

Summer 2014

VOL 28

ISSUE 4

CONQUEST

THE GAME
CHANGER

THE UNIVERSITY OF TEXAS

MDAnderson
Cancer Center

Making Cancer History®

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

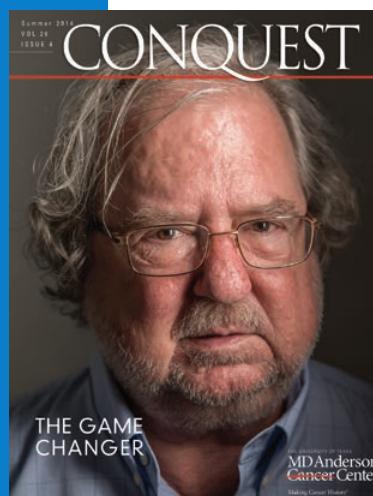
By our words and actions, we create a caring environment for everyone.

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: Scientist James Allison's research on the immune system resulted in the first drug to improve survival for patients with advanced melanoma. Outside of the lab, he's a pretty gifted blues harmonica player.

© Wyatt McSpadden



cancerwise RedLine

Join the conversation with MD Anderson via Facebook or Twitter or follow our YouTube, Google+, Pinterest, RedLine eNewsletter, Cancerwise blog and other publications.

Links:

www.mdanderson.org/redline
www.facebook.com/MDAnderson
www.twitter.com/MDAndersonNews
www.youtube.com/mdandersonorg
plus.google.com/+mdanderson

www.pinterest.com/mdandersoncc
www.cancerwise.org
www.mdanderson.org/publications

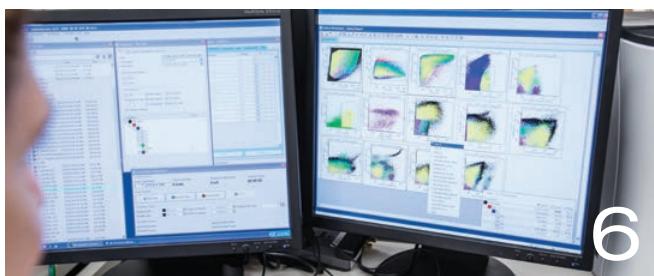
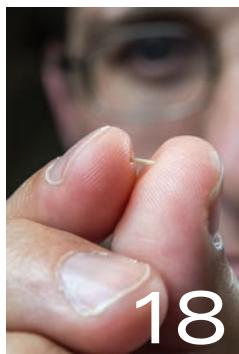


A Comprehensive Cancer Center Designated by the National Cancer Institute

VISIT THE CONQUEST WEBSITE
AT WWW.MDANDERSON.ORG/CONQUEST

CONTENTS

CONQUEST SUMMER 2014



FEATURES

2 CANCER FRONTLINE

Updates on the construction of the Zayed Building, efforts to end tobacco and more.

6 THE BREAKTHROUGH

James Allison proved the human immune system could fight cancer, and his innovative work has earned him a lot of praise, including that of Facebook founder Mark Zuckerberg, who says Allison's discoveries "will change lives for generations to come."

14 STRESS DISORDER

MD Anderson researchers are starting to understand the link between stress and cancer.

18 FROM IDEA TO FDA APPROVAL

Steven Frank is the doctor, inventor and entrepreneur helping make prostate brachytherapy less of a shot in the dark.

20 MEETING THE CANCER GENE HEAD-ON

Those who carry a mutation of the BRCA1 or BRCA2 genes face both a higher risk of cancer and the decision whether or not to have preventive surgery.

23 THANKS, CANCER

Writer Megan Silianoff considers her illness a blessing. Without it, she's not sure she would've found her true calling.

26 THE ADVENTURES OF REZA MEHRAN, M.D.

Whether in the air, operating room or war zone, this surgeon is always up for a challenge.

28 DYNAMIC DUO

The American Cancer Society and MD Anderson have been allies in the cancer war for decades.

30 BE ON THE LOOKOUT

With pediatric melanoma on the rise, doctors are working hard to raise awareness.



MD Anderson's award-winning Conquest magazine is available on the iPad.

Want to combine the design of the print version with the convenience of your tablet? The iPad version is for you. It's filled with multimedia extras and features sleek, user-friendly navigation. To read more about the app and how to download it for free, see Page 5.

Conquest also is available at www.mdanderson.org/conquest.

CANCER FRONTLINE

BUILDING A PERSONALIZED APPROACH TO CANCER THERAPY

In 2011, MD Anderson received a \$150 million gift — the largest in its history — from the Khalifa Bin Zayed Al Nahyan Foundation. Three years later, construction of the Sheikh Zayed Bin Sultan Al Nahyan Building for Personalized Cancer Care is well underway, with the exterior completed and a “move-in” date set for spring 2015.

The 12-floor, 626,000-square-foot facility will be home to the Sheikh Khalifa Bin Zayed Al Nahyan Institute for Personalized Cancer Therapy, an international center of clinical excellence that uses the latest advances in genetic information to develop safer, more effective treatments for patients on a case-by-case basis. That includes support for preclinical research and clinical trials in which each patient’s cancer cells are examined to determine their genetic and molecular mutations so that therapy can be tailored to their needs.

The building also will be the nerve center for the Sheikh Ahmed Bin Zayed Al Nahyan Center for Pancreatic Cancer Research. This will be dedicated to accelerating discoveries that significantly impact a deadly disease that’s on the rise yet remains underfunded compared to other cancers. Each year, some 43,000 cases of pancreatic cancer are diagnosed. Of those, 80-85% are inoperable.

“It’s a revolutionary time to be at MD Anderson if you’re a cancer researcher,” said Anirban Maitra, co-director and scientific director of the pancreatic research center. “It’s an incredible opportunity to build one of the best, most well-rounded pancreatic cancer groups in the country, bringing MD Anderson’s basic scientists, oncologists, surgeons, radiologists and pathologists all under a single umbrella.

“Integrated, multidisciplinary research and patient care will allow MD Anderson to become the vanguard place for pancreatic cancer treatment and research.”

What about the name on the building?

Follow this timeline through the life of Sheikh Zayed Bin Sultan Al Nahyan:

1918

Sheikh Zayed is born in Abu Dhabi, the youngest of Sheikh Sultan bin Zayed bin Sultan Al Nahyan’s four sons. His father was Ruler of Abu Dhabi from 1922-1926.

- At the time of his birth, the emirate was undeveloped. Its economy was mostly based on fishing, pearl diving and some agriculture.
- **Late 1920s and '30s:** Sheikh Zayed spends time in the desert with the Bedouin tribesmen, learning their ways and gaining an appreciation of the environment. It’s here he falls in love with falconry.

1946

Sheikh Zayed becomes the ruler’s representative in the Eastern Region of Abu Dhabi, serving in this post until 1966.



Sheikh Zayed Bin Sultan Al Nahyan Building for Personalized Cancer Care

© F. Carter Smith

1953

Sheikh Zayed makes his first visit to Europe. He is so impressed by the schools and hospital he visits that he's inspired to replicate them for his own people.

1958

Oil is discovered in Abu Dhabi. The discovery will transform the country's economy when export of the region's crude begins four years later. Sheikh Zayed quickly realizes the enormous potential of oil industry revenue.

"Money is of no value unless it is used for the benefit of the people."

— Sheikh Zayed

1960

The first hospital in Al Ain is founded on the instructions of Sheikh Zayed.

1966

Sheikh Zayed becomes ruler of the Emirate of Abu Dhabi. His leadership marks the beginning of a modern administrative structure, while ensuring that traditions of the past are maintained and preserved.

1968

Great Britain announces it will withdraw from the Arabian Gulf by the end of 1971.

1971

The seven-member United Arab Emirates Federation is formed. Sheikh Zayed becomes the first president of the UAE on Dec. 2. During his first years in power, roads are constructed, electricity is installed and schools and hospitals are built. Since 1971, the population has grown from approximately 250,000 to 9.3 million today.

Following Sheikh Zayed's initiative, the UAE, Kuwait, Saudi Arabia, Bahrain, Qatar and Oman form the Arab Gulf Cooperation Council (AGCC) at a summit conference in Abu Dhabi.

1981

United Arab Emirates University is formed by Sheikh Zayed.

1976



مؤسسة خليفة بن زايد آل نهيان
للأعمال الإنسانية
KHALIFA BIN ZAYED AL NAHYAN
FOUNDATION

Sheikh Zayed dies. His son Khalifa Bin Zayed Al Nahyan becomes president of the UAE.

2004

The Zayed Building will be ready for occupancy in the spring.

2015



Exterior of the Zayed Building is completed.

The Khalifa Bin Zayed Al Nahyan Foundation gives \$150 million to MD Anderson in honor of Sheikh Zayed. It makes possible the construction of the Sheikh Zayed Bin Sultan Al Nahyan Building for Personalized Cancer Care.

2014

2011

Read about the latest progress in Making Cancer History® at cancerfrontline.org.

THE BEGINNING OF END TOBACCO

Tobacco use is one of the greatest public health menaces of our time, causing 30% of all cancer cases in the United States. This year, tobacco is expected to kill 480,000 Americans and 6 million people worldwide. In the next half-century, its use will result in 500 million deaths, mostly in low- and middle-income countries.

Motivated in large part by the daily suffering of patients and their families, a cross-functional team led by Ernest Hawk, M.D., M.P.H., vice president and head of Cancer Prevention and Population Sciences, and Mark Moreno, vice president for governmental relations, has developed EndTobacco™. This comprehensive program recommends actions that MD Anderson will take to end tobacco use through policy, education and community-based clinical services. The program will begin within the walls of the institution, then expand to organizations and communities across the state, the nation and the world.

EndTobacco has three primary goals:

- Reduce tobacco use by children, teenagers and adults.
- Reduce nonsmokers' exposure to secondhand smoke.
- Increase attempts by adult and teen smokers to quit, and increase tobacco cessation counseling.

"EndTobacco is one of several initiatives in the cancer prevention and control platform of the Moon Shots Program focused on preventing and reducing cancer through screening, early detection and survivorship," Hawk says.

As part of the program, MD Anderson is adopting a tobacco-free hiring policy. Beginning Jan. 1, 2015, all MD Anderson job candidates offered a position will be screened for tobacco use during the recruitment process.

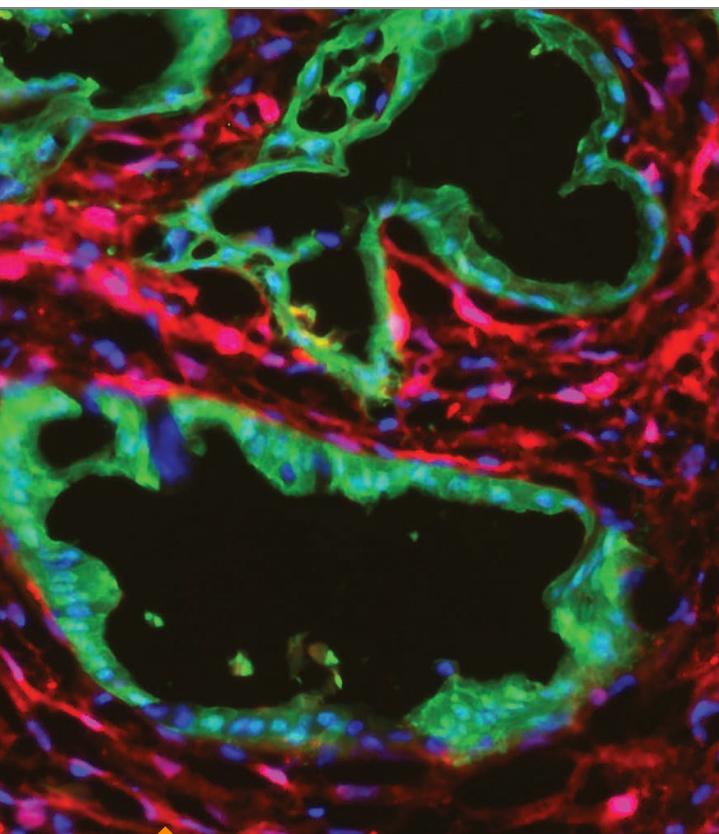


Those who test positive won't be eligible for hire. They may, however, reapply after 180 days.

"If we want to make a serious impact on smoking and tobacco use, we must lead by example and create a healthy environment internally for our patients, visitors, faculty and staff," Hawk says.

EndTobacco, which includes 110 tactical recommendations, is founded on best practices in tobacco control as established by the Centers for Disease Control and Prevention and the World Health Organization.

"For a long time, MD Anderson has worked to eliminate tobacco use at the local, state and national level," Moreno says. "EndTobacco is a perfect opportunity to align our internal goals with our external efforts."



FIBROUS TISSUE BELIEVED TO BLOCK THERAPY ACTUALLY SLOWS CANCER'S SPREAD

Fibrous tissue that was long suspected of making pancreatic cancer worse actually supports an immune attack that slows tumor progression, though in the end the tumor wins, MD Anderson scientists report.

"This supportive tissue that's abundant in pancreatic cancer tumors is not a traitor as we thought, but rather an ally that is fighting to the end. It's a losing battle with cancer cells, but progression is much faster without their constant resistance," says study senior author Raghu Kalluri, Ph.D., M.D., chair of Cancer Biology.

The team's findings point to a potential new avenue for guiding treatment and offer an explanation for the failure of a promising combination drug approach in clinical trials.

"Cancer is one form of tissue injury. When our defense system detects damaged cells, it sends soldiers to contain and repair the damage," Kalluri says. "When it cannot remove the damaged cells and repair the injured area, our defensive fibrotic response tries to put a boundary around it, to contain it and prevent it from spreading."

Kalluri and colleagues used genetically engineered mouse models that allowed depletion of tissue repair cells called myofibroblasts in pancreatic cancer.

Pancreatic cancer cells are green and myofibroblasts are red in this fluorescence microscopy visualization of a tumor section from a genetically engineered mouse with spontaneous pancreatic cancer. (image courtesy of Valerie LeBleu, Ph.D., and Judith Kaye of Cancer Biology)

GET MORE OUT OF CONQUEST WITH THE IPAD APP

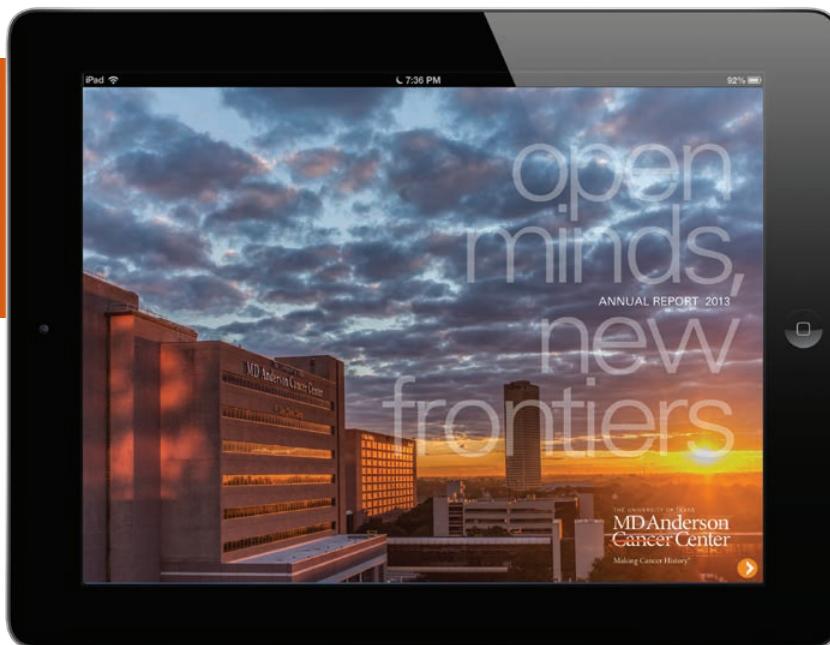


Each issue of MD Anderson's award-winning Conquest magazine is filled with stories about new cancer research and treatments, innovative patient services, cancer prevention and control, and programs and facilities. There are also profiles and features on patients, donors, faculty, staff and volunteers.

And now you can enjoy an even richer and fully interactive experience with Conquest on the iPad.

These days, with more and more people reading books and magazines on tablets, the ability to download Conquest via the iPad app makes it available anywhere and to more people. And along with that comes the convenience of storing it in your online library with other must-reads.

By maintaining the beautiful design of the magazine, this lush digital version differs greatly from what you'll find online. But it's not just a replica of what's in print. The iPad edition includes multimedia extras such as videos and podcasts featuring doctors discussing cutting-edge treatments and research, enhanced photo slideshows and hidden content in the form of additional information and links that delve deeper into stories and complex issues. All of this is enhanced by user-friendly navigation.



It's also easy to enjoy Conquest on your iPad. To get your free subscription, just search "Conquest Magazine" in the iTunes App Store and download the free app. After the download, a subscription banner will appear. Selecting this option enables you to automatically receive push alerts through Newsstand each time a new issue publishes.

If you like the layout and experience of the print version, but want bonus content and the convenience of your tablet, the iPad app is for you.

Myofibroblasts comprise a major portion of supportive tissue called stroma and also produce collagen, which serves as a scaffold for wound-healing and tissue regeneration. Up to 90% of a pancreatic tumor can be fibrotic support tissue.

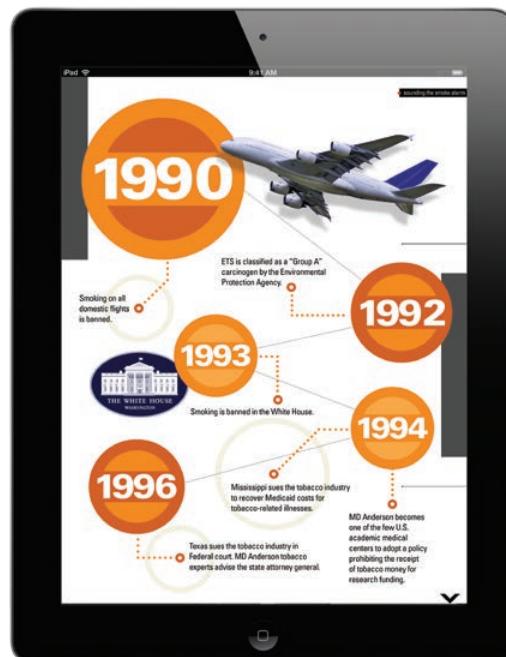
When the scientists depleted myofibroblast production in mice, their tumors became much more invasive, aggressive and lethal.

"We did these experiments thinking that we would show the importance of myofibroblasts and fibrosis in pancreas cancer progression, but the results went completely against that hypothesis," Kalluri said.

Since myofibroblasts and collagen are thought to block chemotherapy, the team treated their myofibroblast-depleted mice with gemcitabine, the standard treatment for pancreatic cancer. The chemo drug didn't have any effect on the disease course or improve survival.

These results track those of a major clinical trial that combined a myofibroblast-depleting drug called a hedgehog inhibitor with gemcitabine to treat pancreatic cancer patients. The trial was stopped in 2012 when an interim analysis showed the patients taking the combination had faster disease progression than the control group that took only gemcitabine.

— Scott Merville





THE IMMUNO MAN

By Scott Merville

📷 Wyatt McSpadden

A blues-loving scientist from a small town in South Texas shook off the immunotherapy naysayers and made believers out of everyone

Back in 1977, James Allison arrived at MD Anderson's Science Park in Smithville, Texas, with an itch to discover something new. It was the music-loving, harmonica-playing scientist's first faculty position, and he was happy to be near Austin, his favorite city.

There was no way of knowing then, but Allison's initial research on the immune system at MD Anderson laid the groundwork for his return in 2012 as the father of immune checkpoint blockade — an entirely new way of treating cancer that's yielding unprecedented results.

Thanks to his clinical collaborators, he's been fortunate enough to meet some of those saved by his drug, ipilimumab (Yervoy®), the first ever to improve survival for patients with advanced melanoma. According to American Cancer Society predictions, the disease will kill more than 9,700 people in the U.S. in 2014.

One of the most dramatic stories belongs to an original phase I clinical trial patient in Los Angeles.

"The patient just wanted to live long enough to see her teenage sons graduate from high school," says Allison, chair of Immunology. "That was 14 years ago. She's lived to see them go to college, go to graduate school, start their own families and get established in their careers ..." His voice trails off and his eyes mist. "I get emotional talking about them. That's what it's all about."

James Allison, Ph.D., loves to sing the blues. The scientist and harmonica player formed a blues band with other immunotherapy experts called The Checkpoints, which has a standing gig at the House of Blues in Chicago during the annual meeting of the American Society of Clinical Oncology each summer.



THE BASIC SCIENCE BEHIND SUCCESS

The journey from Allison’s laboratory research at MD Anderson to Food and Drug Administration approval of ipilimumab for metastatic melanoma in 2011 was arduous and often frustrating. It included stops at other prestigious research institutions such as the Cancer Research Laboratory at the University of California, Berkeley, and Memorial Sloan Kettering Cancer Center, the travails of drug development and the quirks of pharmaceutical companies and clinical trials.

“Jim has great scientific intuition and he’s stubborn — or maybe persistent is a better word. He tells you exactly what he thinks,” Patrick Hwu, M.D., says of Allison, who goes by Jim.

“He had the vision to see the research through to a paradigm-changing treatment strategy,” adds Hwu, chair of Melanoma Medical Oncology, who’s both a scientific and musical collaborator of Allison. “I truly appreciate what he’s done for my patients.”

Follow-up studies show an unprecedented 22% of late-stage melanoma patients treated in ipilimumab clinical trials survived for at least four years. Meanwhile, checkpoint blockade is being extended to treat other cancers, and the journal *Science* named cancer immunotherapy its 2013 Breakthrough of the Year.

Allison lost his mother to lymphoma when he was 11 years old and a brother later on to prostate cancer, a disease he himself has survived.

“My family has suffered greatly from the ravages of cancer, so cancer treatment has always been in the back of my mind,” he says.

“But I didn’t set out to develop a cancer treatment. If I had, I probably would have missed something important because the target we found isn’t on tumors, it’s on T cells,” Allison says. “Checkpoint blockade emerged as a cancer therapy only because we first uncovered the basic science and biology of T cells, the immune system’s primary attack cells. It’s a classic example of how understanding basic science can lead to new disease treatments.”

Allison’s return to MD Anderson in November of 2012 came with a \$10 million recruitment grant from the Cancer Prevention and Research Institute of Texas and an MD Anderson commitment of \$30 million to develop an immunotherapy program that Allison says is unmatched in its scientific and clinical capabilities.

“One appeal of being a scientist is being the first person on the planet to know something. It’s kind of egotistical, but I think most scientists are driven at least in part by that ambition. There was so little known about T cells, their function was a black box.”

— James Allison, Ph.D.

“Immunotherapy is the most exciting and promising area of cancer research today, and its potential is just beginning to be realized,” says MD Anderson President Ron DePinho, M.D. “We’re proud to have Jim leading our efforts to expand and hone this approach as executive director of MD Anderson’s Moon Shots Program immunotherapy platform.”

Allison, who’s encountered a lot of immunotherapy naysayers over the years, acknowledges DePinho’s commitment to advancing the treatment.

“Ron is the first cancer center leader to say ‘we’re really getting into this big,’” he says. “I wouldn’t be here without him.”

FIRST STOP: RESEARCH PARK IN SMITHVILLE

Almost 40 years ago, fresh from a post-doctoral fellowship at the prestigious Scripps Clinic and Research Foundation in La Jolla, Calif., Allison was looking for his first job as a scientist.

A friend in Houston tipped him off to a new MD Anderson program in Smithville, a research center that studies cancer causes. Importantly for Allison, Smithville is just southeast of Austin.



Allison during his early days at MD Anderson's Science Park in Smithville, Texas.

"I grew up in Alice, which is a very small town in South Texas," Allison says. "Summer science programs at The University of Texas-Austin, starting in middle school and continuing through high school, were fun, inspiring and a lifeline to intellectual life."

At 16, he enrolled at UT-Austin and ultimately earned a doctorate in biological sciences. Along the way, he soaked up the city's academic energy and music scene.

In La Jolla, he had played harmonica in a band and once finagled his way into a platinum-record celebration for fellow Texan Willie Nelson. When Nelson asked afterward where he might go pick and play that night, Allison gave him and two other musicians a ride to his regular haunt, The Stingaree.

"A friend of mine was singing 'Blue Eyes Crying in the Rain' when we arrived. He just about gagged. Willie sang that song later and I got to play harmonica," he recalls.

That part of his California stay was fun, but "I loved Austin and wanted to get back," Allison says.

So he packed his car, drove to Smithville and inquired about a job. He became the sixth person hired at the Science Park, an assistant professor in Biochemistry. His initial research involved using components of the immune system — antibodies — to understand liver cancer.

But Allison was intrigued by the immune system itself; dating back to mouse studies he conducted as an undergraduate.

"The complexity and versatility of the immune response fascinated me," he says.

THE T CELL IGNITION SWITCH

"Ellen Richie, my friend and colleague from graduate school, was having a lot of fun studying T cells," he recalls. "She urged me to get into them, which recently had been discovered and were poorly understood."

Richie, today a professor in Molecular Carcinogenesis at Smithville, is an expert on the development of T cells and the thymus — an organ right behind the sternum where these white blood cells mature.

"Somehow, something I said raised his interest in T cells, but I don't recall specifics," Richie says. "I'm really glad that it did, though, because he revolutionized the field."

"From his earliest days, he was always on the cutting edge," she says. "He was never shy or put off by common wisdom or existing methods, challenging them when he found evidence to the contrary. He's persistent — he definitely doesn't give up."

"The big mystery of the time was the T cell antigen receptor. Nobody had any idea what it was," Richie says. "The intellectual challenge that presented itself appealed to Jim."

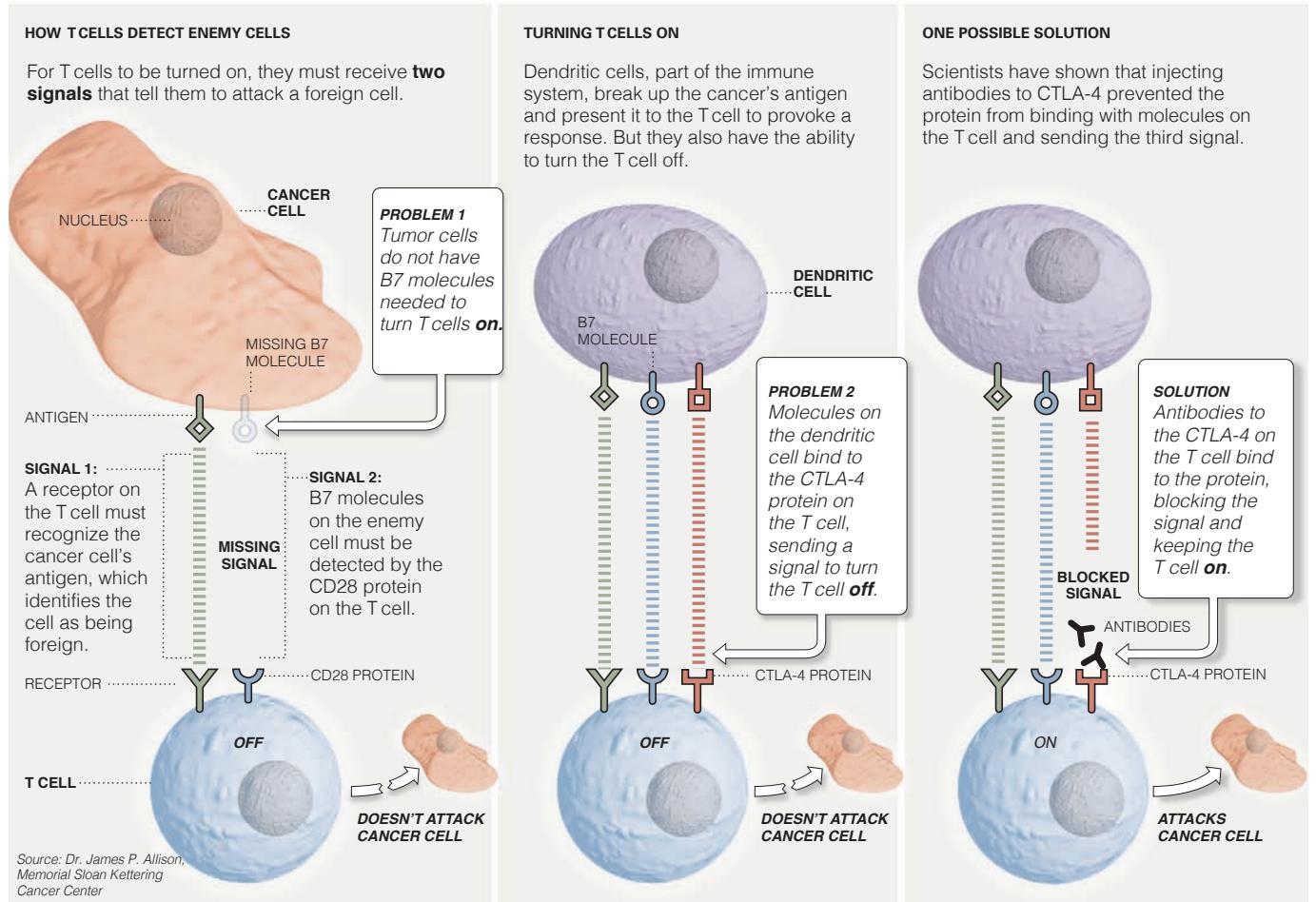
"Immunotherapy is the most exciting and promising area of cancer research today, and its potential is just beginning to be realized. We're proud to have Jim leading our efforts to expand and hone this approach."

— MD Anderson President Ron DePinho, M.D.

T cells seemed to function in a way that required them to recognize an antigen — a distinctive piece of a virus or bacterium, for example — to become activated and attack the invader. Research to identify a T cell antigen receptor had been so plagued by lack of conclusive proof that some scientists thought it might not exist at all, that T cells worked by some other mechanism.

Cancer and the Immune System

For years, scientists have questioned why the immune system does not aggressively fight off cancer cells. New evidence suggests that T cells, which are crucial to the body's immune response, have a protein (CTLA-4) that actually suppresses their ability to attack cancer cells. Researchers are focusing on that protein in hopes of creating a more aggressive immune system that could kill cancer cells.



This graphic originally appeared in a 2005 New York Times article about cancer and the immune system that featured Allison and his research. Allison, who was at Memorial Sloan Kettering Cancer Center at the time, is credited as the source.

Allison recalls a graduate-level immunology textbook that closed with some advice for budding immunology researchers: "Don't try to find the T cell antigen receptor because it's ruined more careers and wasted more time than any other single thing.

"So we tore that page out and stuck it to the wall in our lab because we figured we already had it, or at least an antibody to it."

In a 1982 paper in the *Journal of Immunology*, Allison and colleagues identified an antibody that bound only to a specific type of lymphoma cell. Its specificity was a surprise — it didn't connect with any other lymphoma cell line or with normal spleen, thymus, lymph node or bone marrow tissue.

Intrigued, they tapped their biochemistry expertise to determine the underlying protein structure on the lymphoma cell surface that

held the antigen. Then they looked for similar proteins on the surfaces of other types of cells, finding them only on T cells and their precursor cells, but not on the better-known immune system B cells or in the bone marrow.

Their findings suggested that the protein complex made up a T cell-specific surface structure with both constant and variable regions, ideal for acting as the versatile, long-sought T cell antigen receptor.

After publication, the young scientist was invited to a Gordon Conference on immunology, an elite meeting of the leading researchers in the field. A major paper in *Cell* soon confirmed what Allison's team had suggested.

"The T cell antigen receptor is the ignition switch of the immune response," Allison explains. But it wasn't enough to fully ignite immunity by itself.

CD28: THE GAS PEDAL

The next step was to identify the genes responsible for the T cell antigen receptor, and, at the time, MD Anderson simply wasn't equipped for such research. Allison took a visiting professorship at Stanford in the lab of Irv Weisman, a leading scientist who once gave a speech at MD Anderson that had set Allison's mind abuzz with research possibilities.

As it happened, other scientists beat them to the genes. While in the Bay Area, Allison gave an invited talk at the University of California, Berkeley, and made a strong impression. He was soon recruited to lead the immunology department there.

Leaving MD Anderson in 1984 was difficult.



“Smithville was wonderful for several reasons,” Allison recalls. “I had no administrative duties, I didn’t teach, I just did science all of the time. Had a great team, good support and a few National Institutes of Health grants.

“I owned a house and 18 acres in the Lost Pines area close enough to walk through the woods every day to work (the Science Park is located within Buescher State Park) and had a house in Austin.”

At Berkeley, Allison turned his attention to a molecule on the surface of T cells called CD28. By then, researchers knew that an antigen presented to a T cell was not enough to activate it, and CD28 seemed like a good candidate as a co-stimulatory molecule.

In a study published in *Nature*, Allison and his colleagues showed that CD28 is cross-linked to the antigen receptor and, when activated, sparks an immune response, much like a gas pedal applied after ignition moves a car.

CTLA-4: THE BRAKES

French scientists identified another T cell surface protein they named Cytotoxic T-Lymphocyte Antigen

4, or CTLA-4. Because it greatly resembled CD28 and was activated by the same binding molecules, the initial thought was that CTLA-4 was another co-stimulator.

Allison’s research, and additional work done by Jeff Bluestone, Ph.D., then at the University of Chicago, indicated otherwise. In July 1994, they presented data at another Gordon Conference showing CTLA-4 inhibited immune responses. Subsequently, they published papers demonstrating that effect in mice.

“CTLA-4 is cross-wired with the antigen receptor and CD28, so the brake is activated at the same time to help ensure that the immune response doesn’t go on and on, destroying healthy cells,” Allison says.

For decades, research had shown that activated T cells often penetrate tumors, indicating an activated immune response, but one insufficient to overcome the cancer. It occurred to Allison that the CTLA-4 checkpoint might be shutting down those immune responses and that blocking it might free T cells to more effectively find and kill cancer.

A mouse experiment in 1995 using an antibody against CTLA-4 worked so well that Allison wanted to repeat it immediately. He didn’t know which mice, all with colon cancer, had been treated with the antibody to block CTLA-4. All developed tumors, but by the third week, distinct differences developed. For some, tumor growth slowed, then stopped and the tumors went away completely, while others progressed rapidly.

When the experiment was unblinded after six weeks, nine of the 10 treated mice were fine, all of the untreated had died. These results were repeated in a variety of cancers, including melanoma.

“I thought, ‘we need to get this to people as soon as we can,’” Allison says.

THE SLOW ROAD TO DRUG APPROVAL

Translating Allison’s antibody against CTLA-4 into the clinic was a frustrating grind, so his legendary persistence became crucial. He shopped it to 12 companies over two years, none of which were interested.

Some were intimidated that Bristol-Myers Squibb had a patent on another antibody to CTLA-4. Others scoffed at yet another immunotherapy idea — a field plagued by earlier therapies that didn’t come close to living up to their hype.

Finally, a small company licensed the patent and tried unsuccessfully to make a small-molecule drug to block the brakes rather than use an antibody to CTLA-4 that he and colleague Alan Korman had made. The project stagnated.

“It got pretty ugly. I tried to get it back,” Allison says.

In 1998, a small biotech called Medarex bought the drug rights and made the human antibody to CTLA-4.

KNOWLEDGE HAS BEEN ITS OWN REWARD FOR ALLISON, GOING BACK TO CHILDHOOD.

“I’ve always wanted to know how things work. My father was a doctor in Alice, Texas, so I had a pretty good look at what it’s like to be a physician. As a doctor, you can’t make mistakes,” says Allison.

“The scientist’s job is to generate and test hypotheses, which are wrong most of the time, otherwise the answer would be obvious. So you go back and do another experiment,” Allison says. “Scientists only need to be right some of the time — preferably about something important.”

Allison has been right often enough about important things that honors have been pouring in — including seven major awards since April 2013.

restigious awards given to Allison recently:

The Economist’s 2013 Innovation Award for Bioscience

The Breakthrough Prize in Life Sciences, which recognizes researchers whose work extends human life and is worth \$3 million

The 2014 Canada Gairdner International Award, which recognizes seminal medical discoveries

The 2014 Szent-Györgyi Prize for Progress in Cancer Research from the National Foundation for Cancer Research

The inaugural AACR-CRI Lloyd J. Old Award in Cancer Immunology from the American Association for Cancer Research and the Cancer Research Institute. It’s named in honor of Old, an immunology trailblazer.

Elected as a fellow of the American Association for Cancer Research Academy

2014 Tang Prize for Biopharmaceutical Science



Tsvetelina Hoang, Ph.D., instructor in Immunology, at work in Allison's laboratory at MD Anderson.

An early clinical trial was deemed a failure after tumors didn't shrink by three months of treatment — the usual clinical-trial standard for new chemotherapy — and in some patients, tumors appeared to grow.

Fortunately, physicians involved in the clinical trial noted that many of the patients showed tumor shrinkage later than three months and continued to live well beyond the expected survival period for late-stage melanoma. As it turned out, immune responses in those patients were sometimes slow to get started.

Bristol-Myers bought Medarex in 2009 for \$2.4 billion and advanced ipilimumab through clinical trials, culminating in a successful phase III study that finally led to FDA approval in 2011. In the meantime, Allison had moved to Memorial Sloan Kettering in New York in 2004 to head its immunology efforts and work with clinicians conducting clinical trials there.

IMPROVING OVERALL SURVIVAL

Eight other immune checkpoint or co-stimulatory molecules have been identified, and drugs to block the PD-1 checkpoint currently are advancing through clinical trials.

When the FDA approved ipilimumab for metastatic melanoma, it cited the traditional measure of success: an increase of four months in the median overall survival (the point where half of treated patients remain alive) of treated patients.

But that's not what has oncologists excited about the drug and the checkpoint blockade approach. When ipilimumab works, it works for a long time — complete remission or disease so tamped down that life returns to normal for patients who once faced certain death from the disease. This is an uncommon result not just for metastatic melanoma, but for any type of solid tumor that has spread to other organs.

"Long-term follow-up, so far, indicates that once a patient survives for three years, if they die after that, it's from something other than melanoma," Allison says.

One of the important mysteries that has yet to be solved is why the drug doesn't work for more patients. Testing new combinations is an exciting area, as are discovering new checkpoints and co-stimulatory molecules, as well as developing drugs to address them. Research at MD Anderson addresses all of these.

Five pharmaceutical companies have signed collaborative agreements with

MD Anderson's immunotherapy platform to develop new drugs.

Allison points out that one of MD Anderson's strengths is the ability to conduct innovative clinical trials that include the measurement of scientific endpoints.

These protocols, developed by Padmanee Sharma, M.D., Ph.D., associate professor in Genitourinary Medical Oncology, allow patients to consent to presurgical treatment with an immunotherapy. This permits in-depth analysis of the molecular effect of the drug after the tumor is removed.

This approach allowed Sharma to discover that activation of a protein called ICOS increases ipilimumab's effectiveness. The details of this co-stimulatory molecule and its effect were then worked out in a mouse model. ICOS activation to improve treatment now is being explored by Jounce Therapeutics, a company co-founded by Allison and Sharma.

"Immunotherapy for cancer is really just beginning," Allison says. "As we learn more and develop immunotherapy drug combinations, we can start thinking about curing cancer in many patients. MD Anderson is a center of immunotherapy excellence that will grow, improve and contribute significantly to that cause."



FRUSTRATION

WORK

FEARS

PAIN

MARRIAGE

EXPENSES

FATIGUE

MORTGAGE

FAMILY

PE

COMPLICATIONS



STRESSING OUT

CALCULATING THE REAL COST

By Katrina Burton

What stresses you out?

Are financial challenges getting you down? Maybe a challenging work environment is causing persistent, nagging headaches. Perhaps relationship trouble is keeping your blood pressure at an all-time high?

We all know that stress is unhealthy. And we now know that chronic stress can shorten a person's lifespan. It also can lead to unhealthy behaviors such as smoking or drinking too much alcohol.

Hans Selye, the Hungarian-born endocrinologist touted as being the first person to recognize the existence of biological stress, once said, "it is not the stress that kills us; it is our reaction to it."

Research has shown stress increases the risk of developing chronic diseases such as depression, diabetes, obesity and heart disease. New data adds cancer to that troubling list. These conditions are difficult to treat. They also have an unhealthy effect on your wallet.

The connections between stress and cancer are being discovered by MD Anderson researchers and clinicians. They hope to understand the relationship to determine its implications for prevention, treatment and survivorship.

"There's not a significant amount of research on the stress and cancer link compared with work linking stress to other conditions such as heart disease. However, there is growing evidence," says Christopher Fagundes, Ph.D. "In my lab, we're particularly interested in why certain populations don't benefit from the same health status as others, and how early-life adversities contribute to a person's health."

The dangers of childhood stress

Fagundes, an assistant professor in Health Disparities Research, is charting new territory with his research on stress and cancer. As

director of the Behavioral Mechanisms Explaining Disparities lab, Fagundes and his colleagues use psychology, autonomic psychophysiology and psychoneuroimmunology to investigate the body's response to life stresses and their link to cancer.

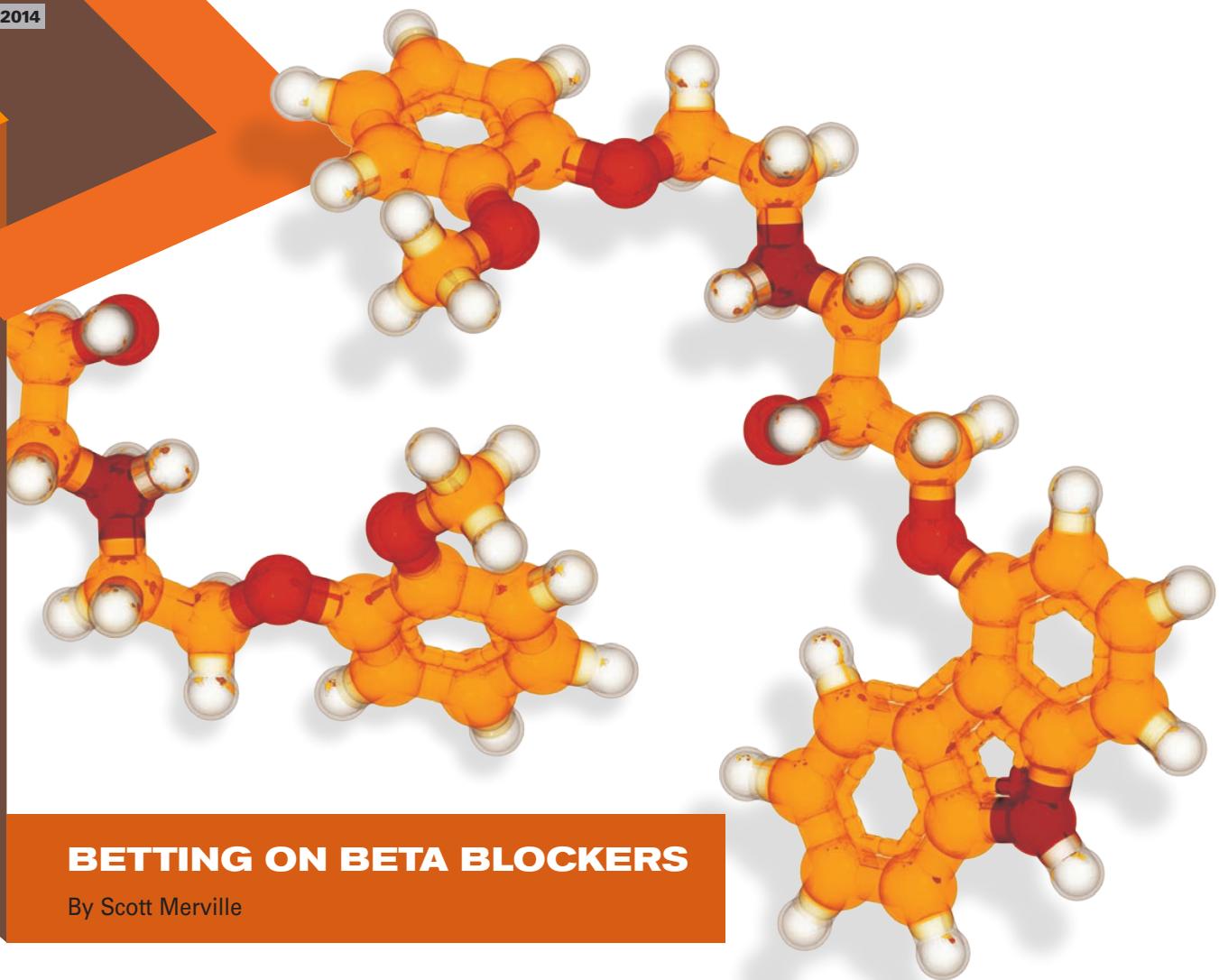
"Combining the three methods allows for evaluation of interaction between psychological processes and the nervous and immune systems, while also studying the interface of mind and body and its behaviors," Fagundes says.

In a recent study published in *JAMA Psychiatry*, Fagundes investigated the impact of early-life stress on basal cell carcinoma. The study showed that people who experience childhood adversity such as abuse, neglect and family problems are at a greater risk for a poor immune response to the tumor.

"This can have a significant impact on a person's physical health later in life and has been linked to morbidity and mortality from many chronic diseases," Fagundes says.

Fagundes also is investigating how stress impacts post-treatment symptoms, such as fatigue, pain and sleep, in breast cancer survivors. For example, a study underway examines how stress among married couples impacts inflammatory levels. A key biological mechanism underlying post-treatment cancer symptoms, these levels are associated with cancer recurrence. The study involves intentionally creating conflict between breast cancer survivors and their partners to measure stress levels. It also tracks how well they manage conflict and resolve their differences. It examines the effect of other stressors, including the couple's socioeconomic status.

"While all marriages have stress, that combined with a serious illness such as cancer can negatively impact patients' quality of life," Fagundes says.



BETTING ON BETA BLOCKERS

By Scott Merville

Tracking down the molecular details of how stress accelerates tumor growth and progression is pointing to a potential new role for a class of drugs used to treat cardiovascular disease and related conditions.

Years of research by Anil Sood, M.D., professor in Gynecologic Medical Oncology and Cancer Biology, show that stress hormones fuel progression of ovarian and other cancers, and that beta blockers might be a new way to stifle that effect.

“Beta blockers treat a variety of conditions, such as heart disease, high blood pressure, glaucoma and migraines, targeting a receptor protein in heart muscle that causes the heart to beat harder and faster when activated by stress hormones,” Sood says. “Our research has shown that the same activation helps ovarian cancer progress and spread, so these drugs might have a new role for cancer.”

Sood’s findings include:

- When mice with ovarian cancer are stressed, their tumors grow and spread more quickly, but the effect can be blocked by the beta blocker propranolol.
- Chronic stress triggers a chain of molecular events that protects breakaway ovarian cancer cells from automatic destruction. Heightened levels of the fight-or-flight hormones epinephrine and norepinephrine permit malignant cells to safely leave the primary tumor — a necessary step in cancer metastasis and progression — and avoid a cell-death mechanism called anoikis.
- When norepinephrine hits its target — the beta-adrenergic (ADRB) receptor — on tumor cells, it activates Src, a master regulator of cancer cell survival proteins, through another protein called PKA. Stress-activated Src is like a dam opening, only the flood is a chain reaction inside cells that promotes cell survival, mobility, invasion of neighboring tissue

and creation of new blood vessels to supply the tumor.

Beta blockers plug the ADRB receptor, blocking activation by norepinephrine and other hormones. Norepinephrine is the most abundant stress hormone found in ovaries.

Sood and colleagues analyzed data on outcomes of cancer patients treated with beta blocker drugs from the Food and Drug Administration Adverse Event Reporting System. They found that mortality in patients treated with a beta blocker fell by an average of 17% across all major cancer types, with a nearly 15% decrease in mortality among patients with ovarian and cervical cancers.

Sood continues to study biological mechanisms that may be affected by stress with the aim of identifying cancer patients who are most likely to benefit from beta blockers and other stress interventions.

NOT OVERLOOKING HOW PATIENTS SEE THEMSELVES

By Katrina Burton

Many times, the focus for cancer patients is on making it through treatment. They're asked to "keep calm and carry on." But the internal stress patients endure — particularly related to ways their bodies change as a result of treatment — can torpedo their confidence level and ability to enjoy everyday activities.

Feeling good about your appearance not only builds self-confidence, it also can have a positive effect internally by reducing stress.

Michelle Fingeret, Ph.D., works with patients and cancer survivors as the director of MD Anderson's Body Image Therapy Program, which supports patients who undergo reconstructive surgery after cancer treatment. Fingeret sees firsthand how low self-esteem and body image concerns foster negative stress.

"Body image often is an overlooked component of cancer treatment," says Fingeret, associate professor in Behavioral Science. "Patients and survivors typically won't address body image concerns with their doctor because they don't want to appear ungrateful for surviving cancer."

After all, not everyone survives cancer, and shouldn't they be happy with just beating this horrible disease?

In reality, the majority of patients who undergo reconstructive surgery resulting from breast and head and neck cancers, for example, often are worried about how their body changes will affect their relationships with loved ones and friends, what others will think about their changed appearance and how they themselves will come to terms with these changes. Survivors often struggle with anger, depression, anxiety and feelings of isolation. Getting back into the swing of things or adjusting to their new "normal" can be difficult. The emotions associated with treatment and the physical changes resulting from treatment can be intense and trigger internal distress.

"It's important that we address all of the patient's concerns at the beginning of any kind of treatment, so the patient knows that being worried about body image is normal and appropriate," Fingeret says.



MORE TO WORRY ABOUT THAN CANCER

By Katrina Burton

Ever feel as if you overcome one obstacle only to encounter another? Or maybe you believe the old superstition that bad things always come in threes. If you think about stress and its many debilitating effects on a person's body, that saying may not seem so irrational.

Understanding the science behind stress and how it negatively impacts a person's health are important topics being investigated at MD Anderson. Researcher Eileen Shinn, Ph.D., who specializes in psychosocial oncology, is redefining how clinicians might view stress and how to better connect the dots between stress and cancer.

"I feel there are aspects of a cancer patient's health, such as psychological stress, that are overlooked or not addressed, that may have an impact on their survival," says Shinn, assistant professor in Behavioral Science.

She believes that many cancer patients suffer from multiple afflictions that should be treated along with the cancer. "Patients could suffer from heart disease or diabetes, as well as cancer."

"It's important to address these comorbidities so we can ensure that the treatments and interventions developed for each patient will offer a better chance for survival," Shinn says.

Most recently, Shinn and her colleagues investigated whether hypertension and chronic stress had an impact on the survival of ovarian cancer patients, who, overall, have a five-year survival rate of 35%. Results from the study showed that women with tachycardia (rapid heart rate) lived an average of four years after diagnosis. In comparison, women without the condition lived, on average, 5.9 years. The study also revealed that patients who didn't experience cardiovascular events such as venous thromboembolism and pulmonary hypertension also lived longer.

"These findings were significant in that a blockbuster cancer drug typically leads to a 3 to 7% improvement in survival, whereas these cardiovascular comorbidities were associated with reductions in survival between 32 to 42%," Shinn says.

Shinn expects these types of cardiovascular events are related to stress, but more research is necessary.

F R O M
P A T E N T T O
P A T I E N T S

By Will Fitzgerald

📷 Wyatt McSpadden

STEVEN FRANK IS THE DOCTOR, INVENTOR
AND ENTREPRENEUR WHO TOOK THE
UNCERTAINTY OUT OF A CANCER TREATMENT

When Steven Frank, M.D., had an idea to improve the effectiveness of a common prostate cancer treatment, he didn't know his vision would result in the creation of an innovative device that would win Food and Drug Administration (FDA) approval and subsequently be spun off into a startup company.

It all began when Frank tackled a decades-old problem plaguing the field of prostate brachytherapy, a treatment in which tiny radioactive seeds are implanted in the body to destroy cancer cells. Because the seeds are difficult to view through imaging such as computed tomography (CT) scans, which are necessary to evaluate the success of treatment, uncertainties are created that can impact the therapy's effectiveness.

Frank proposed that a highly visible marker of sorts, or implantable contrast agent, could be developed and placed between the seeds to guide treatment.

"The best analogy to describe this technology is looking at footage of machine gunners in World War I who would spray bullets everywhere and not have any idea where the bullets were going," says Frank, associate professor in Radiation Oncology. "Finally, someone had an idea to insert a tracer every few rounds to increase accuracy. That's essentially what we've created."

In 2006, Frank collaborated with a biomolecular engineer at the University of Houston and together they began testing compounds believed to be visible under an MRI scan, the most accurate way to monitor brachytherapy seeds. The answer arrived in a compound called cobalt chloride, which to their surprise, lit up the scans during the investigation.

After discovery, taking on the 'beast'

Armed with this new finding, Frank's next steps propelled him into unfamiliar — yet necessary — territory that he had to navigate if his idea was to become reality. He needed guidance to understand the very complex process required to commercialize this technology and bring it to patients.

For that he turned to Oliver Wenker, M.D., clinical professor in Anesthesiology and Perioperative Medicine, and Tom Lee, director

of Technology Commercialization's Active Venture Development, who are responsible for unearthing innovations within MD Anderson's walls and determining commercial potential. The laborious process, which Frank describes as "a beast," involves raising capital and obtaining financing, patents and regulatory approval.

"The ultimate goal is not just discovery, but taking that achievement from the laboratory to the patient, which is a very complicated process in medicine," Frank says. "I was at a crossroads because I needed to license the technology out of MD Anderson, otherwise it would die."

With Wenker and Lee's mentorship, and the help of outside counsel experienced in negotiating licensing agreements, Frank successfully transferred his discovery out of MD Anderson over the course of nine months. With an agreement in place, the institution would receive royalties and Frank would be free to incorporate a business of his own.

A maze of regulations

In 2009, three years after making his initial discovery, Frank established C4 Imaging. He immediately began the first of two fundraising rounds that would generate more than \$3 million in total startup capital.

But challenges remained. Before any new medical technology can be used clinically, it must be approved by the FDA. In anticipating the regulatory phase, Frank hired a CEO to lead the important next steps. Around that time, he also learned of an innovative program that would prove especially beneficial.

"The National Institutes of Health created a mechanism where experts with regulatory experience hand-select aspiring companies to help navigate their way through the FDA, and we were selected," Frank says. "During this process we were also busy conducting trials and evaluating toxicity, so it was a critical time to make sure everything happened correctly."



Steven Frank, M.D., invented the first FDA-approved permanently implantable MRI marker (seen on the facing page) for use in prostate brachytherapy.

After three years of discussions with the FDA, the world's first permanently implantable MRI marker for use in prostate brachytherapy was approved.

Frank, who worked tirelessly on the development of his idea while his family — including four children less than 10 years old — slept, achieved an incredible feat without any formal business training, and in an industry known for high failure rates.

This past March, the first group of patients received the marker during their therapy. While Frank credits his success to a team of advisers and supporters, the end goal was always focused on improving patient care.

"We can now limit uncertainty, provide optimal quality assurance and minimize side effects," Franks says. "This technology could change the way brachytherapy is planned and evaluated for future patients."

Let us explain ...

The Office of Technology Commercialization (OTC)

The OTC identifies technologies suitable for startup company formation. These companies help create institutional value for the intellectual property resulting from inventions made by MD Anderson researchers and clinicians. Since 1987, the OTC has been involved in the creation of 11 affiliated companies that have raised more than \$300 million on the strength of MD Anderson-based discoveries. Four portfolio companies listed on NASDAQ have raised more than \$230 million and funded \$25 million in sponsored research at the institution.

Surgically removing cancer risk

By Laura Sussman
Wyatt McSpadden

Carriers of mutated BRCA genes face the difficult decision of if and when to have preventive surgery

For Denise Megarity, the decision to have her ovaries removed at a young age — and thereby dramatically reduce her risk of multiple cancers — was an empowering one.

Her mother, Margarita Wight, is a cancer warrior. First diagnosed with breast cancer in 1987, she's survived the disease three times. Seven years ago, Wight was diagnosed with ovarian cancer — and again beat the odds.

In fact, Megarity and Wight's family tree is dotted with cancer caused by a defective gene.

"Looking back at our family history on my mother's side, there are all kinds of cancer associated with the BRCA genes," explains Megarity. "My mother's father died of pancreatic cancer. My mother's first cousin had male breast cancer, and his daughter had breast cancer, too. And my first cousin was diagnosed with breast cancer when she was just 27."

BRCA genes repair damaged cells and make sure they grow normally. But the mutation of tumor suppressor genes BRCA1 or BRCA2 is associated with a hereditary risk for both breast and ovarian cancers, as well as other cancers. According to the American Cancer Society, approximately 50 to 65% of women with either BRCA mutation will develop breast cancer, and 35 to 45% will develop ovarian cancer before the age of 70.

Initially, Megarity's mother didn't conclusively test positive for BRCA abnormalities — leaving the mother-daughter duo and their MD Anderson physicians puzzled. Years later, when Wight

was diagnosed with ovarian cancer, a follow-up test uncovered the BRCA1 mutation. Immediately, her daughter made the decision to undergo genetic testing. Like her mother, Megarity carried the BRCA1 mutation. At 42, Denise opted to undergo an oophorectomy to remove her ovaries.

A recent study published in the *Journal of Clinical Oncology* may encourage women even younger than Megarity with either BRCA mutation to strongly consider undergoing preventive surgeries.

The international registry study followed nearly 5,800 women with either BRCA mutation for as long as 19 years and found that those who had the oophorectomy reduced their risk of ovarian and other gynecological cancers by 80%. They also cut their risk of dying by age 70 from any cause by 77%.

The most striking survival benefit was found in women with a BRCA1 mutation who underwent an oophorectomy before the age of 35. The surgery dropped their risk for ovarian cancer to 1% — on par with the risk of women who don't have the gene mutation. The researchers found that women with an abnormal BRCA2 could wait longer and still achieve the same benefit.

In addition, the research found that women more than doubled their chance of developing ovarian cancer if they opted for the surgery after age 40; they also were at an increased risk for breast cancer.



Survivor Margarita Wight (left) and her daughter, Denise Megarity, both carry the BRCA1 mutation.

“As clinicians, we really struggle with the conversation about when is the right time for women with BRCA mutations to remove their ovaries,” explains Shannon Westin, M.D., assistant professor in Gynecologic Oncology and Reproductive Medicine. “This is a patient population that’s incredibly knowledgeable about its risk and is faced with a very personal decision.”

Also, before this study, there were concerns about removing the ovaries too early because of possible co-morbidities and the known side effects associated with the surgery.

“Yet the study’s overwhelming survival benefit for women with both BRCA1 and 2 mutations should make us more confident that if you have cause — and BRCA is certainly considered cause — then surgery at a young age is beyond appropriate,” Westin says.

National organizations currently recommend that women with BRCA mutations remove their ovaries at age 35, or after completion of childbearing, says Westin. While she isn’t sure this research will amend those recommendations, the study conclusively finds that, for women with BRCA abnormalities, earlier is better.

And while, as a society, women are waiting longer to have children, Terri Woodard, M.D., assistant professor in Gynecologic Oncology and Reproductive Medicine, hopes that recent advances in fertility treatment will help quell the concerns of those with BRCA mutations struggling to balance their desire to have a family with their decision to proceed with the surgery.

“Now younger women can move forward with their surgery, but first, take steps to preserve their ability to have children,” says Woodard, a reproductive endocrinologist and director of MD Anderson’s Oncofertility Consult Service.

“If they’re not partnered, women with BRCA may choose to freeze their eggs prior to their oophorectomy. Or, if they’re married, perhaps they’ll opt to freeze embryos. It’s important for these women to know that they do have options for family planning.”

For Megarity, the decision to undergo an oophorectomy wasn’t overly difficult. A mother to three boys, she and her husband had completed their family.

“While there was a feeling of finality that I dealt with, having the surgery definitely has eased my worry and allowed me to be at peace knowing that I’ve taken steps to decrease my personal cancer risk.”



Terri Woodard, M.D., a reproductive endocrinologist and director of MD Anderson’s Oncofertility Consult Service, hopes that advances in fertility treatment will help ease the concerns of women who have BRCA mutations and are struggling with the decision to proceed with preventive surgery.

The risks of carrying a mutation

Both men and women with mutations of the BRCA1 or BRCA2 gene have an increased risk of breast cancer.

BRCA1 and BRCA2 mutations account for 20 to 25% of hereditary breast cancers and 5 to 10% of all breast cancer, as well as 15% of ovarian cancers.

The mutation can come from the mother or father. A child of a parent with the mutation has a 50% chance of inheriting it.

Other cancers linked to the mutations:

Women with BRCA1 mutations have an increased risk of developing fallopian tube and peritoneal cancers.

BRCA2 mutations and, to a lesser extent, BRCA1 mutations raise a man’s risk of breast cancer.

Both mutations increase a man’s risk of prostate cancer.

Both men and women with BRCA1 or BRCA2 mutations may be at a higher risk of pancreatic cancer.

National Cancer Institute

99 problems but cancer ain't one

My diagnosis
changed my life.
And for that I'm
very thankful

By Megan Silianoff

📷 Wyatt McSpadden

I was a newlywed, a self-appointed Chicago socialite and an Urban Outfitters' patron. I was working as a recruiter and harboring an obsession with Jay-Z. I was all of these things and 28 years old when I found out I had ovarian cancer.

Looking back, the only thing more shocking than the blindsiding diagnosis was the fact I'd eventually be genuinely happy this happened to me.

After several days of deferring to my mom to break the news to friends and family, and watching her sob through it every time, I realized I needed to take matters into my own hands. This whole thing was too scary. Too depressing. I wanted to lighten the mood and the message.

I decided to start a Caringbridge.org blog, which allowed me to control how and what people learned about my ongoing prognosis. I could also tell people about the cancer in my own voice; a voice that turned out to be quite irreverent and mildly profane.

My cancer prognosis initially was dire and confusing, consisting of opposing opinions from prestigious hospitals. Originally, I was told I had both breast and ovarian cancer and that chemo would be necessary. However, after seeking second and third opinions, it was determined I didn't have breast cancer and didn't need chemo. (I had serous, low malignant potential tumors, which tend to be unresponsive to chemo and radiation. That's why I got to skip that hell on earth.) Although I had four surgeries in 17 months, I considered myself incredibly lucky.

Shortly into remission I realized I missed my blog. I didn't miss the cancer aspect — but I did miss the writing. My Caringbridge blog allowed me to find my voice and writing style, and establish an audience that responded to what I had to say.

Blogger Megan Silianoff and her daughter, Macy, in her home office.



So, in January of 2011, I started “Greetings from Texas,” a lifestyle blog in which I explore and write about whatever it is I feel compelled. Whether it be my obsession with Kylie Jenner’s hair, a recipe for black-bean brownies, an outfit I want to show off or my sexual attraction to Harry Connick Jr.

Eventually, “Greetings” began to cultivate an audience outside of my friends and family. I began to work with brands and attend blogging conferences — at some of which I was a speaker. As my traffic grew, the blog even became mildly profitable.



In the process of building “Greetings” and pursuing domestic adoption with my husband of our daughter, I felt I had more in me than one-off posts. I wanted to share my experiences with cancer and adoption — somber subjects told in a light-hearted way, just like I’d done in my Caringbridge blog.

So I decided to write a book. After about a year and half of plugging away, I had my title: “99 Problems But a Baby Ain’t One — A Memoir About Cancer, Adoption, and My Love for Jay-Z.” It was published by Brown Books this past September.

These days, I continue to promote “99 Problems But a Baby Ain’t One.” I conducted a four-city book tour in 2013 and continue to do signings and speaking engagements at various blogging conferences. I’ve presented my story to companies such as Facebook and the U.S. Navy, hoping to inspire them with my experiences. I’m also working on two new books: a children’s book and an adoption book, which I’m co-writing with an Atlanta author.

Every day I wake up I’m genuinely excited about my work. Whether it’s writing blog posts for “Greetings from Texas,” working on my books or writing freelance pieces for clients, I’m in love with what I do and my life — a life I never would’ve had without cancer.

Cancer is the best thing that ever happened to me. Without cancer my husband and I would never have adopted Macy, the crazy, whip-smart, Elmo-obsessed little girl who makes us laugh and experience love in a whole new way. Without cancer I never would have become a writer, a career that fulfills and energizes me every day. Without cancer I wouldn’t know how capable and strong I can be when push comes to shove.

I’ll say it again because I acknowledge it’s a provocative thing to declare, but I don’t want to be misunderstood.

Cancer is the best thing that ever happened to me.

Megan Silianoff is a writer from Chicago who started her well-known blog, “Greetings from Texas,” after moving to Houston in 2011. Her ovarian cancer diagnosis paved the way for a successful writing career, which includes a published memoir and two more books in the works. In her spare time, she manages social media for Langford Market and Cheeky Vintage, two Houston boutiques. She also has been a contributor to MD Anderson’s Cancerwise blog. She and her husband, Danny, have been married for six years and have a 19-month-old daughter, Macy, and a 7-year-old Vizsla-beagle mix named Booker.

Excerpts from "99 Problems But a Baby Ain't One"

We leave for MD Anderson this week. I have no idea when I'll be back, but I do know I plan to be poolside for the majority of the trip. How did I end up with ovarian cancer and not skin cancer? It's like God doesn't know me at all.

.....
The tumor board at MD Anderson, arguably the most prestigious cancer hospital in the world, is stumped by my case. I don't know whether to be proud or pissed." (I'm leaning towards proud.)

.....
I heard from Cara, my genetic counselor, today. It appears my genetic shortcomings are limited to the areas I'm already aware of: height, math and math. (Seriously, I'm really bad.)

.....
I like my new allergy doctor. He's a smooth cat. He fist bumps. He fist bumped me on his way out of the examination room, which I think should be the new standard for anyone who practices medicine. Any of you doctors reading this, write this down. Patients like fist bumps.

.....
The nurse asked the usual stuff: current medications, if I was in pain, had I fallen recently. I actually had fallen recently, but I'm pretty sure it wasn't cancer-related. Just drunk-related. I decided not to share.

.....
I can't tell you how nice it is to be back home. My dog, my bed, the 4 a.m. gunshots. (Totally kidding prospective buyers of our condo! Non-prospective buyers: Help! I'm scared!)

From "Greetings from Texas":

Megan Silianoff, 28, is a healthy young woman consistently mistaken for Rachel Bilson. (She wishes.) Megan resides in Chicago and is married to Danny Silianoff, 35, consistently mistaken for Kevin James. (Despite his wishes.)

.....
Easter came and went and we embraced the holiday fully. Easter baskets? Nailed it. Easter egg hunt? Obviously. Church? Radio silence.

.....
While Macy has agreed to participate in her budding fashion career, she's made it clear that it's a commitment that will come secondary to her true passion of throwing toys in the toilet.

.....
Everyone I know thinks I'm a terrible driver. Including the police. I have to take defensive driving soon.

From her Caringbridge blog:

Hi. I'm Megan. As you now know, I have cancer. If you're shocked, take comfort in knowing that I am, too.

.....
I had 48 hours until my appointment with the oncologist. I spent 40 of them obsessing about losing my hair. The other eight were spent watching "The Rachel Zoe Project."

.....
I spent the next few days in the hospital. I eventually proved to the nurses and doctor that I was ready to go home. I could walk. I could eat. I could say "I want to go home now."



Silianoff, Macy and the family's Vizsla-beagle mix, Booker

The adrenaline-fueled life

By Madylan Eskridge

When Reza Mehran, M.D., isn't in the operating room, he may be piloting a twin-engine plane or flying a helicopter. When he's not taking to the skies, he may be scuba diving or hunting for dinosaur fossils.

"I'm an old-fashioned adventurer," he says. "If I had lived in the 16th century, I probably would've sailed the world searching for unexplored lands."

His colleagues call him a Renaissance man, but Mehran attributes his extraordinary personal résumé to an affinity for trying new things and visiting new places.

For example, he studied what appeared to be a tumor on the left scapula of a Gorgosaurus (an older cousin of the Tyrannosaurus rex) on display at Houston's Museum of Natural Science. Turns out, the growth was a callus, which implied the dinosaur had suffered a bone-breaking injury. Mehran's discovery gave scientists a unique perspective on the creature's ability to heal and survive. He'll continue pursuing his interest in paleontology this summer when he participates in a fossil dig in South Dakota.

Linguist, soldier and survivor

A professor in Thoracic and Cardiovascular Surgery, Mehran also is co-director of the Thoracic Surgery and Thoracic Medical Oncology Outpatient Clinic. But he's fluent in more than mediacese.

The multilingual native of Switzerland grew up speaking French. Thanks to several years of living in Iran, he knows Persian. While earning his medical degree in Montreal, he learned English. Later on, he added Spanish to the list.

Following his postgraduate training, Mehran served two tours of duty as the commanding officer for an advanced surgical team with the United Nations peacekeeping efforts during the Yugoslav wars of the 1990s.

"My war experience was a lot like the TV series 'M*A*S*H,'" Mehran explains. "Our medical team was deployed with the troops in the danger zone. We went where help was needed."

Years later, he and many of those with whom he served waged their own personal battles against cancer, likely caused by exposure to depleted uranium that commonly was used in aircraft, armor and ammunition during the wars. But Mehran's experience with leukemia and a sarcoma in his knee took him to even greater heights.

Always looking for his next adventure. That's how this surgeon operates

Taking flight

"I'm quite the outdoorsman. But after my knee surgeries, I wanted to find activities that weren't high impact but still challenged me. So I started earning my pilot's license," Mehran says.

After moving to Houston to join MD Anderson in 2001, Mehran bought an airplane and started a small commercial airline company.

A few years later, he learned to fly helicopters in Central America, where he picked up Spanish to communicate with his instructors and the air traffic controllers. Now a commercial pilot of planes and helicopters, Mehran considers himself an aviator as much as anything else.

"In many aspects, flying is similar to performing in the operating room," he explains. "It's a very strict environment. I like the discipline involved."

Always more to learn

Though he's adventured near and far, Mehran feels a strong connection to MD Anderson.

"It's truly a unique place to work as a thoracic surgeon," he says. "I always want to offer the best to my patients, and here I'm able to because I can count on the expertise of the specialists around me. I'm thankful for the strong rapport with my colleagues and our common goal to cure our patients' malignancies."



Adolfo Chavez III

Mehran's colleagues say his cardiac and vascular surgical training, coupled with his precision and speed, have resulted in a fearless cancer surgeon willing to tackle any tumor. He's described as a master surgeon, one who distills a complex operation into precise and deliberate steps with no wasted moves. His operations often are completed in half the time they may normally take, allowing his patients smoother recoveries thanks to his skill and their reduced time under anesthesia.

Furthermore, he's an early adopter of approaches such as minimally invasive esophagectomies, in which small incisions are made and video-assisted thoracic surgery is performed with laparoscopic instruments to remove the esophagus. He's developed techniques to minimize post-operative pain through nerve blocks and the infusion of local anesthetics, which have resulted in improved outcomes. He's also skilled in a variety of palliative procedures.

Despite Mehran's expertise in many areas, there's always more he wants to learn.

"One day I won't be able to physically keep up with my current hobbies," he says. "So I'm trying to look for new ones that will continue to stimulate my brain without being so dangerous."

This story originally ran in the April/March issue of Messenger magazine, which is published for MD Anderson employees, retirees and their families.



Pilot and surgeon Reza Mehran, M.D., is also a budding paleontologist. He recently helped scientists with a discovery about a Gorgosaurus on display at Houston's Museum of Natural Science. © F. Carter Smith

PREVENTION: the ultimate cure for cancer

By Victor Scott

Given their shared commitment to understanding and eliminating cancer, it should come as no surprise that the partnership between MD Anderson and the American Cancer Society (ACS) has existed almost as long as the cancer center itself.

Shortly after opening in 1941, MD Anderson received its first research grant from ACS. In the almost 70 years since, it's awarded the institution approximately 670 grants, equaling more than \$80 million of support for its mission of eliminating cancer.

"In 2013, we celebrated our 100th birthday," says John R. Seffrin, Ph.D., CEO of ACS. "If there's one thing we've learned about defeating cancer during that time, it's that an investment in cancer research has gone from a good bet to a sure bet. What that means is, if we continue to stoke the engines of discovery at institutions such as MD Anderson, we're hopefully going to get the answers needed to end the unnecessary suffering caused by this disease."

Prevention, Seffrin adds, is an area both ACS and MD Anderson view as crucial to achieving their shared goal.

"We have to work together to turn prevention into public policy," Seffrin says. "More than half of the new cancer cases diagnosed each year could be prevented, and I think most people would prefer never to be diagnosed with cancer to being cured of it."

ACS is working to enact prevention policies such as smoke-free laws; educating lawmakers about providing more access to quality, affordable health care that includes cancer screenings and treatment; and pushing for increased federal funding for cancer research.

Ernest Hawk, M.D., vice president and head of Cancer Prevention and Population Sciences at MD Anderson and co-leader of the cancer prevention and control platform of the Moon Shots Program, agrees with the need for changes in public policy.

"The momentum the American Cancer Society has generated with its multidisciplinary approach to fighting cancer matches our mission stride for stride," Hawk says. "Our longtime partnership through research funding and prevention awareness continues to grow. We're excited now to be working even more closely to develop new public policy that will accelerate our common goal of significantly reducing cancer deaths."

In 2009, MD Anderson honored ACS for its decades of generous support with induction into The Anderson Assembly, an organization created to recognize donors who've made a lifetime commitment of \$1 million or more to support MD Anderson programs.



American Cancer Society CEO John R. Seffrin, Ph.D., (right) and MD Anderson's Ernest Hawk, M.D., are committed to turning prevention into public policy.

by F. Carter Smith

\$448,143,101

Total amount of current grants

\$4 billion

Amount given since 1946

Research engine

The American Cancer Society is the largest private funder of cancer research, contributing to nearly every major cancer research breakthrough in recent history. Their grants are the result of a nationwide competition, which has a peer-review process to ensure donor dollars are invested in the best research and training.

Hope Lodge

Many patients come to MD Anderson from outside of Houston, and about one-third travel from outside of Texas. To help those seeking treatment far from home, ACS has established Hope Lodges, which provide a free place to stay, in 31 cities. Currently, ACS seeks to raise \$30 million to cover construction and operating costs for Hope Lodge Houston, which will be built in the Texas Medical Center on land donated by MD Anderson. Upon completion, it will be the largest Hope Lodge in the country, providing free accommodations and transportation for 62 patients and their caregivers. That's approximately 23,000 nights of free lodging each year.

883

Current grants funded in the U.S.

Current grants funded in Texas

58

Total amount of current grants

MD Anderson faculty members currently receiving extramural grants from the American Cancer Society

\$37,501,166

22

Artist's rendering of Hope Lodge Houston





The rise of melanoma in kids

As awareness of the pediatric cancer grows, so do efforts to teach valuable lifelong prevention habits at a young age

By Julie Penne

📷 Wyatt McSpadden

When 14-year-old Kai Dunbar bursts out of the starting blocks while training with her high school track team, she has a single focus: crossing the finish line first.

It was that same philosophy of pushing on to the finish that brought Kai through a rare diagnosis of malignant melanoma, news that she and her family received when she was only 9 years old.

Born with a mole on her right cheek, Kai says the mark grew and eventually spread behind her ear. When it started bleeding and itching, her mother knew the changes were unusual and took her daughter to a dermatologist. After a biopsy and initial diagnosis, the dermatologist recommended the Dunbars go to MD Anderson Children's Cancer Hospital for specialized care.

In the five years since, Kai has had three surgeries and several rounds of the immunotherapy drug interferon, which uses an antiviral protein produced by the body. She experienced a number of difficult side effects and was away from school for a full year. Now an incoming sophomore at Manvel High School, a half-hour's drive south of Houston, Kai comes back to the children's hospital outpatient clinic once a year for checkups, scans and labs.

Kai's experience with the most deadly form of skin cancer has given her a new role among her growing social circle. In addition to hanging out with her friends, going to movies, performing hip-hop dance and running track, Kai is an advocate for sun protection and a walking example of why prevention and awareness are so vital.

"I try not to think about my cancer experience too much, but I always tell my friends to wear their sunscreen, be aware of

any unusual moles, warts or freckles on their skin, and stay in the shade whenever possible," she says. "When I tell them what happened to me, they're shocked. They've never met anyone their age who's been diagnosed with or survived cancer, let alone a cancer that is so much more common in adults."

A rare diagnosis comprising about 3% of all childhood cancers, pediatric melanoma is on the rise in the United States. According to the American Academy of Dermatology, the number

"We live in a culture that loves tanning. Let's help our kids navigate the pressures of tanning and arm them with answers when they encounter others who question their sun safety habits."

— Dennis Hughes, M.D., Ph.D.

of cases diagnosed in the U.S. each year has doubled since 1973, from less than 250 cases to about 500 today.

But even as the number of diagnoses increases, the American Cancer Society reports that treatment may be delayed in up to 40% of cases, often due to a low level of awareness that the disease can affect children.



“A child doesn’t have to be fair-skinned and light-haired to be diagnosed with melanoma,” warns Dennis Hughes, M.D., Ph.D.

© Wyatt McSpadden

Dennis Hughes, M.D., Ph.D., associate professor in Pediatrics at Children’s Cancer Hospital, can attest to the increased cases — and the need for greater awareness of melanoma in children.

Hughes, who came to MD Anderson in 2004, sees an average of 16 new cases each year. His patients range in age from toddlers to teens and represent a variety of ethnic backgrounds.

Hughes and his Children’s Cancer Hospital colleagues are among a handful of pediatric oncologists in the U.S. who provide specialized care for children with melanoma. Over the past decade, no patient diagnosed with melanoma under the age of 18 and treated at the children’s hospital has been lost to the disease, which is well above the national average. According to Hughes, it’s a combination of experience, expertise and a more aggressive approach to treatment — along with a child’s young and more-responsive immune system — that have led to the positive outcomes over the years.

“Deaths due to pediatric melanoma are preventable through early screening, the proper use of sunscreen and decreasing exposure to dangerous ultraviolet (UV) rays, which can come from the sun or tanning beds,” Hughes says. “A child doesn’t have to be fair-skinned and light-haired to be diagnosed with melanoma. It’s important for parents to tune in to an unusual mole or wart and behaviors that may increase risk.”

Teaching, encouraging and practicing positive sun protection habits can pay off for children now and later in life. And teaching sun safety to children and teens can remind adults about the life-long risks of melanoma.

“Instilling strong habits of sun protection not only keeps children safe now, but it also helps reduce risk in their adult years,” Hughes says. “We know that bad sunburns as a child can increase the risk of melanoma later on, so let’s teach our kids now about the importance of wearing sunscreen, playing on a playground or swimming at a pool shaded by a cover, staying away from tanning beds and doing skin checks regularly. These truly are life lessons.”

Tips for sun protection from Children’s Cancer Hospital

- Consider multiple sunscreens for the family, not just one bottle for everyone to share. Let kids select their own sunscreen to make sure it’s something they’ll wear. Take into consideration that some kids don’t like fruity or floral scents and some don’t like a greasy feel. The most effective sunscreen for children is one they’ll wear properly.
- It’s not necessary to wear a sunscreen with an SPF greater than 30. Higher SPF numbers really don’t mean anything in terms of protection.
- Look for play areas with a protective cover or shade, but still apply sunscreen.
- Apply sunscreen to your child before putting on his or her bathing suit for the pool or beach.
- Always pack wide-brimmed hats, umbrellas or shades, sunscreen, sunglasses and protective clothing when heading outdoors.
- Stay indoors between 10 a.m. and 3 p.m., the sun’s peak hours.
- Babies less than 6 months old should be completely shielded from direct sun exposure.
- Talk to your children and teens about the importance of sun safety.

THE UNIVERSITY OF TEXAS SYSTEM BOARD OF REGENTS

Paul L. Foster, *El Paso*
Chairman

Wm. Eugene Powell, *San Antonio*
Vice chairman

R. Steven Hicks, *Austin*
Vice chairman

Ernest Aliseda, *McAllen*

Alex M. Cranberg, *Austin*

Wallace L. Hall Jr., *Dallas*

Jeffery D. Hildebrand, *Houston*

Brenda Pejovich, *Dallas*

Robert L. Stillwell, *Houston*

Nash M. Horne, *Austin*
Student regent

Francie A. Frederick
General counsel to the Board of Regents

THE UNIVERSITY OF TEXAS SYSTEM ADMINISTRATION

Francisco G. Cigarroa, M.D.
Chancellor

Raymond S. Greenberg, M.D., Ph.D.
Executive vice chancellor for Health Affairs

THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER EXECUTIVE COMMITTEE

Ron A. DePinho, M.D.
President

Ethan Dmitrovsky, M.D.
Provost and executive vice president

Thomas A. Buchholz, M.D.
Executive vice president and physician-in-chief

Thomas W. Burke, M.D.
*Executive vice president,
MD Anderson Cancer Network**

Leon J. Leach, Ph.D.
*Executive vice president and
chief business officer*

R. Dan Fontaine, J.D.
Executive chief of staff

Helen Pivnicka-Worms, Ph.D.
Vice provost for science

Maureen K. Cagley
Vice president for academic operations

Margaret B. Row, M.D.
Vice president for operations

Amy C. Hay
Vice president for business development

Wenonah B. Ecung
Vice president for clinical administration

MD ANDERSON CANCER CENTER BOARD OF VISITORS OFFICERS

Harry J. Longwell
Chair

Melvyn N. Klein
Chair-elect

James J. Mulva
Vice chair

Nancy B. Loeffler
Immediate past chair

LOCATIONS

MD Anderson has Houston-area locations in the Texas Medical Center, Bay Area, Katy, Sugar Land, The Woodlands, Bellaire (diagnostic imaging) and Memorial City (surgery). MD Anderson physicians also provide cancer care to the underserved at Lyndon B. Johnson General Hospital in Houston. In addition, there are two research campuses in Bastrop County, Texas. The institution also has developed a network of national and international locations.

MD ANDERSON CANCER NETWORK*

www.mdanderson.org/cancernetwork

PARTNER MEMBERS

- Banner MD Anderson Cancer Center (Gilbert, Ariz.)
- MD Anderson Cancer Center at Cooper (New Jersey)

CERTIFIED MEMBERS

- 13 health systems and hospitals in 11 states

AFFILIATES

- MD Anderson Cancer Center Madrid (Spain)
- MD Anderson Radiation Treatment Center at American Hospital (Istanbul)
- MD Anderson Radiation Treatment Center at Presbyterian Kaseman Hospital (Albuquerque, N.M.)

Sarah Newson, *associate vice president, Communications*

Jim Newman, *director, External Communications*

EDITOR

Andy Olin, *program director, External Communications*

DESIGNER

Michael Clarke

Conquest is published by the MD Anderson Cancer Center Board of Visitors on behalf of MD Anderson.

All correspondence should be addressed to the Communications Office - Unit 700, MD Anderson Cancer Center, 6900 Fannin St., Houston, Texas 77030-3800, 713-792-3457.

Email: RLKimmons@mdanderson.org. Articles and photos may be reprinted with permission.

For information on supporting programs at MD Anderson, please contact Patrick B. Mulvey, vice president, Development, 713-792-3450, or visit the myGiving website at www.mdanderson.org/gifts/q0414.

For information on patient services at MD Anderson, call askMDAnderson at 877-632-6789, or log on to www.mdanderson.org/ask.

© 2014 The University of Texas MD Anderson Cancer Center
Not printed at state expense. Printed with soy-based ink.

Visit the Conquest website at www.mdanderson.org/conquest.