasty surgery.

and questions from friends and family, and especially strangers."

Elise, however, wanted to give it a try. She likes playing sports, and rotationplasty would allow her to remain active.

"Most sports are possible," Lewis says, "especially those where knee motion is important, such as bicycling, skating and soccer."

Elise's other two options were an amputation or limb salvage – a surgical procedure that replaces a diseased bone with a replacement constructed from a metal implant, a bone graft from another person, or a combination bone graft and metal implant. Neither would allow Elise to remain as active as a rotationplasty because both rule out participation in high-impact sports. In addition, limb salvage would require Elise to undergo several more operations in the

future, while any further surgery is rare following rotationplasty.

Elise's treatment was aggressive. She underwent chemotherapy for 10 weeks before surgery and 20 weeks after surgery, as well as a year of healing before she was able to wear her prosthetic leg.

She now walks unassisted, and with physical therapy soon will be running. Brimming with confidence, she's looking forward to taking the field for softball this fall, plays double bass in her school's orchestra and walks the runway at the annual back-to-school fashion show hosted by MD Anderson Children's Cancer Hospital and the Galleria.

"Elise is extremely proud of her prosthetic leg and shows it off whenever she has a chance," boasts her mom.

# UTILIZING THE BODY'S NATURAL BORN KILLERS

Unique access to cord blood gives MD Anderson cancer experts a big advantage in harnessing and using these immune cells against the disease

By Scott Merville  
Photos by Nick de la Torre

**N**atural killer cells sound menacing, but they play a friendly role in keeping us healthy. And they might do much more in stopping cancer.

After years of diligent, groundbreaking research, MD Anderson physician-scientists are putting natural killer cells – NK cells for short – to work in a series of clinical trials for a variety of cancers through the cancer center's Moon Shots Program™.

“These white blood cells are the scouts, the sentinels of our immune system,” says Elizabeth Shpall, M.D., professor of Stem Cell Transplantation and Cellular Therapy.

They're constantly surveying our bodies for invading microbes and abnormal cells – the type that can become cancer if they aren't already. Equipped with an array of detection techniques, natural killers also are heavily armed to deal with the threats they discover.

“They're poised to kill. They can kill over and over again,” says Katy Rezvani, M.D., who is also a professor in the department. “That's why we're trying to harness them for cancer immunotherapy.”

To do that, Shpall, Rezvani and their colleagues have been systematically identifying and overcoming disadvantages that hinder NK cells as cancer-fighting tools.

High on the list: There aren't enough of them – they make up only 10% to 15% of our blood cells – and they don't persist, lasting only two to three weeks. And perhaps most importantly, by the time a patient's cancer has matured, it's already evolved ways to evade that patient's NK cells, so cells from a donor are required.



**Natural killer cells are gathered from units of umbilical-cord blood such as this one.**







**Daniel Esqueda, senior clinical cell therapy specialist, retrieves frozen cord blood to be thawed for natural killer cell production when a patient is scheduled for treatment.**





**A technique pioneered at MD Anderson almost 10 years ago makes it possible to greatly increase NK cells in the lab.**

**Enter umbilical cords**

To get donor cells, Shpall and her colleagues have tapped a resource that's unique for a cancer center, an umbilical-cord blood bank. MD Anderson's was established as a source of blood stem cells for patients with certain blood cancers. Today, the bank stores 27,000 units of cord blood cells donated by mothers from Houston-area hospitals.

This resource means there's no need to search for donors willing to go through safety screening and cell collection. Another advantage:

The cord blood units have been thoroughly analyzed, so it's simple to select a good match with high potential for expanding in the lab.

To increase the supply of cord blood NK cells, Shpall's team applies a technique pioneered by researchers in MD Anderson's Pediatrics department nearly a decade ago for patients needing their own supply of stem cells expanded. The technique makes it possible to isolate and stimulate the NK cells in the lab, increasing their numbers 200- to 500-fold.

These NK cells can be given to patients without fear of dangerous side effects like graft vs. host disease. NK cells have been given to hundreds of patients, and so far there have been no toxicities.

"With the cord blood bank, we can have off-the-shelf products, NK cells that can be given to patients without a need to individualize them," Rezvani says.

Having overcome two major barriers – the need for donor cells and lots of them – the team now is working on ways to genetically modify NK cells so they last longer, even though cord-blood-derived NK cells provide some improvement in lifespan.

And the team is looking to add specialized receptors to identify and destroy specific targets.

"Some tumor types are more resistant to NK cells than others, and our preclinical models show that adding one of these receptors to NK cells makes those cancers more sensitive to NK cells," Rezvani says.

**Clinical trials underway**

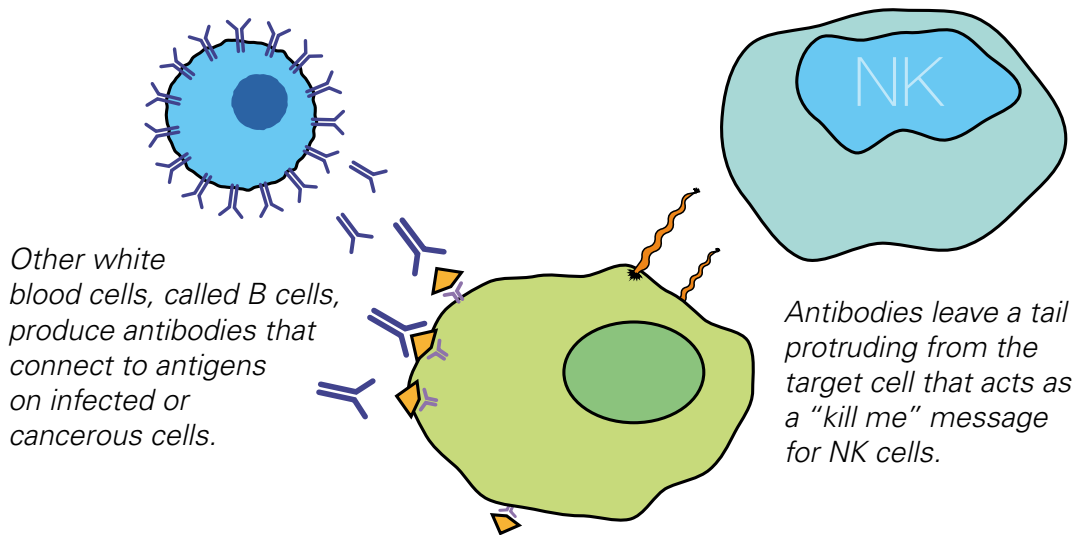
Five clinical trials at MD Anderson deploy NK cells against Hodgkin and non-Hodgkin lymphoma, several types of leukemia, myelodysplastic syndrome and multiple myeloma.

Three of the trials administer NK cells from cord blood in conjunction with transplants using blood stem cells from donors.

THREE WAYS  
NK CELLS  
TRACK DOWN  
ENEMY CELLS

1

**HOMING IN ON ANTIBODIES**



“NK cells are the first cells to recover after a blood stem cell transplant, and many studies show NK activity prevents disease relapse,” Rezvani says. So adding cord blood NK cells is a logical attempt to strengthen transplants.

A fourth trial, for multiple myeloma, combines an infusion of cord blood NK cells with an autologous transplant, in which a patient’s own blood is used.

“Autologous stem cell transplants can result in prolonged remission for some patients, but they aren’t curative,” Shpall says. “If we add cord blood NK cells to the stem cell transplant, maybe we can break that barrier. The same applies to our acute myeloid leukemia studies.”

Early results in the multiple myeloma trial showed that NK cells took hold and were well tolerated by patients; however, the impact on remission and survival remains to be seen.

The fifth trial combines NK cells with chemotherapy and an immune-altering drug called lenolidamide in a variety of blood cancers.

Rezvani and Shpall expect NK cells to be deployed against solid tumors as well, with the first trial planned against glioblastoma multiforme, the most common and deadliest of brain tumors.

To further extend the reach of this approach, MD Anderson has signed agreements with three pharmaceutical companies to test its NK cells in combination with the companies’ own experimental therapies.

NK cells remain in the early stages of development as a cancer treatment. While others also are studying these cells, MD Anderson has unique advantages.

## MOON SHOTS AND NK CELLS

Shpall is co-leader of the Adoptive Cell Therapy Platform™ of MD Anderson’s Moon Shots Program™ to reduce cancer deaths by accelerating development of therapies from scientific discoveries.

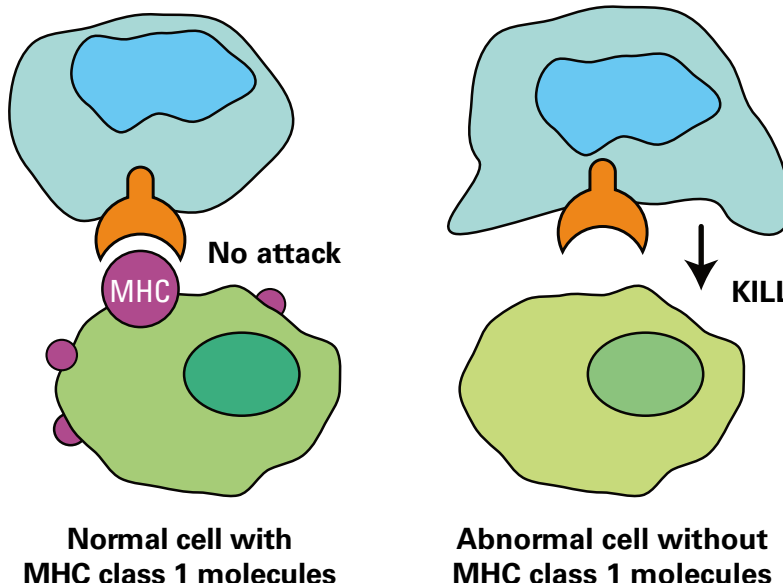
The platform provides NK cell and T cell therapies to the individual Moon Shots. Those currently using NK cells in clinical trials and those that have studies planned include:

- Acute Myeloid Leukemia/Myelodysplastic Syndrome Moon Shot
- High-Risk Multiple Myeloma Moon Shot
- Chronic Lymphocytic Leukemia Moon Shot
- B Cell Lymphoma Moon Shot
- Glioblastoma Moon Shot

2

### CHECKING IDs

Normal cells have MHC class 1 molecules on their surface. Cancer cells do not. Without these molecules, the disease is invisible to T cells. NK cells, on the other hand, kill cells that lack these molecules.



3

### SNIFFING OUT STRESS

Even cancer cells without antibodies attached and an intact MHC1 complex can express various “stress” molecules that mark them for NK attack.

# In life and in the lab, he never gives up

By Ron Gilmore  
Photo by Nick de la Torre



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**L**ife in the small village in southeast India where Sendurai Mani, Ph.D., grew up had remained unchanged for many generations.

There was no hospital – there still isn't, few people were educated past the sixth grade, and running water and electricity were luxuries that existed only in dreams.

Mani's village of Sendurai is in Tamil Nadu, literally "land of the Tamils," a state replete with an abundance of natural and man-made wonders. The monsoon-fed region features the Pillaiyarnatham rainforest near Sendurai, tiger and elephant reserves, endless beaches, prehistoric dinosaur nesting areas and soaring ancient Hindu temples – many which are UNESCO World Heritage Sites. Mani's world, however, revolved around his parents' subsistence lifestyle.

"We had no expectations. We had no money. So we accepted what we had," he says.

Acceptance included having just one name, common in parts of rural India. It wasn't until he was much older that he took the name of his village as his given name. In his youth he was simply Mani.

Sleeping outdoors on a woven mat with his brothers was an accepted part of life as the son of a peanut farmer whose one acre also supported rice paddies, a milk cow, and a family destined to follow in the subsistence farming lifestyle that was the only world Mani knew.

"You see when it rained, we had to go indoors, and there was no place to sleep so we stayed up," explains Mani, who is now an associate professor of Translational Molecular Pathology and renowned for his work on cancer metastasis.

## **A head for problem solving**

When Mani completed sixth grade, his parents took the unusual step of allowing him to pursue an additional four years of education in the nearby town of Melur, accompanying his Uncle Palanisamy, who would prove to be a constant mentor in the years ahead.



## Mani's on a mission

“In my village, if you fail in school, there is no going forward to further education. Fortunately, I did not fail,” Mani says, flashing an infectious smile.

In Melur, Mani was introduced to the English alphabet, but found using English in addition to his native Tamil to be challenging. He didn't let that stop him. His parents' wishes, however, were another story.

“At the end of 10th grade, my parents said ‘OK, you're done with your education. It's time to come home to the farm,’” Mani recalls.

With no money for further schooling, he returned home. Once again, his uncle stepped in with an offer to help him continue his education in Chinnalapatti, where Mani hoped to study mathematics and computer science. But his lack of English sent him in another direction.

His path included some time studying botany, another return to his parents' farm after completing the 12th grade and – at his uncle's urging – college in Madurai, where he studied zoology.

After earning his undergraduate degree, Mani applied for a master's program at several colleges and universities, but wasn't accepted. Eventually he entered the biology program at Kamaraj University in Madurai.

After Kamaraj, Mani was accepted into the Ph.D. program at the India Institute of Science in Bangalore. Like so much of his education, this seemed to happen by chance.

“There was one slot in the lab of a leading Indian genetic scientist, and the student who had been selected decided against coming, so I got his slot,” explains Mani.

It was in 1998 at the Indian Institute of Science where he met Robert Weinberg, Ph.D., one of the top cancer researchers in the world. The connection would change his life.

### From Bangalore to MIT and MD Anderson

Weinberg, an internationally known scientist whose work as a founding member of the Massachusetts Institute of Technology's Whitehead Institute for Biomedical Research led to the hallmark discoveries of the first

human oncogene – Ras – and the first tumor suppressor gene – Rb – had a penchant for mentoring brilliant young minds. Mani intuitively sensed that Weinberg was someone who would influence his career.

“He came to give a lecture at the Indian Institute of Science, and I made a point to introduce myself,” says Mani. “I asked to join his laboratory.”

Weinberg must have seen great promise in the young postdoctoral student. Upon meeting him, he asked Mani to “wait right there” when he was called away for a few minutes. When Weinberg returned – two hours later – Mani was still waiting.

“By the end of the day he offered me a position in his lab at the Massachusetts Institute of Technology (MIT).”

For Mani, MIT might as well have been Mars. His understanding of the international science community was minimal. All he knew was that a truly great man had asked him to join his team. It was an event that would transform his life. But when he arrived at MIT's Whitehead Institute, Mani wasn't prepared for scientific study at a pre-eminent laboratory.

But within a short time Mani began to prove his merit. He worked with two colleagues looking at breast cancer metastasis and it intrigued him.

“I knew then that I wanted to determine what made cancer cells metastasize.”

In 2004, his team's discovery of the Twist gene, a key player in metastasis, was published in Cell. Today, it continues to rank among Cell's most-cited articles. By 2008, Mani was regularly interviewed by the media and was featured in a New York Times article that touched on the huge departure from his childhood “studying by kerosene lamp” to his work in Weinberg's lab identifying similarities between cancer cells and stem cells. That work, which resulted in another landmark Cell article, could lead to new ways to stop cancer metastasis.

Mani joined MD Anderson in December 2007. It was a move that allowed him to interact more closely with clinicians and to continue studying the biology of tumor initiation, invasion and metastasis.

His most recent work examines similarities between mouse embryos and metastatic tumors. This led to the discovery that tumors have gene expression signatures similar to mouse embryos at an early stage, when they are more prone to develop metastasis.

This first-of-its-kind signature stands out in its ability to predict metastasis in breast cancer patients by analyzing the bulk of the primary tumor, rather than residual tissues or scarce circulating tumor cells.

Today, as Mani continues to make significant contributions to understanding the molecular basis of how tumors progress, he relishes the atmosphere of collaboration at MD Anderson.

“I'm able to work closely with patients and also be a part of the clinical side of research, in addition to the laboratory work,” he says. “In general, MD Anderson seems to be accepting of both success and failure – as failure is often a stepping stone to success.”

The same year Mani came to work in Houston, he married well-known Indian actress Poornima Bhat, who is his “strong supporter.” They have a 5-year-old daughter, Prisha.

Despite his scientific successes, Mani's thoughts are never far from his Indian village roots. In 1998 he founded the Sakthi Foundation with his mentor Pradheepkumar Challiyil, whom he met at Madurai Kamaraj University. The foundation provides educational funds for young people in Sendurai, and offers eye camps for checkups and vision care.

When Mani visits the village, he offers the same advice he shares with his trainees at MD Anderson.

“I encourage them to go after their dreams. And to never give up.”

# Some of MD Anderson's own spend their free time giving back

Current staff members and two retirees talk about the fulfillment they find in volunteering

By Lany Kimmons



photo by Nick de la Torre

Each weekend Eunice Murage exchanges her white lab coat for a light-blue MD Anderson volunteer jacket.

Murage is a research scientist and belongs to a select group whose members work and volunteer at the cancer center. During the week she's in the lab, studying ways to detect cancer early. On weekends, she's visiting patients in their rooms, making their days a little brighter.

Current and retired MD Anderson employees who volunteer are highly valued for the time and energy they devote to helping others. All have their own reasons for wanting to help.

## Ericsteven Abordaje

In college, Ericsteven Abordaje and his girlfriend studied hard but still had spare time. They decided to use it helping others. Together, they applied and were accepted to MD Anderson's volunteer program. Abordaje was assigned to the Children's Hospital, where he helps in many ways.

On Fridays, he accompanies Child Life Specialists to patients' rooms for "bedside play."

"If I child is too tired or sick to visit the hospital's playroom, we bring the playroom to them," he says.

On Friday evenings, he transforms the playroom into a theater and serves pizza and popcorn while children enjoy movie night.

And three Saturdays a month, he's a pediatric liaison – a "jack of all trades." He does whatever's needed, including visiting with patients and their families, delivering supplies and supervising pet-therapy visits.

"I help patients associate their hospital experience with fun memories – not scary or unpleasant ones."

Abordaje has now graduated from college and works at MD Anderson as a patient transportation trainer.

He still volunteers at the Children's Cancer Hospital, and is studying to become a child life specialist.

"Volunteering has shown me how meaningful it is to make a lasting and positive impression in the lives of children and their families," he says.



photo by Wyatt McSpadden

**Maxine Hill**

A breast cancer diagnosis in 2010 led Maxine Hill to volunteer.

“During my six months of chemotherapy, radiation and surgery, volunteers checked on me, brought me warm blankets, and made sure I had everything I needed,” she says. “I knew how much the volunteers helped me through my cancer journey, and I wanted to do the same for others.”

Hill retired from MD Anderson in 2014 after 30 years of service in Accounts Payable and Grants and Contracts. Since then, she’s volunteered at the MD Anderson Pavilion information desk, helping patients find their way to appointments and anywhere else they need to go.

“It’s so rewarding to help others who are going through a difficult time,” says Hill. “Sometimes just a smile or a ‘hello’ makes patients feel better.”

Today, Hill is cancer free and enjoying life. She enjoys traveling with her daughter, who plans destination weddings, and spending time with her new granddaughter.

**Eunice Murage**

As a senior research scientist at MD Anderson, Eunice Murage, Ph.D., looks for chemical markers in the body that signal the early onset of cancer.

“I’ve always been curious and like to solve mysteries,” she says.

When she’s not working in the lab at MD Anderson’s McCombs Institute for the Early Detection and Treatment of Cancer, Murage volunteers as a patient advocate. Every Saturday she visits hospitalized patients and educates them about the MD Anderson resources designed to make their stay easier.

“I tell them and their families about all our amenities, like dining services, gift shops and the onsite beauty shop, library and post office,” she says.

And because she’s a tireless advocate for science, Murage always adds a plug for MD Anderson’s behind-the-scenes research that may someday help cure and prevent cancer.

“Patients see their doctors and nurses every day,” she says. “I remind them that scientists play an important role, too.”



photo by Adolfo Chavez III

**Isaac Rosen**

During his career as a medical physicist, Isaac Rosen, Ph.D., saw firsthand how difficult cancer treatment can be, not only for patients but for their families as well.

“Being treated in an institution as large as MD Anderson can be especially overwhelming, so I decided I wanted to help make a difficult time less confusing for patients and their families,” says Rosen, a retired professor of Radiation Physics who now holds the title Professor Emeritus.

As a volunteer in the outpatient surgery waiting area, he keeps families informed while they wait for their loved ones to come out of surgery. Once an operation is finished, he escorts family members to the recovery area where they’re reunited with their relatives.

Rosen chose to volunteer in the waiting area because he wanted to interact directly with families.

“They respond so warmly and are grateful for the help and attention volunteers provide,” he says. “I always tell them that MD Anderson is a great institution, the best place in the United States to be treated for cancer, and I am enormously proud to be associated with it.”



photo by Wyatt McSpadden





## Prom night All Stars

Whether it be a pair of red Chuck Taylors or a piece of custom-designed Kendra Scott jewelry, teen patients from MD Anderson Children's Cancer Hospital were encouraged to add their own style to the formal attire at the "Beauty and the Beast"-themed Prom Party Palooza on the 24th-floor observation deck of the cancer center's Main Building. Patients and their families enjoyed music, dancing and a lot of great food throughout the evening, which included visits from Houston Astros legend and Major League Baseball Hall of Famer Jeff Bagwell and Houston Texans defensive end Christian Covington. The event capped a week of excitement that began with the teens selecting tuxedos and choosing from hundreds of dresses at a two-day "dress-and-suit shop."

"Many patients miss the opportunity to attend their school proms while undergoing treatment," says Kevin Long, director of Pediatric Operations at MD Anderson. "But thanks to our wonderful and caring community of businesses that donate goods and services, we have the privilege of bringing the prom experience to them."

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[www.mdanderson.org/cancernetwork](http://www.mdanderson.org/cancernetwork)

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