

CONQUEST

THE UNIVERSITY OF TEXAS
MD Anderson
Cancer Center

Making Cancer History®

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**SHE DOESN'T HAVE CANCER,
AND SHE PLANS TO KEEP
IT THAT WAY**

Women who inherit elevated cancer risks are taking action to sidestep the disease

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On the cover: Like most parents, Jenna Arnold is doing all she can to ensure that she'll live a long life to see her son, Jack, grow up and pursue his dreams. Women such as Arnold, who carry BRCA gene mutations, are participating in a first-in-the-nation MD Anderson clinical trial to reduce their risk of cancer while leaving menopause for later. The trial involves a surgery known as salpingectomy, which removes the fallopian tubes while leaving ovaries intact.  Eric Kayne

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.

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

CANCER FRONTLINE

BLOOD TEST COULD REVEAL PANCREATIC CANCER EARLIER

MD Anderson researchers believe they may have found a way to detect pancreatic cancer at an early stage, before it has spread to other organs and becomes too difficult to treat.

Their study, which was published in the science journal *Nature*, shows a protein present on cancer exosomes was found in the blood of pancreatic cancer patients, but not in the blood of those who don't have the disease or who have chronic pancreatitis. The findings could lead to an accurate, noninvasive diagnostic and screening tool to detect the deadly cancer, which often is only diagnosed in the later stages after metastasis has occurred.

Close to 50,000 people are diagnosed with pancreatic cancer in the United States each year, and almost 41,000 deaths are caused by the disease annually. The average five-year survival rate is 7.2%.

Exosomes are tiny, virus-sized particles released by cancer cells and contain DNA, RNA and proteins. Scientists isolated and monitored the circulating exosomes (crExos) enriched with the glypican-1 (GPC1) protein — called GPC1⁺ crExos — from pancreatic cancer patients' blood.

"GPC1⁺ crExos were detected in small amounts of serum from about 250 pancreatic cancer patients with absolute specificity and sensitivity. It importantly distinguished patients with chronic pancreatitis from those with early- and late-stage pancreatic cancer," said Raghu Kalluri, M.D., Ph.D., chair of Cancer Biology.

The study also found that the levels of the exosomes were significantly lower in patients following surgery to remove the tumors. Circulating exosomes from healthy donors and breast and pancreatic cancer patients were examined, and elevated levels of the GPC1⁺ exosomes were seen in both cancers.

"GPC1⁺ crExos can be detected and isolated in blood samples that were stored in freezers almost 30 years ago, unlike circulating tumor cells, which require large amounts of fresh blood," said Kalluri. "DNA, RNA and proteins can be isolated from cancer exosomes

taken from a stored specimen for further genetic and biological analyses. Therefore, cancer exosomes aren't just a biomarker. Isolating them provides a trove of cancer-specific information."

That information could be used to help physicians choose the best treatment for particular cancers, as well as show the effectiveness of treatments.

These markers appear to be a more reliable screening tool than the commonly used CA 19-9 biomarker, which results in many false negatives and false positives. The study showed that the presence of GPC1⁺ exosomes predicted pancreatic cancer 100% of the time. And GPC1⁺ crExos detected the possibility of pancreatic cancer in mouse models of pancreatic cancer at a time when the mice showed no signs of pancreatic disease by MRI.

"Routine screening of the general population for pancreatic cancer using MRIs or CTs would be prohibitively expensive with the likelihood for many false positives," said David Piwnica-Worms, M.D., Ph.D., chair of Cancer Systems Imaging. "Our study suggests the potential for GPC1⁺ crExos as a detection and monitoring tool for pancreatic cancer combined with imaging, with an emphasis on its application in early detection."

If detected early, surgery involving a pancreatoduodenectomy or the Whipple procedure can be a cure for pancreatic cancer patients. Since pancreatic cancer is often diagnosed after the disease has spread, only about 15% of patients qualify for the surgery.

"Studies comparing stage of disease with outcome following surgery suggest that death rates for pancreatic cancer would be reduced if the disease were diagnosed at an earlier stage," said Kalluri. "This presents an unprecedented opportunity for informative early detection of pancreatic cancer and in designing potential curative surgical options."

— Ron Gilmore



MD ANDERSON NAMED THE TOP CANCER HOSPITAL ONCE AGAIN

MD Anderson has been ranked the No. 1 hospital for cancer care in the nation by U.S. News & World Report's "Best Hospitals" survey.

Since the annual survey launched in 1990, the institution has been named one of the top two cancer hospitals in the United States. It has ranked first 11 times in the past 14 years.

"We're honored by this tremendous national recognition, but the true measure of our success is the number of lives we've impacted with our care, research and support," said Ron DePinho, M.D., president of MD Anderson. "We owe our gratitude to the more than 20,000 cancer fighters, including world-class faculty and nurses, and 1,000-plus volunteers working every day to end cancer for our patients and others around the world. Our culture of exceptional care and genuine caring is second to none."

Specialty rankings

Two subspecialties also were ranked highly in this year's survey. In the Ear, Nose and Throat specialty, MD Anderson's Head and Neck Surgery service was ranked No. 5, the same ranking as last year. In Gynecology, MD Anderson's Gynecologic Oncology and Reproductive Medicine service moved forward one ranking, coming in at No. 7.

These specialty rankings are particularly notable because they include care provided at general hospitals across the nation, not just cancer centers. Both of these specialties have been consistently ranked high for the past two decades.

The survey also named MD Anderson as "high performing" in Urology, meeting the survey's standards for excellence.

DON'T LET THE SUN CATCH YOU UNPREPARED

This time of year, kids are out of school, families are vacationing and people are heading to the beach and the pool. Yes, summer is on full blast, which means it's a good idea to brush up on your sun safety skills. To prevent skin cancer — the most common type of the disease — it's important to be informed about the sun's harmful effects and diligent about using sunscreen correctly. (And don't forget to wear protective clothing.) More than 3.5 million people are diagnosed with skin cancer each year in the United States. Follow these tips from MD Anderson experts to help keep your skin healthy.

Even a few minutes in the sun increases your skin cancer risk. So don't head outside without sunscreen — not even for vitamin D.

Seek shade between 10 a.m. and 4 p.m. That's when the sun's UV rays are strongest and you're more likely to burn.

Your skin takes 30 minutes to absorb sunscreen, so apply sunscreen with SPF 30 or higher 30 minutes before you head outside.

There's no such thing as a safe tan.

Tan skin is a sign of skin damage that can lead to skin cancer.



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Spray sunscreens wash off more easily than lotions, so make sure you re-spray every 60 to 90 minutes.

You'll use sunscreen more often if you like its texture. Test different sunscreens and find one with a texture you like.

Don't skimp on the sunscreen this summer.

A family of four should use a whole bottle of sunscreen on vacation in two days.



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Shopping for sunscreen? Choose one with titanium dioxide or zinc oxide. They both block UV-B and UV-A rays.

Talk to your kids about the dangers of tanning beds. Tanning bed use before age 30 increases melanoma risk by 75%.

Your age doesn't matter when it comes to skin cancer. What matters is your exposure to UV radiation. Seek shade when the sun's rays are strongest.

Anyone can get skin cancer. No matter your skin color, monitor your skin and contact your doctor ASAP if you spot unusual changes.

Tanning beds are not safer than natural sunlight. Tanning beds emit the same harmful UV rays as the sun, so avoid using them.

No skin color is safe from skin cancer.

Even people with dark skin need sunscreen.



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E-CIGARETTES' GROWING POPULARITY UNDERScores THE NEED FOR REGULATION

In April, new federal data was released showing that while smoking combustible cigarettes continues to go down among teenagers, e-cigarette use has tripled among students in middle and high school.

We asked MD Anderson's head of Cancer Prevention and Population Sciences, Ernest Hawk, M.D., to share his thoughts on the trend:



Ernest Hawk, M.D.

Parents, cancer researchers, physicians and public health practitioners should all be encouraged by substantial declines in the use of traditional

cigarettes among teenagers. From 2011-2014, the percentage of high school students that smoke cigarettes fell from 16% to 9%, according to Centers for Disease Control and Prevention's annual youth tobacco survey.

The same report, however, showed an increase of nearly 9% — from 4.5% to 13.4% — between 2013 and 2014 in the use of e-cigarettes among high-schoolers. That's a jump from 660,000 to 2 million in the span of just one year.

This dramatic rise in the use of e-cigarettes, which may be related to the decline in the use of combustible tobacco, is troubling.

There's been no shortage of theorizing about whether e-cigarettes are less dangerous than smoking. But at this time, there is no sufficient evidence-based research to support e-cigarettes as a healthy alternative to tobacco products for current smokers.

Paul Cinciripini, Ph.D., MD Anderson's chair ad interim of Behavioral Science, shared these concerns last year:

"The absence of smoke, which is replaced by the odorless vapor, gives smokers a false sense of security that there's less risk involved with using e-cigarettes, known as vaping," said Cinciripini. "Because e-cigarettes aren't regulated by the Food and Drug Administration (FDA), we have no evidence to prove they're safe."



Illustration by Kellye Sanford

More than a year ago, the FDA proposed regulations for the e-cigarette industry, which operates with little oversight and uses marketing tactics such as candy flavoring that likely contribute to the swell of younger users. The proposals would ban the sale of e-cigarettes to those below the age of 18, halt the distribution of free samples, place health warnings about nicotine on packages and disclose their ingredients. To date, no action has been taken by the federal government.

As tobacco use is ultimately a result of nicotine addiction, the uptake of e-cigarettes among non-smokers is of particular concern. Regardless of what science tells us about the potential long-term health effects of e-cigarettes, we must not forget these are products intended to deliver nicotine, an addictive substance that can be detrimental to developing adolescent brains and can potentially lead to future tobacco use.

At this time, 42 states prohibit the sale of e-cigarettes to minors. That number may soon increase.

Texas lawmakers are considering extended restrictions on tobacco products to e-cigarettes. We're pleased that Texas and other states are taking seriously the health impacts of e-cigarettes on future generations. And we're hopeful the FDA will quickly follow suit.

HARNESSING A MUSHROOM'S TOXIN TO KILL CANCER

For some time, cancer researchers have considered alpha-amanitin, the toxin derived from "death cap" mushrooms, as a possible cancer treatment. However, because of its penchant for causing liver toxicity, its potential as an effective therapy has been limited.

MD Anderson scientists looked at antibody-drug conjugates (ADCs) based on alpha-amanitin as one solution. They found that ADCs, when aimed at a gene called POLR2A, are highly effective in mouse studies in treating colorectal cancer. The drug caused complete tumor regression and greatly reduced toxicity. ADCs combine powerful anticancer toxins linked to antibodies that allow for improved targeting of cancer cells, resulting in less impact on healthy cells.

Xiongbin Lu, Ph.D., associate professor of Cancer Biology, observed that when the common tumor suppressor gene TP53 is deleted, resulting in cancer growth, another nearby gene, POLR2A, also is deleted. Normal cells have two copies of POLR2A and TP53 genes. Lu's study targeted cancers that had a single copy of both genes, representing 53% of colorectal cancers, 62% of breast cancers and 75% of ovarian cancers.

"POLR2A is an essential gene for cell survival, including cancer cells," said Lu. "Because there's only one copy, the cancer cells are more susceptible to suppression of this gene."

Lu's study was published in *Nature*.

The discovery that POLR2A is deleted at the same time as TP53 means that therapies can more specifically target the genetic processes that allow cancer cells to thrive. Understanding that one copy of POLR2A can allow cancer to grow gives researchers a new target to hit. As it turns out, it can be suppressed by an ADC based on the mushroom toxin. Lu's team tested alpha-amanitin because it was believed to specifically inhibit POLR2A.

— Ron Gilmore



Jesse Selber, M.D., a reconstructive plastic surgeon at MD Anderson, conceptualized the partial skull and scalp transplant for Jim Boysen. 📷 Mayra Beltran / Houston Chronicle via Associated Press

MD ANDERSON COLLABORATES ON WORLD'S FIRST SKULL-SCALP TRANSPLANT

Doctors from MD Anderson and Houston Methodist Hospital have performed what is believed to be the world's first partial skull and scalp transplant on a man whose treatment for a rare cancer of the scalp muscle left him with a deep head wound that wouldn't heal.

During the same surgery, the patient also received a donor kidney and pancreas.

"This has been a long journey, and I'm so grateful to all the doctors who performed my transplants," said Jim Boysen, a 55-year-old software developer from Austin, Texas. "I'm amazed at how great I feel and am forever grateful that I have another chance to get back to doing the things I love and be with the people I love."

Boysen's first kidney-pancreas transplant was in 1992, to treat diabetes he's had since age 5. The immune suppression drugs he took at the time to prevent organ rejection raise his risk of cancer, and he developed leiomyosarcoma, a rare type of cancer affecting the smooth muscle under his scalp.

Radiation therapy for the scalp cancer left Boysen with a large head wound, and the immune suppression drugs kept his body from repairing the damage. In addition, the transplanted organs he received 23 years ago were starting to fail.

Yet doctors could not perform a new kidney-pancreas transplant as long as he had an open wound.

Jesse Selber, M.D., a reconstructive plastic surgeon at MD Anderson, conceptualized a solution: give Boysen a new partial skull and scalp, a new pancreas and a new kidney, all at once.

"When I first met Jim, I made the connection between him needing a new kidney and pancreas and the ongoing anti-rejection medication to support them. Receiving a full scalp and skull transplant at the same time that would be protected by those same medications," Selber said. "This was a truly unique clinical situation that created the opportunity to perform this complex transplant."

The surgery took place on May 22 at Houston Methodist Hospital. A team of about a dozen doctors and 40 health care professionals participated, led by Selber and Houston Methodist's A. Osama Gaber, M.D., director of the Houston Methodist J.C. Walter Jr. Transplant Center.

LifeGift, a Houston-based organ procurement agency, obtained the organs for transplant.

Last year, doctors in the Netherlands replaced most of a woman's skull with a 3-D printed plastic one. The Texas operation is the first skull-scalp transplant from a human donor.

— Julie Penne


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in Making Cancer History®
at cancerfrontline.org.



Treating the cancer patient, not just the patient's cancer

Palliative medicine isn't
hospice care, it's a support
system devoted to improving
quality of life

By Ronda Wendler

Shalini Dalal and other members of the Palliative Care Medicine team help patients like Bre Tipps deal with the physical side effects and emotional stress that come with cancer treatment and diagnosis.  Eric Kayne

Bre Tipp's life turned upside down in January 2012 after she underwent routine surgery to remove benign fibroid tumors from her uterus.

"I woke up in the recovery room to see my doctor standing over me, looking concerned," she recalls. "He told me I didn't have fibroids after all. I had ovarian cancer."

The 26-year-old mother of three was given six months to live. That's when she decided to make the five-hour drive to Houston from her tiny hometown of Grand Saline in northeast Texas. She wanted a second opinion from MD Anderson cancer specialists. And she wanted to fight.

"I have a husband. My kids are still young," she says. "I have a lot to live for."

At MD Anderson, Tipp's sailed past her six-month end-of-life prognosis, and today at age 29, she's well into her third year of treatment. Her cancer was advanced when detected and is still there, but she's managed to stay a few steps ahead of it with chemotherapy, surgery and experimental drugs.

Sometimes the medical procedures are grueling and the side effects severe. Tipp's has suffered pain, nausea, fatigue and, occasionally, depression.

"I know I'm getting the best medical treatment," she says, "but I need somebody to help me deal with the side effects and everything else cancer brings."

ONE-STOP SHOP

That "somebody" is a team of health care providers, counselors, clergy members and others who are specially trained in palliative care — a branch of medicine that helps patients deal with the physical side effects and emotional stress that come with cancer treatment and diagnosis.

At MD Anderson, outpatients receive palliative care in the hospital's Supportive Care Center. Each new patient undergoes a 10-point checkup, much like a car in a mechanic's garage, explains Eduardo Bruera, M.D., chair of Palliative, Rehabilitation and Integrative Medicine. From that initial visit, a team is assembled to address each patient's requirements.

"One person may need a gastroenterologist for nausea, a psychiatrist for anxiety and a pain specialist for discomfort," Bruera explains. "Another may need a sleep specialist for insomnia, a respiratory therapist for shortness of breath and a chaplain for spiritual support. Others

may benefit from having a social worker, pharmacist, nutritionist or oncology massage therapist on their teams."

When visiting the Supportive Care Center, patients meet with their team members in one appointment, under one roof.

"Instead of visiting five specialists in five clinics, your custom-designed palliative care team is here in the Supportive Care Center," Bruera explains. "In one day you see them all, then you go home."

Hospitalized patients can receive palliative care in their hospital room as well. On the 12th floor Andreas Beck Inpatient Palliative Care Unit, patients with advanced cancer are preparing to transition to hospice or end-of-life care, but first need their symptoms brought under control. Each morning, teams of palliative care professionals visit each patient, dispensing comfort and care.

"I've seen patients with unrelenting pain and nausea arrive on our unit, and within 48 hours they're calm and comfortable," says licensed professional counselor Martha Aschenbrenner. "Our palliative care team works magic."

On other floors, patients battling various stages of cancer are visited by mobile palliative teams.

EXTRA LAYER OF SUPPORT

The goal of palliative medicine, Bruera says, is to give patients the best quality of life possible, not by providing primary cancer care — the oncologist does that — but by delivering pain and symptom relief, as well as spiritual and psychosocial support.

"Think of it this way," he says. "Oncologists treat the patient's cancer; palliative care teams treat the cancer patient. The emphasis is on the patient's needs, not the disease."

Modern medicine offers wonderful therapies to treat cancer, Bruera says, but many of those treatments produce unpleasant side effects. Palliative care, sometimes called "comfort care" or "symptom management," provides an extra layer of support, beyond the medical care provided by oncologists.

"Palliative care helps patients tolerate their treatments and get on with their lives," Bruera says.



Tipps has been able to continue working as an office assistant at a natural gas pipeline company and even organized a “Paint the Town Teal” ovarian cancer fundraising event in Grand Saline. Last year she attended the National Ovarian Cancer Coalition’s annual conference in Washington, D.C., and testified before Congress about the need for increased ovarian cancer research funding.

Throughout her cancer journey, Tipps has had a strong support network of friends and family, including her husband, Terry; her parents, Liz and Ronald; and her hometown church family.

“My family and friends are wonderful, but my palliative care team keeps me going,” she says. “They tell me things like, ‘You don’t need to suffer. We can lessen your pain.’ I’m grateful for their help. I couldn’t have made it this far without them.”

PACKAGE DEAL

Derived from the Latin *palliare*, “to cloak,” palliative care addresses a patient’s “total pain.”

“Cancer patients may question why God is letting them suffer,” says Aschenbrenner. “They may fear their treatment won’t work or worry about cancer’s effect on their marriage or children. They’re in physical, spiritual and psychological pain.”

These various forms of pain are deeply interconnected, Aschenbrenner says.

“It’s hard to control physical pain in a person who’s having a spiritual crisis, and it’s difficult to soothe psychological pain in someone whose physical pain is uncontrolled,” she explains. “They’re all part of one big package.”

“We want to help people live as well as they can, as long as they can.”

ANY AGE, ANY STAGE

Palliative care often is confused with hospice. That’s understandable because it’s an important component of hospice care, says Suresh Reddy, M.D., director of Palliative Care Education.

But while hospice is tailored to patients whose life expectancy is generally six months or less, palliative care “is in no way limited to those who are at the end of life, have a terminal disease or whose outcome is expected to be terminal,” Reddy says.

From infants to the elderly, from the newly diagnosed to the critically ill, palliative care is appropriate “at any age, at any stage.”

“Most people who need palliative care are not dying, but living for a long time with serious and complex illness,” Reddy says.

If a patient’s cancer cannot be treated, only then does the palliative care focus shift to end-of-life care, which is often provided by a hospice.

THE CONVERSATION

At the heart of palliative medicine is a conversation, or series of conversations, about a patient’s goals and preferences for care.

This requires skill, compassion, a good listening ear and, if the patient is terminally ill, a level of comfort with topics many people would rather avoid.

Palliative care specialists help patients and families weigh the benefits and drawbacks of various treatments. Some patients want to “pull out all the stops” and try everything, while others may prefer comfort-focused care or something in-between.

“We ask our patients their understanding of their disease,” explains Paul Walker, M.D., medical director for the hospital’s inpatient Palliative Care Unit. “We find out what they know and, if their disease is terminal, what they hope to achieve

“We’re adding life to their days, not just days to their lives.”

— Eduardo Bruera, M.D., *chair of Palliative, Rehabilitation and Integrative Medicine*



The Rev. Christiana Liem is available to counsel patients dealing with the spiritual pain of cancer. Spiritual health can play an important role in the cancer journey.

Eric Kayne

in the time they have left. Then we help them achieve those things that are important to them.”

Aschenbrenner says the inpatient palliative care team is privileged to witness some extraordinary events.

“We’ve had several weddings on the unit,” she says. “Families are so willing, at one of the most daunting times of their lives, to let us come in and walk alongside them. I’ve witnessed vulnerability and sadness, along with remarkable tenderness, resilience and healing.”

Aschenbrenner readily admits to shedding a tear with families.

“This job is not a piece of cake,” she says, “but I wouldn’t dream of doing anything else.”

Every doctor who sees seriously ill patients should possess the skills to lead conversations that put patients’ desires first, says Bruera. But research shows that between one-quarter and two-thirds of patients with advanced cancer don’t have such talks with their physicians, and when they do occur, the conversations often take place in the hospital just a month or so before death.

“In fact, palliative care is most useful when it’s started early, along with cancer treatment,” Bruera says. “This way, it can help treat common symptoms caused by treatment and ensure the best quality of life.”

It boils down to this, Bruera says:

“People have priorities in their lives besides just living longer. We must find out what their priorities are by asking, but we don’t ask. As physicians we’re not rewarded for having conversations. We’re rewarded for doing operations or procedures well.”

Regardless of a patient’s prognosis, Bruera says his message to patients is this: “We hope you get better, but if you don’t, what do you want? We push the envelope on what’s important to the patient.”

Just knowing that there’s a plan in place offers families peace of mind,” he says. “And that helps them concentrate on their loved one.”

RACHEL’S STORY

After battling bile duct cancer for two years, Rachel Henry was tired. She’d made countless round trips from her home in Huntsville, Texas, to MD Anderson, endured numerous chemo and radiation sessions, tried a host of different drugs and been confined to the intensive care unit four times.

Earlier this year, the palliative care team helped Henry clarify how she’d like to spend the time she had left. Instead of more medical procedures, she opted for “comfort care,” or treatment of symptoms. No more poking and prodding, no more machines.

“It took Rachel all of 10 seconds to make that decision,” says her sister, Mary Gail Doddridge. “She was ready.”

Before she died on April 17 at age 64, Henry, a retired home economics teacher, was able to spend valuable time with her children and grandchildren and share family recipes from her hospital bed.



Massage therapist Curtiss Beinhorn does his part in treating the whole patient.  Wyatt McSpadden

That extra time focusing on loved ones and quality of life is something the family will always cherish, Doddridge says.

GROWING FAST

Palliative care has come a long way since it was first introduced in the United States in the 1970s.

“At first, physicians and other health care providers were suspicious of palliative care practitioners, because they didn’t understand our role,” Bruera says. “They thought of us as ‘grim reapers.’ Acceptance was slow.”

Today, palliative care is the fastest growing medical specialty in the United States, and the fastest growing department at MD Anderson. Almost 90% of large hospitals — those with 300 beds or more — now have palliative care programs, and most cancer centers have added palliative care supportive services.

Several groundbreaking studies have fueled this growth, including results from a lung cancer patient trial published in the *New England Journal of Medicine* in 2010. The study revealed that lung cancer patients who received palliative care at the same time as their cancer treatment felt better, had fewer emergency room visits, were less depressed, less likely to die in the hospital and lived three months longer than similar patients getting excellent cancer care but no palliative care.

Recognizing these benefits, the Institute of Medicine last fall issued a report that said every patient should have access to high-quality, affordable palliative and hospice care when and where they need it. The report, which Bruera helped author, is expected to produce sweeping changes in patient care across the country.

“Helping people live longer is great,” says Bruera. “But what’s really important is that we’re improving quality of life for our patients. We’re adding life to their days, not just days to their lives.”

The engines powering the moon shots

By Scott Merville

10 platforms of expertise and technology support the program's progress

Since discovering that leukemia cells contain a target that can attract an immune attack leading to remission, Jeff Molldrem, M.D., and his colleagues have doggedly sought ways to help the immune system home in on the cancer.

In 2011 the team developed an antibody that recognizes and binds to that target, a peptide called PR1/HLA-A2. This attack triggers destruction of acute myeloid leukemia (AML) cells by the complement system, a component of our overall immune system.

The antibody, named h8F4, became a prime candidate for a clinical trial — one that could potentially result in a new drug to treat AML. However, that step from successful preclinical research to first clinical trial is where many ideas falter and die.

“Unfortunately, advancing novel discoveries from the laboratory to drug development has been historically challenging,” says Molldrem, a professor of Stem Cell Transplantation and Cellular Therapy. “Antibodies pose their own difficulties, including a more complex and expensive manufacturing process than other types of drugs.”

ANTIBODIES IN ORBIT

Molldrem connected with Carlo Toniatti, M.D., Ph.D., a scientist with a long record of research achievements in the pharmaceutical industry and executive director of a platform for MD Anderson's Moon Shots Program called Oncology Research for Biologics and Immunotherapy Translation, or ORBIT. The plat-

form is designed to help accelerate and execute the translation of MD Anderson immune system discoveries into therapeutic treatments.

ORBIT accelerated development of H8F4 by funding the start of the manufacturing process for the antibody, developing a detailed, three-year plan to bring the drug to clinic, and reaching out to potential pharmaceutical company partners.

As a result, in April, MD Anderson signed an agreement with the international drug company Astellas Pharma Inc., to develop h8F4, with clinical trials set for 2017.

“Jeff Molldrem's connection with ORBIT is a good example of how the Moon Shots Program meets its promise of applying existing scientific knowledge to bring new therapies to patients at an accelerated pace,” says Giulio Draetta, M.D., Ph.D., co-leader of the Moon Shots Program and director of the Institute for Applied Cancer Science (IACS).

ORBIT is one of 10 platforms, or research engines, built by the moon shots, which are designed to harness established knowledge and new, disruptive technologies to dramatically reduce cancer deaths through prevention, early detection and treatment. The platforms provide an empowering infrastructure of expertise and technology to support the program's efforts.



Carlo Toniatti (from left), Giulio Draetta and Jeff Mollidre are working to translate immune system discoveries into drug development.

📷 F. Carter Smith

“Platforms are a unique aspect of the program,” says MD Anderson President Ron DePinho, M.D. “We’ve embedded these industry-quality capabilities in an academic organization to allow scholars who are really good at discovery to translate their findings more systematically, rapidly and deliberately to save as many lives as possible in the next five to 10 years.”

The initial moon shots are targeting chronic lymphocytic leukemia, breast and ovarian cancer, melanoma, myelodysplastic syndrome (MDS)/acute myeloid leukemia (AML) and lung and prostate cancers. A number of additional moon shots pilot programs have been initiated.

With their expertise and capabilities in drug development, prevention, cancer genetics and proteomics, immunology, preclinical cancer modeling, and the storage, processing and use of massive amounts of medical and scientific information, the platforms are primed to deliver on the cutting edge of science and medicine.

NEW DRUGS AND CELLULAR THERAPIES

ORBIT, IACS and the Center for Co-Clinical Trials (CCCT) and Applied Cell Therapy (ACT) are platforms devoted to novel drug development. They discover potential medicines to offer the moon shots and MD Anderson clinical departments and also collaborate with the institution’s investigators who have ideas for new drug targets.

The institute specializes in small-molecule drug development and functions much like a biotech company, if one was embedded in an academic institution. Many IACS scientists honed their craft in the biotech/pharmaceutical sector and apply that insight in their collaboration with MD Anderson’s clinical experts.

As an example, IACS, collaborating with the CCCT platform and the MDS/AML Moon Shot, is in the final stages of Food and Drug Administration-mandated safety testing of IACS-10759, a novel inhibitor of a key cellular component required for energy production to which some tumors appear addicted.

“Platforms are a unique aspect of the program. We’ve embedded these industry-quality capabilities in an academic organization to allow scholars who are really good at discovery to translate their findings more systematically, rapidly and deliberately to save as many lives as possible in the next five to 10 years.”

— MD Anderson President Ron DePinho

Working together, the team rapidly advanced IACS-10759 through preclinical development and plans to start clinical trials in early 2016, beginning with AML.

“The drug discovery team designed, synthesized and evaluated multiple rounds of compounds, steadily improving their overall profiles over 18 months to identify a single compound to move into clinical development. IACS-10759 is in the final stages of preclinical testing leading to an Investigational New Drug submission,” says Phil Jones, Ph.D., head of Drug Discovery at IACS. “IACS-10759 starves certain vulnerable cancer cells of energy in a new way.”

In addition to AML, preclinical work on the drug indicates it might also work for some patients with lymphomas, colon, pancreatic and skin cancers, and glioblastoma.

CELL THERAPIES

ACT is a new platform that develops customized cellular therapies, including immune system T cells, to attack cancer, and will guide the moon shots in this promising area of research. Clinical trials of T cells genetically engineered to more efficiently find and kill cancer are in the works.

Another trial cultivates different types of immune cells, called natural killer cells, from donated umbilical cord blood and gives them to patients as immunotherapy in the Chronic Lymphocytic Leukemia Moon Shot, along with chemotherapy.

IMPROVING AN INNOVATIVE COMBINATION

The CCCT focuses on how genomic alterations drive tumor growth and progression, and seeks to identify vulnerabilities that will enhance treatment. It conducts comprehensive preclinical research using patient-derived tumor models, cancer cell lines and unique engineered mouse models to position novel drugs with distinct patient populations.

In collaboration with the Melanoma Moon Shot, MD Anderson scientists developed a promising new two-drug targeted therapy for a specific group of melanoma patients. The dosing schedule used in a first-in-human phase I clinical trial showed promise but also significant toxicity, says Tim Heffernan, Ph.D., CCCT co-director.

“We’ve taken what we learned from the clinical trial back into the mouse model to develop an effective but less toxic treatment schedule,” he says.

This repeat process, from preclinical insight to clinical trial, then back to the lab to improve treatment before returning the therapy to the clinic, is a hallmark of the CCCT. The same drug combination is being tested in colorectal and pancreatic cancers.

“Based on initial clinical experience, the CCCT’s approach will likely be critical to maximizing the clinical impact of these very promising approaches by identifying safe and effective treatment regimens,” says Michael Davies, M.D., Ph.D., associate professor of Melanoma Medical Oncology and co-leader of the moon shot.



SWIFT, DEEP GENOMIC ANALYSIS

The Cancer Genomics Laboratory (CGL) is a platform that provides genomic tumor sequencing on an accelerated schedule. Samples are sequenced and analyzed within 10 to 12 weeks after submission. In addition to supplying information for an investigator's specific project, everything is deposited into MD Anderson's big data platform, where it's available to all researchers.

"CGL provides rapid, high-quality sequencing with open access to data," says Maggi Morgan, the platform's scientific manager.

Earlier this summer, eight projects were in the CGL platform's pipeline, and that number is expected to increase. Investigators in the pilot moon shot for human papillomavirus (HPV)-related cancers are using CGL sequencing results to better understand how the virus inserts its DNA into a person's DNA, and the role that genomic integration plays in the development of cervical and head and neck cancers.

A follow-up study of nine HPV-positive and 50 HPV-negative cell lines and patient samples will further examine the role of HPV in tumor origination, patient outcomes and as a biomarker for personalized treatment.

EMERGING IMMUNOTHERAPY

Tumor and matched blood samples also are sent to the immunotherapy platform led by James Allison, Ph.D., the scientist who opened up a new way to treat cancer by unleashing the immune system to attack it.

Allison's platform conducts preclinical and clinical research to identify and evaluate new single-agent and combination therapies, including immune monitoring of tumors before, during and after treatment. More than 60 MD Anderson immunotherapy clinical trials for a variety of cancers rely on the platform for immune analysis.

Long-term research shows that 22% of patients with untreatable, late-stage melanoma survive 10 years or longer when treated with Allison's drug, Yervoy. Drugs such as Yervoy, which amp up the immune system, have shown similar improvements in clinical trials for lung, bladder, kidney, liver, head and neck and other cancers.

Allison believes combination therapies will yield even better results. The key is to identify the most promising combinations out of a multitude of potential choices.

"I think with immunotherapy drugs we're going to succeed very quickly in improving survival in patients with a number of cancers," Allison says. "Patients will survive decades — not just months or weeks as they did with conventional therapies."

HOMING IN ON PROTEIN TARGETS

The proteomics platform identifies and analyzes the thousands of proteins in cancer cells to find the few that can be used as drug targets or biomarkers for screening or diagnosis.

"The platform is helping the MDS/AML Moon Shot understand drug resistance and identify new targets for these diseases," says moon shot leader Guillermo Garcia-Manero, M.D., professor of Leukemia.

One outcome: An agreement with drug company Amgen to provide and test proteins for a new type of therapy the company is developing to connect immune T cells to cancer cells.

10 PLATFORMS PROPEL THE MOON SHOTS FORWARD:

PUTTING INFORMATION TO WORK FOR PATIENTS

Two other platforms are focused on efficiently gathering and managing information and combining it with medical data to improve patient care and research.

Adaptive Patient-Oriented Longitudinal Learning and Optimization (APOLLO) provides a framework to comprehensively and systematically gather relevant clinical information, tumor genomics and samples over time for each patient and to integrate it with research information. This improved system is designed to benefit individual patients and inform research for better treatment for future patients.

All these data are aggregated in the big data platform to improve physicians' and scientists' access to relevant information. APOLLO and big data are being piloted in the MDS/AML and Lung Cancer Moon Shots.

"The idea is to have each patient contributing to and benefiting from research," says Andy Futreal, Ph.D., co-leader of the Moon Shots Program and the APOLLO and big data platforms.

"Thanks to these platforms and our world-leading clinical trials engine, we now are positioned to precisely match any one of hundreds of novel drugs for our patients in so-called smart clinical trials," DePinho says. "Nowhere else is there such a powerful confluence of in-depth molecular profiling, clinical data integration and myriad clinical trials."

PREVENTION RESEARCH AND OUTREACH

Through its Moon Shots Program, MD Anderson offers ways to help people stay healthy and avoid cancer altogether.

The Lung Cancer Moon Shot includes smoking cessation and research programs such as ASPIRE (A Smoking Prevention Interactive Experience) — a multimedia, Web-based smoking cessation and prevention program for adolescents.

The Melanoma Moon Shot supports legislation that bans minors from using tanning beds. And the moon shot developed a sun safety program for preschoolers called Ray and the Sunbeatables. The program is a project of the CATCH Foundation, a national organization that promotes healthy lifestyles for children. The cancer prevention and control platform supports these efforts and launches them in the community.

MD Anderson has always been strong in developing evidence-based prevention programs, says Ernest Hawk, M.D., vice president of prevention, and it now devotes greater effort to translating those findings into public policy, patient care and education.

"Our platforms and the moon shots are central to our efforts to translate evidence-based cancer prevention to the clinic and community," he says.

MOLECULAR DIAGNOSTICS

Cancer genomics laboratory

Provides rapid, high-quality genomic sequencing services and institution-wide access to genomic data

Proteomics

Sifts through thousands of cancer-related proteins to find those useful for diagnosis, imaging or as targets for treatment

Immunotherapy

Enables design of preclinical studies and clinical trials to evaluate novel immunotherapies as single treatments or in combination with other drugs

PREVENTION RESEARCH AND OUTREACH

Cancer prevention and control

Develops and implements evidence-based programs involving public policy and public/professional education, and service delivery to advance prevention, screening, early detection and survivorship

IMPROVING PATIENT CARE AND RESEARCH

Big data

Integrates MD Anderson's information systems to improve patient outcomes with efficient, secure use of research and clinical data

APOLLO – Adaptive Patient-Oriented Longitudinal Learning and Optimization

Provides an operational framework to accelerate research-driven patient care by standardizing clinical workflows and sample collection. The goal is to ensure that high-quality clinical/research data are captured systematically over time for each patient to enhance learning and improve outcomes

DRUG DEVELOPMENT

Center for Co-Clinical Trials

Functions as an industrialized pharmacology unit to test the impact and tolerability of single drugs or combinations in appropriate preclinical models

Institute for Applied Cancer Science

Applies scientific knowledge of factors that drive tumor formation and progression to develop small-molecule cancer therapies for specific cancer patients, targeting areas of unmet medical need

Applied Cell Therapy

Innovates, develops and implements novel cell-based immunotherapies, including customized T cells to attack cancer

ORBIT – Oncology Research for Biologics and Immunotherapy Translation

Focuses on the rapid discovery and development of innovative monoclonal antibodies — targeted biologic drugs to treat cancer



Jenna Arnold
is reducing risk
while leaving
menopause
for later

By Ronda Wendler

📷 Eric Kayne

New procedure allows women who carry BRCA gene mutations to lower their chances of developing cancer by removing their fallopian tubes, but not their ovaries

Jenna Arnold inherited her mother's love of traveling, passion for volunteering and strong religious faith. But she's determined not to inherit the cancer that took her mother's life.

Arnold's mother, Judy Kenesson, was battling ovarian cancer when she took the blood test that detects inherited genetic mutations that greatly increase a woman's chance of developing breast and ovarian cancer. When her results came back positive, she urged her daughter to be tested as well.

"My mom knew her mutation could be passed on to future generations, so she wasted no time warning me," says Arnold, who also tested positive. "She's my hero."

The test looks for mutations in the BRCA1 and BRCA2 genes, known as the breast and ovarian cancer susceptibility genes. Normally, these genes protect people from getting cancer. But when mutated, the genes' protective abilities are weakened and cancers can arise more readily.

Women with BRCA1 mutations have a 39% risk of ovarian cancer compared to the general population's risk of 1.3%, while women with BRCA2 mutations fare slightly better with a 17% risk, according to the National Cancer Institute. Breast cancer rates are similarly elevated.

"But here's the good news," says Denise Nebgen, M.D., Ph.D., associate professor of Gynecologic Oncology and Reproductive Medicine. "If you know that you carry a BRCA mutation, there are steps you can take to greatly reduce your chance of getting cancer. Knowledge is power."



Denise Nebgen is leading a pilot trial at MD Anderson that's exploring the option of fallopian tube removal for some BRCA-positive women.

Wyatt McSpadden

ESTROGEN'S ROLE

In women at high risk for ovarian cancer, the common prevention strategy is to remove fallopian tubes and ovaries after childbearing is completed — typically between the ages of 35 and 40.

“It seems drastic, but removing ovaries and fallopian tubes reduces the risk for ovarian cancer by 80 to 90%,” Nebgen says.

And there's an added benefit, she says. Because the ovaries make the hormone estrogen — which fuels many breast cancers — removing the ovaries reduces breast cancer risk by 50%.

The downside is that removing the ovaries and their accompanying supply of estrogen plunges women into instant menopause and all the unpleasant symp-

“I didn't want to have my ovaries out yet. But I wanted to feel like I was doing something to reduce my risk.”

— Jenna Arnold

toms that come with it, including hot flashes, vaginal dryness and painful intercourse, and may place them at a higher risk for developing cardiovascular disease and osteoporosis.

Arnold, who's 37 and has a 10-year-old son, didn't want that.

“My husband and I were confident that we were done having children, but I felt far away from menopause,” she says. “I was afraid of the hormonal changes and imbalances it can cause.”

Nebgen understands.

“It's life-changing to have your ovaries removed 10 to 15 years before menopause would happen naturally,” she says.

ANOTHER OPTION

Now, women participating in a first-in-the-nation MD Anderson clinical trial have a way to reduce their risk while leaving menopause for later: a surgery known as salpingectomy removes the fallopian tubes while leaving ovaries intact.

The technique is built on intriguing science that suggests most cases of high-grade serous cancer — the most common and lethal form of ovarian cancer — arise from the fallopian tubes rather than the ovaries. A scientific literature review authored by Karen Lu, M.D., chair of Gynecologic Oncology and Reproductive Medicine at MD Anderson, suggests that in the future, ovarian cancer may be described as fallopian tube cancer. The study was published in the April 2015 edition of *Cancer Prevention Research*.

“For about 30 years, almost everyone thought ovarian cancer arose on the surface of the ovaries,” says Nebgen, who works closely with Lu. “But within the last five years, we've come to understand that many genetic ‘ovarian cancers’ appear to start in the fallopian tubes. So removing these tubes may greatly reduce risk.”

Researchers were tipped off by two phenomena: First, women who practiced birth control by having their fallopian tubes tied developed ovarian cancer 50% less often than women whose tubes weren't tied. Second, the initial wave of surgeries performed on BRCA mutation carriers in the 1990s showed early evidence of cancer in the fallopian tubes but not in the ovaries.

Nebgen considers removing only the fallopian tubes as an intermediary step before later removing the ovaries, and recommends it only as part of a clinical trial.

“I tell women that salpingectomy is an interim measure we can take. Eventually these women will also want their ovaries out to decrease not only ovarian cancer risk, but also breast cancer risk due in part to the ovaries' production of estrogen,” she says. “But having the tubes out early, and then the ovaries out later, can be a stop-gap that reduces risk in this window without initiating menopause.”

The MD Anderson trial, led by Nebgen and conducted through the High Risk Ovarian Cancer Screening Clinic, is following 80 BRCA-positive women who choose one of three paths: screening only, the recommended traditional combination of ovary and fallopian tube removal, or, Arnold's choice — fallopian tube removal followed by ovary removal years later.

Nebgen suggests removing the fallopian tubes while sparing the ovaries may be appropriate for women who don't plan to have more children, are below age 40 and are strongly opposed to the idea



Jenna Arnold is taking action to prevent cancer later in life.  Eric Kayne

of immediate menopause, to the point of refusing the current risk-reducing surgery that removes both ovaries and tubes.

Arnold fits that description and is comfortable with her decision.

“I didn’t want to have my ovaries out yet,” she says. “But I wanted to feel like I was doing something to reduce my risk.”

YOUNG AND INVINCIBLE

As BRCA testing becomes more common, clinicians are encountering more and more women who have been blindsided in their 20s and 30s — in the prime of their reproductive life — by the knowledge that they carry a potentially life-threatening genetic mutation.

“They could dramatically reduce their risk of cancer with surgery, but some women simply refuse,” Nebgen says. “They want to keep their options open until they marry or until they have one or two more children.”

These women believe they’re invincible, Nebgen says, and don’t realize they’re gambling with their lives.

Unlike breast cancer, no reliable screening test has been developed to detect ovarian cancer. And because the disease produces no obvious symptoms, it remains undetected as it silently grows. Nearly two-thirds of ovarian cancers aren’t caught until they’ve spread beyond the ovaries to elsewhere in the body. By then, the five-year survival rate is 45% — far below the 92% survival rate for ovarian cancer that’s found and treated before it spreads outside the ovaries.

EVOLVING ALTERNATIVE

Exactly how much salpingectomy reduces cancer risk is a question yet to be answered. The procedure is fairly new, and Nebgen is quick to point out that proving its effectiveness will require multiple studies in the years to come.

This spring, MD Anderson became one of five institutions chosen to participate in a new Ovarian Cancer Dream Team funded by Stand Up to Cancer, an organization started in 2008 by film and media leaders to quickly translate lab research into treatments for cancer patients. Dream Team members will pool their different areas of expertise and work together to prevent ovarian cancer in high-risk women. MD Anderson’s role on the team is headed by Lu, who this fall will be principal investigator of a new Dream Team-funded clinical trial that looks at fallopian tube removal in 350 women with BRCA mutations. The multi-site trial builds on Nebgen’s pilot study, which concludes as this larger trial gets underway.

“Dr. Nebgen is conducting a proof-of-concept study — a smaller-scale study that is confirming for us that women are interested in salpingectomy to reduce cancer risk and stave off menopause,” Lu says. “Now we’re ready to build on that initial research with larger studies that give us data on salpingectomy’s safety and effectiveness.”

Until then, Nebgen considers salpingectomy an option for women who say “absolutely no” to the recommended, more aggressive fallopian tube and ovary removal surgery.

“Salpingectomy is not yet the standard of care,” she says. “But it’s an evolving alternative.”

MD Anderson's got talent

When they aren't fighting cancer, these faculty and staff members are expressing themselves

By Ron Gilmore

Given that his father's big band once opened for Nat King Cole at New York's Paramount Theater, it's no surprise that music's in Geoff Giacco's blood.

Giacco is among many MD Anderson faculty and staff members with artistic sides, which they pursue outside the confines of their labs, offices and nursing stations. This wealth of talent is one reason the institution annually offers avenues for showcasing creativity such as "MD Anderson Idol" and the Faculty Art Exhibition.

For Giacco, a manager of MD Anderson's Tumor Registry, which catalogs and tracks patient information, music provides much-needed balance to his work life.

"It helps free my mind for the analytical thinking that's required in my job as an epidemiologist," he says. "It's a great way to relieve the stress of the day."

For more than 30 years, Giacco has performed guitar and vocals with his band, Cowjazz. The group can be heard on musician-development website Reverbnation and regularly plays at Houston venues such as Bohemeo's, Last Concert Café and Natachees. Giacco's 89-year-old father occasionally joins them on stage to play flute.

During the last three years, Giacco has been a finalist in "MD Anderson Idol." He also participates in the employee choir.

"It's a lot of fun to entertain my co-workers and our patients. It's a very different experience from the normal workday," he says



Tami-Maury, Dr.Ph.

📷 F. Carter Smith

ART LOVER

Despite a demanding schedule, Hagop Kantarjian, M.D., chair of Leukemia, finds time to paint. In fact, many of his paintings, stunning in their use of vibrant primary colors and eclectic in style, line the hallways of his department's suite.

For Kantarjian, who's modest about his artistic abilities, the impetus of his work is enjoyment, not fame.

"I'm not good enough to exhibit my work," he says. "Perhaps never. Painting is just fun and it relaxes me and alleviates my anxieties. I will be a long-time amateur painter."

Amateur or not, his work adheres to styles that he prefers, particularly those of an artistic movement popular at the turn of the 20th century known as fauvism. French for "the wild beasts," fauvism emphasizes strong, bold colors. Among its leaders are Henri Matisse and André DeRain. Kantarjian's work also is influenced by artists from other genres including post-impressionists Paul Cézanne and Paul Gauguin, and impressionist Edgar Degas.

"I call myself a post-modern surreal impressionistic neo dada-fauvist," he says with a grin. "I love fauvistic colors, post-impressionist and abstract work. My style has evolved over the years and is often influenced by my evolving love of different artists."

Born and raised in Beirut, Kantarjian began painting as a child, but put down his brush for several years because of the Lebanese civil war, which lasted from 1975 to 1990.

"I picked it up in 1993 under the tutelage of a Russian émigré from St. Petersburg named Efim Fruman," he says. "I evolved with his mentorship over the next four years, and then decided to paint as I like."

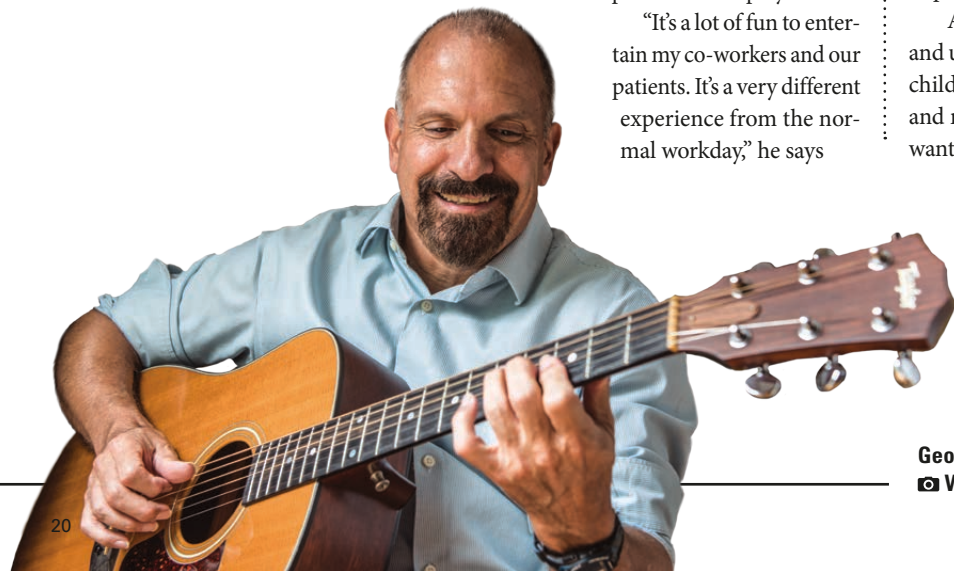
Although several of Kantarjian's paintings depict cityscapes and urban settings — including neighborhood scenes from his childhood — he also enjoys other subjects including still life and nudes. Of the nudes, he jokes: "No one else likes them or wants them, so they end up in the garage."

Beyond providing him with a relaxing hobby, Kantarjian says he gets some of his best ideas in leukemia research when he's painting.

"However," he adds, "at my age, I often forget them as soon as I leave the studio."

Geoff Giacco

📷 Wyatt McSpadden



TAKING TIME TO TANGO

During the day, Karen Stepan dedicates her time to addressing the emotional, spiritual, social and practical needs of MD Anderson patients and their families through her work with the Psychosocial Council.

But at night, she slips on her dancing shoes.

We're not talking about two-stepping at the local honky-tonk. Stepan is an accomplished ballroom dancer. In 2013, she won the National Dance Council of America's World Pro-Am Bronze Rhythm Championship and took second place in the World Pro-Am Smooth Championship.

"I've always enjoyed watching others dance, especially in the Rodgers and Hammerstein musicals," says Stepan. "When I was growing up, I wanted to jump into one of those stories and be part of that experience. I hope audiences I perform for feel the same way."

Stepan's competitive dance journey began in 2008 by training with professional dance partner Christopher Muller. She participated in local competitions, winning her dance level and age group. As her confidence grew, she set her sights on national and international competitions.

"It's an entirely new experience at that level," says Stepan, who has mastered the waltz, tango, fox trot, cha-cha, rumba and swing. "I really didn't know what to expect, but I knew it would be tough."

Dancing has also helped Stepan in her work at MD Anderson. It's helped her lead as well as follow, which has been useful because her job calls for guiding and supporting those she serves.

"It's important to be mindful of the balance between being a leader and a follower," she says. "Both are important roles, and the key is being able to excel at either one."

PARAKUPÁ-VENÁ PAINTER

Although Irene Tamí-Maury, Dr.PH, says her paintings hang mostly at home or in friends' houses, she shared her colorful, expressive work at the MD Anderson Faculty Art Exhibition in early May.

She has shown before, taking first place at an art exhibit for one of her sculptures while attending dental school in Venezuela.

Tamí-Maury, an assistant professor of Behavioral Science, gravitates toward landscapes. One of her paintings, Parakupá-Vená, portrays a magnificent waterfall in pastel tones, emulating stained glass. Parakupá-Vená is the indigenous name for Angel Falls, the world's highest waterfall located in Canaima National Park, Venezuela. Tamí-Maury created her favorite painting, Twilight, with her son when he was 13. The work portrays moody, dark colors applied with sponges, a technique that allows colors to overlap and fade into one another. She prefers landscapes because wilderness has always served as an emotional retreat.

"Painting is therapeutic," she says. "It provides me a sense of tranquility and helps me focus on something else besides work. It also keeps my brain oxygenated and open to new ideas and thinking."



Hagop Kantarjian, M.D.
 © F. Carter Smith



Karen Stepan
 © Wyatt McSpadden

Where in the world is MD Anderson?

More than 14 million cancer cases are diagnosed worldwide each year — and that number is expected to grow.

In fact, World Health Organization scientists predict that number will reach 24 million cases a year by 2035. To avoid a “tidal wave” of cancer tomorrow, MD Anderson and other health care institutions are taking action today.

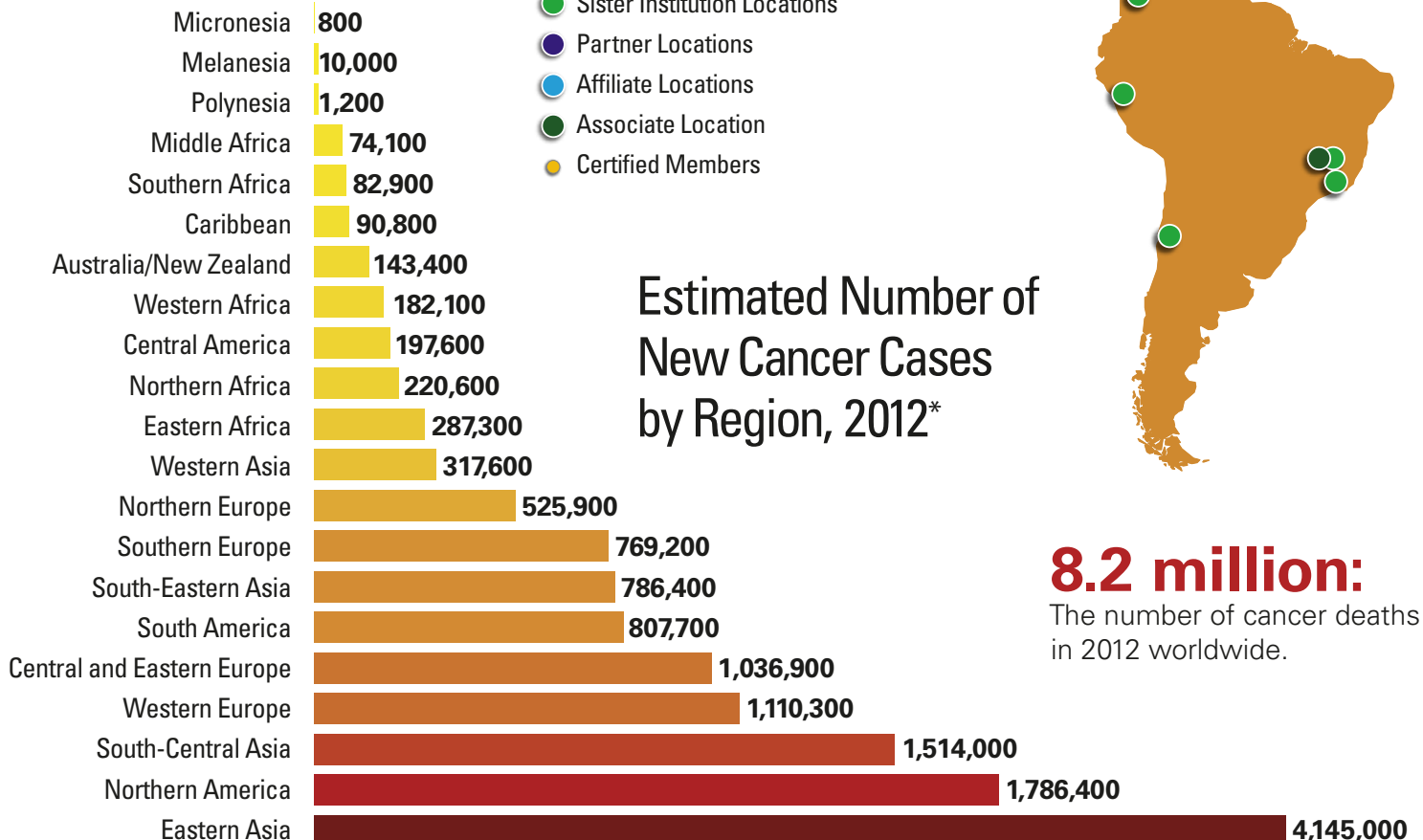
“Our mission and vision challenge us to be the single most impactful institution in relieving the burden of cancer globally, and we can achieve this by extending our brand of prevention, care, research and education to like-minded organizations worldwide,” says MD Anderson President Ron DePinho, M.D.

To do that, the institution’s Global Academic Programs (GAP) facilitates the Sister Institution Network — the largest global network of cancer centers (32 institutions in 23 countries) working collaboratively on research and education. Currently, MD Anderson is involved in 93 international research projects in 24 countries. The MD Anderson Cancer Network® allows the institution to collaborate with healthcare providers to provide MD Anderson’s model of multidisciplinary care to patients in the communities where they live. Here’s a look at new cancer cases by region and where the Cancer Network and GAP are teaming with hospitals, health systems and institutions across the nation and around the globe in Making Cancer History®.



- MD Anderson
- Multiple Sister Institution Locations
- Sister Institution Locations
- Partner Locations
- Affiliate Locations
- Associate Location
- Certified Members

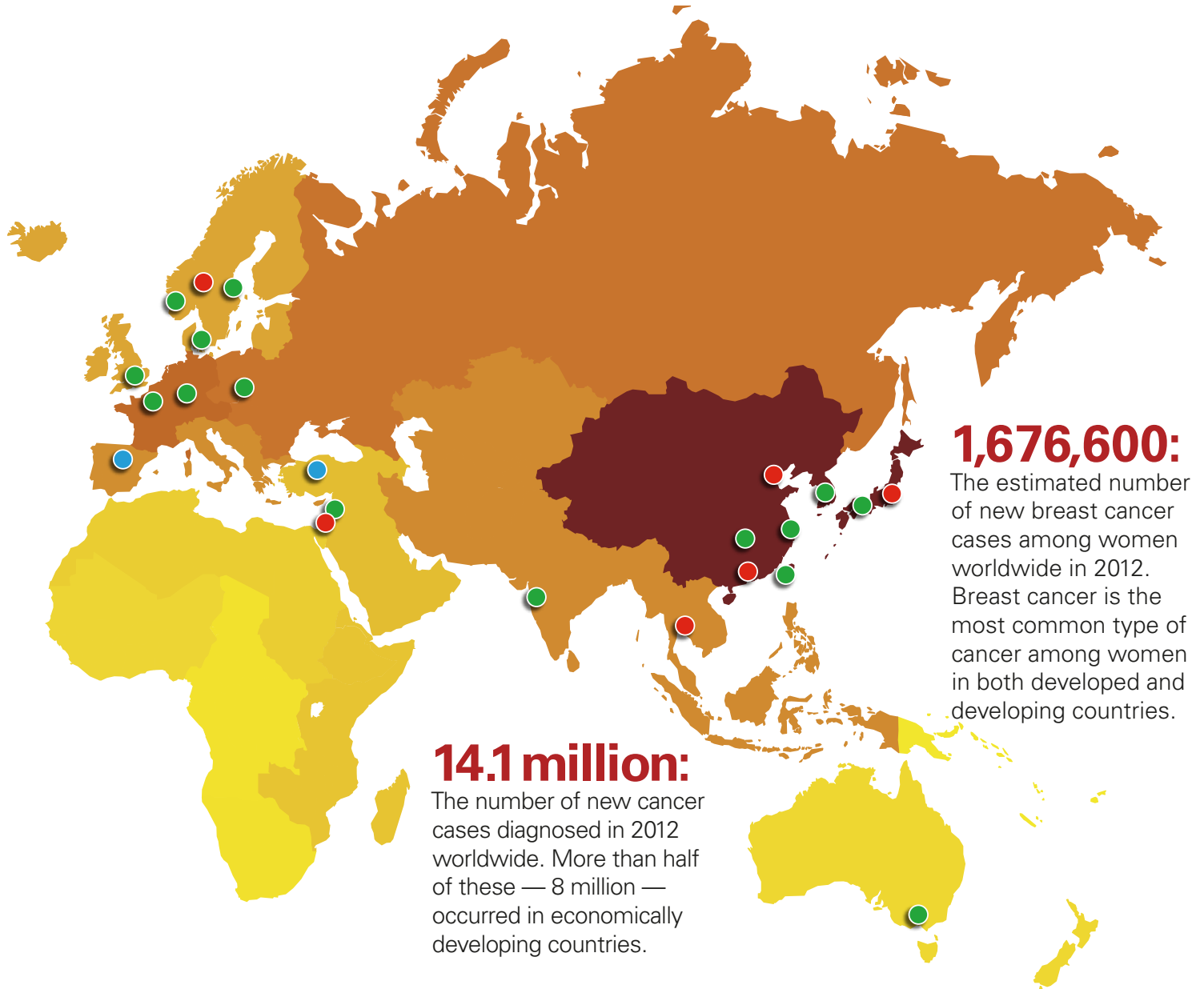
Estimated Number of New Cancer Cases by Region, 2012*



8.2 million:
The number of cancer deaths in 2012 worldwide.

* GLOBOCAN 2012 (Based on the most recent data available from the International Agency for Research on Cancer)

179: The number of countries, out of the 196 that are eligible, that have signed on to the Framework Convention on Tobacco Control (FCTC), a treaty led by the World Health Organization to help combat the global tobacco pandemic. A number of major tobacco-producing countries, including the United States, have not ratified the treaty. The report notes that tobacco use is the cause of nearly 6 million premature deaths annually.



1,676,600: The estimated number of new breast cancer cases among women worldwide in 2012. Breast cancer is the most common type of cancer among women in both developed and developing countries.

14.1 million:

The number of new cancer cases diagnosed in 2012 worldwide. More than half of these — 8 million — occurred in economically developing countries.

58%: The percentage of all newly diagnosed cancers in economically developed countries that occur among those aged 65 and older. This figure is 40% in developing countries. The report notes that this "difference is largely due to variations in age structure of the populations."

21.7 million: The number of new cancer cases expected to be diagnosed in 2030. And, by 2030, 13 million cancer deaths are predicted. However, these projections only reflect population growth and aging, so these figures will likely be much larger "due to the adoption of lifestyles that are known to increase cancer risk, such as smoking, poor diet, physical inactivity, and fewer pregnancies, in economically developing countries."



The gift that's giving life to discoveries

By Miriam Spradling

Ten years ago, San Antonio businessman Red McCombs and his wife, Charline, made a transformative, unsolicited \$30 million gift to establish the Red and Charline McCombs Institute for the Early Detection and Treatment of Cancer at MD Anderson. The donation was the largest the institution had received to fund research at the time, and led to the most aggressive expansion of cancer research in its history.

The 87-year-old McCombs says his desire to give comes from examples set by his parents.

"My father made 25 bucks a week, which he'd give to my mom so she could put \$2.50 aside for the church," he says. "And although we didn't have any extra space, and certainly no extra money, Mom would take in children and keep them while their families worked out their problems."

McCombs first encountered MD Anderson as a college student while visiting a patient. He was impressed by what he saw, and the experience stuck with him. Years later, he reached out to then-President Charles LeMaistre (1978-1996) to offer some praise.

"I called Mickey LeMaistre and complimented him on the care I saw being offered to everyone there," he says. "Mickey explained how everyone they see is troubled, either because they're a patient or because a loved one is a patient, so they take extra care not to add to that. I told him it was the best program I'd ever seen."

Through the years, McCombs's relationship with MD Anderson continued to develop. He joined the MD Anderson Cancer Center Board of Visitors (BOV) in 1986, led the Institutional Initiatives Committee (1993-1994) and chaired the BOV (1995-1997). His daughter, Marsha Shields, joined the BOV in 2009.

"I have a soft place in my heart for MD Anderson because they're the best in the world at what they do," he says.

A decade after Red and Charline McCombs gave \$30 million to MD Anderson, the funds are fueling groundbreaking advances in cancer research

Adolfo Chavez III

A GIFT FOR PREVENTION

In 2005, McCombs received a brochure describing the South Campus Research Initiative (SCRI), and its potential impact on cancer care and research immediately appealed to him. Once again, he picked up the phone.

“I told John Mendelsohn (MD Anderson president, 1996-2011) the SCRI was the greatest approach to this dreadful problem, and I’d give \$25 million to support it,” he says. “Then Dr. Mendelsohn called back and said for \$30 million they could put my name on the facility. I said, ‘For \$5 million more, we’d like that.’”

From there, given McCombs’ belief in the value of early detection, the McCombs Institute for the Early Detection and Treatment of Cancer was born.

“The best treatment we have in the world — with all the billions of dollars and brilliant scientists working on this — is early detection and prevention. Period,” McCombs says.

Sam Hanash, M.D., Ph.D., who was recruited to lead the McCombs Institute in 2009, shares McCombs’ passion. About 20 years ago, he met a patient who changed the trajectory of his career.

“I diagnosed a patient with an advanced-stage brain tumor,” Hanash says. “The father was so distraught and wanted to know why we couldn’t have detected the cancer earlier when it probably could’ve been cured. That’s

what locked me into wanting to see how we can prevent cancer and detect it earlier.”

Now, 10 years after the McCombs’ gift, more than one-third of MD Anderson research is channeled through the McCombs Institute and its seven centers, each devoted to a particular area of cancer research (see sidebar).

ALWAYS PUSHING THE NEEDLE

The numerous groundbreaking advances made in the first decade of the McCombs Institute are extremely promising. Yet, McCombs didn’t become a legendary entrepreneur by being satisfied with standing still. In a letter to Hanash, he indicated that “the institute is on the right track but must press onward — because if you’re on the right track and stop, you’ll be run over.”

“Mr. McCombs is eager to see scientific discovery applied in the clinic. And that’s exactly what we’re committed to — translational medicine — so that the discovery passes what’s known as the ‘valley of death’ — the abyss that must be crossed when laboratory research is translated into drugs or therapies that help patients,” says Hanash. He adds that in another 10 years he expects early detection to have a marked impact on cancer mortality worldwide.

“This disease is a bigger threat to the world than terrorism,” McCombs says. “Someone in every extended family is going to go down with cancer. It’s that big of a robber of life and dignity, and we all need to do everything we can to stop it.”



Red McCombs

More than one-third of MD Anderson’s research is channeled through the Red and Charline McCombs Institute for the Early Detection and Treatment of Cancer. Here’s an update on the impact being made by some of the institute’s many centers:

CENTER FOR CANCER IMMUNOLOGY RESEARCH

Develops vaccines and immunotherapies to induce potent immune responses for treating and preventing cancer

Impact: Vaccination with Dickkopf-1, a protein expressed in myeloma cells but highly restricted in normal tissues. The vaccine protected mice from developing myeloma and also served as a therapeutic agent against myeloma in mice.

CENTER FOR RADIATION ONCOLOGY RESEARCH

Advances the science of radiation therapy and helps integrate radiotherapy into multidisciplinary care

Impact: Established a new treatment for patients with head and neck squamous cell cancer using the antibody therapy cetuximab, which makes cancer cells better receive radiation

CENTER FOR ADVANCED BIOMEDICAL IMAGING

A multidisciplinary center that conducts basic, translational and clinical biomedical imaging of cancer research

Impact: Synthesized ^{18}F -PEG6-IPQA, a solution that is attracted to tumor cells, and conducted a first-in-human clinical trial in non-small cell lung cancer patients to determine if the solution may help doctors see cancer cells better during imaging scans

CENTER FOR TARGETED THERAPY

Identifies targets, develops biological therapies and drugs, and conducts clinical trials to personalize medicine

Impact: The siRNA Screening Service has completed more than 100 RNAi screens, shutting down about 21,000 known human genes to help identify new therapeutic targets, while developing libraries of cancer cells for gene editing studies that will validate identified targets

CENTER FOR GLOBAL CANCER EARLY DETECTION

Brings together investigators to develop strategies for the early detection of cancer

Impact: A global lung cancer screening clinical trial involving 30,000 patients is in the works. The trial will use blood-based biomarkers to detect lung cancer in its earliest stages, when it's still treatable. The goal is to eventually apply this technology to all common cancers.

CENTER FOR RNA INTERFERENCE AND NON-CODING RNAs

Identifies, engineers and accelerates breakthroughs in non-coding RNA discoveries leading to cancer biomarkers and therapeutics

Impact: Developed a systemically deliverable siRNA therapeutic called Epharna, which helps individual cells control gene functionality. The target, EphA2, is overexpressed in several cancers and associated with a poor prognosis, yet is generally absent from normal adult tissues, and when silenced, leads to tumor regression in pre-clinical animal models.



On track for success

Mentors' guidance is invaluable for young scientists and clinicians

By Ron Gilmore

“I am not a teacher, but an awakener.”

With that line, poet Robert Frost captured the essence of what it means to be a good mentor, a key to success for young physicians and researchers new to the world of academic medicine.

New scientists and clinicians rely on the guidance and wisdom of their more senior colleagues as they “awaken” their own inspirations and abilities. The end result? More informed caregivers, teachers and scientists who can better help MD Anderson’s patients, educate future cancer specialists and spur next-generation innovations in cancer treatment.

“I had terrific mentors as a student, as a postdoctoral fellow and as a fellow at the National Institutes of Health,” says Sharon Dent, Ph.D., chair of Epigenetics and Molecular Carcinogenesis at MD Anderson. “They provided me opportunities to meet leaders in the field and to present my research findings at conferences. They also gave me very practical advice.”

Dent recalls her NIH mentor advising her to look carefully at faculty members who worked in institutions where she was applying for jobs.

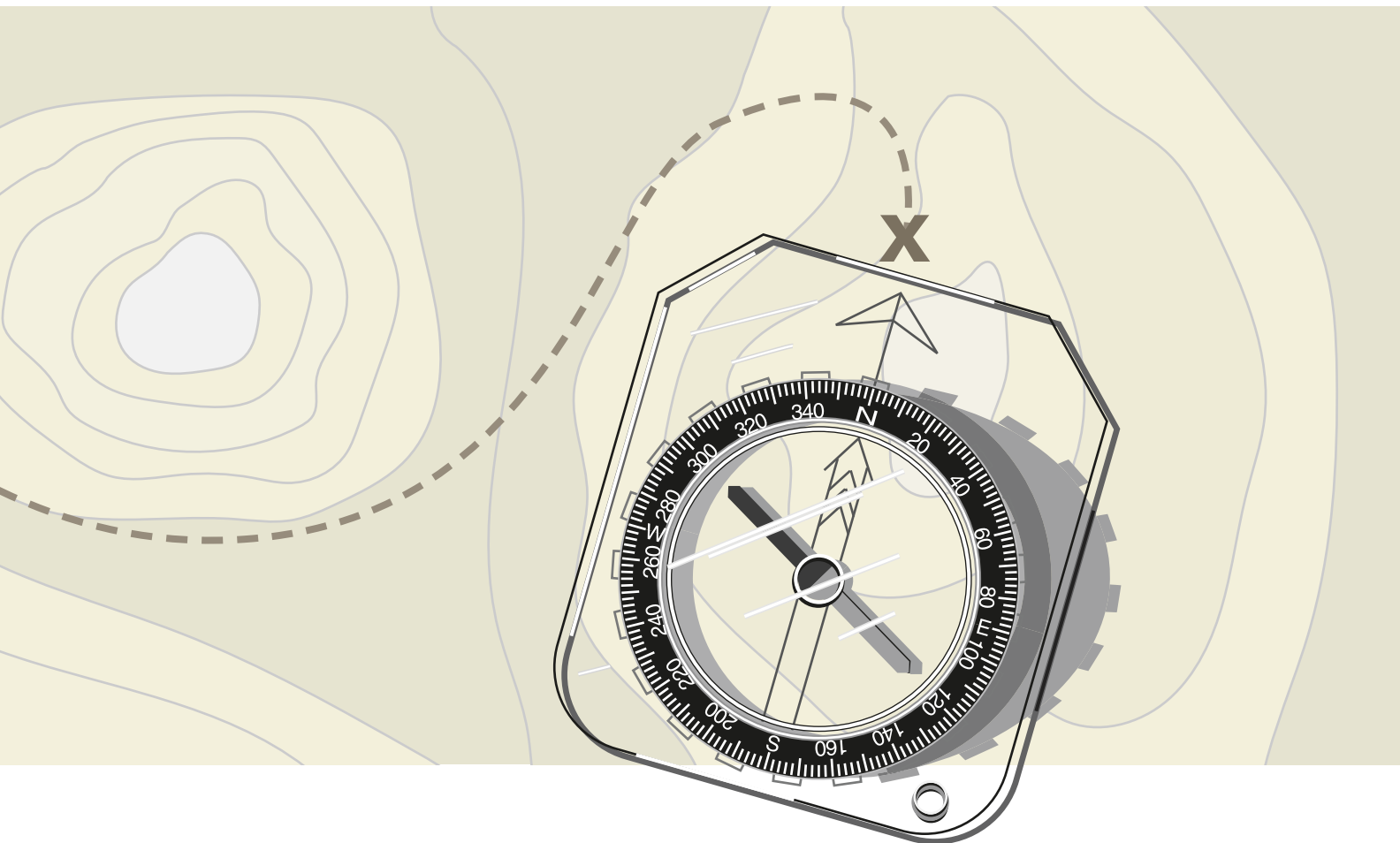
“He knew they would influence my thinking, my students’ thinking and my opportunities going forward,” says Dent. “He was absolutely right.”

HELPING TO CHANGE CAREERS ... AND LIVES

The department of Faculty and Academic Development’s *raison d’être* is helping junior faculty succeed personally and professionally.

To promote collegiality among faculty, trainees and students, the department hosts social gatherings and offers exercise programs, stress reduction programs, and counseling and advising. To help develop participants professionally, it offers workshops that teach grant writing, lab management, teaching skills and how to plan for promotion and tenure.

“The testimonials from faculty who have benefited from good training and mentoring are inspirational and heart-warming,” says Janis Yadiny, associate vice president for Faculty and Academic Development. “That’s why we offer mentoring materials on our website and events that support mentors and mentees. We also support faculty members establishing new programs in their departments and divisions.”



The department sponsored the first Faculty Mentoring Day in 2008, and annually selects winners of the Distinguished Faculty Mentor Award. Last year, recipients included Michael Keating, M.B.B.S., professor of Leukemia, Elizabeth Grimm, Ph.D., professor of Melanoma Medical Oncology, and Gordon Mills, M.D., Ph.D., chair of Systems Biology.

SHARING THE PASSION

Han Liang, Ph.D., associate professor of Bioinformatics and Computational Biology, says he was “tremendously impacted” by Mills’ mentoring.

“I joined MD Anderson with little knowledge or training about cancer research,” says Liang. “Gordon’s passion about helping our patients through science, his creative thinking about big ideas, his unconditional support for junior faculty and trainees, and his high standard for scientific research are amazing.”

Liang says he feels “extremely lucky” to work with Mills.

“I’m trying my best to adopt his characteristics and, hopefully, pass on these traits to my trainees,” he says. “Without Gordon’s support, I wouldn’t have achieved half of what I’ve been able to accomplish.”

Today, Liang is a talented scientist and mentor.

“The most enjoyable thing about research,” he says, “is working with trainees and discussing science daily.”

KEEPING IT SIMPLE

One mentor, George Calin, M.D., Ph.D., professor of Experimental Therapeutics, adheres to a basic but time-honored approach.

“The simplest philosophy is to keep pushing my trainees to think outside the box, ask them to think and write science all the time, and let them prove to themselves just how good they are,” Calin says.

Creativity, imagination and the “desire to discover” are traits he cultivates in his mentees. Calin recalls his own experiences as a young scientist.

“I had the opportunity to have three mentors in Romania, Italy and the United States,” he says. “They contributed fundamentally to my way of understanding science and making discoveries.”

Mein-Chie Hung, Ph.D., chair of Molecular and Cellular Oncology, mirrors Calin’s experience with his mentors.

“I’ve been very lucky to have some great and inspiring mentors throughout my career,” says Hung. “As a naïve young man in Taiwan interested in science, two mentors in particular really opened my eyes to the powers of modern science. They turned on my curiosity and passion.”

Hung says he learned from his mentors how to be happy and successful and to follow his heart. Today, he looks for that same passion, commitment and innovation, along with a solid track record, to ensure his mentees will succeed. His advice to young faculty is to be persistent.

“A career in science will have many ups and downs,” he says. “It’s important to always get right back up.”

One woman's tale of conquering
cancer and Kilimanjaro

THE SURVIVOR AND THE SUMMIT

By Julie Penne



Stephen and Bree brought home lessons they learned on their climb to their 8-year-old twin sons, Beck and Elliott.
 📷 Wyatt McSpadden

Breast cancer survivor Bree Sandlin's inner strength and inner voice helped her overcome two of the toughest challenges she's ever faced.

"Keep going. Put one foot ahead of the other," the mother of two told herself as she battled aggressive, Stage III triple-negative breast cancer in 2012. "I have a great team supporting me."

Two years later, the 39-year-old cancer survivor whispered similar encouraging words as she and husband Stephen scaled Tanzania's Mount Kilimanjaro, the world's tallest freestanding mountain.

"I'm learning from this every day," Bree told herself during the challenging eight-day climb. "My life will be better for this experience."

Always active and adventurous, the Sandlins participated in Survivor Summit, sponsored by the LIVESTRONG Foundation. Each year, the program teams cancer survivors and caregivers with seasoned guides who navigate the mountain as they raise pledge funds to benefit cancer patients. For the Sandlins, the trip was a way to honor the more than 32 million people affected by cancer worldwide.

Averaging about five miles a day, it took the climbers six days to reach Kilimanjaro's 19,000-foot summit. Their descent took another two.

It was a climb that mirrored Bree's arduous year of treatment in many ways.

"The analogy of climbing Mount Kilimanjaro and the cancer journey is remarkable," says Bree. "Every day we climbed I was reminded that it was really hard and something you couldn't do alone. You tell yourself to keep going and not give up. You also remind yourself that this climb is nothing compared to chemotherapy."

With the terrain, altitude and conditions, Stephen says the trek was "the equivalent of doing 14 miles per day and climbing six mountains over eight days." The climbers worked their way through a rain forest

and warm temperatures at the base, but as they advanced, the trees thinned out and the climate became windy and cold. Only 20% of Kilimanjaro climbers make it to the summit. Most are content to walk the rim instead of going the full distance to the peak.

At 15,500 feet, Bree was hit with altitude sickness, and the ensuing nausea and headache almost prevented her from continuing. The physicians on the trip gave her a steroid that kept her going. That experience reminded her that a great team is invaluable and the importance of leaning on others.

Once she was back on her feet, Bree and Stephen were determined to reach the summit with their team.

On the last day of their ascent, the group woke early and climbed until lunchtime. They then rested for about nine hours in camp. At 10 p.m., they climbed in the dark almost straight up until they reached the top of Kilimanjaro at 8 the next morning.

When they arrived at the summit, the temperature was zero degrees, the wind was wailing at 40 miles per hour and the sun was rising.

The group had an hour at the top of the mountain to savor the view, reflect on their accomplishments, think about the people for whom they climbed and how the experience will influence the rest of their lives.

For Bree, it was about the beauty of the moment and the people who helped get her there, especially Stephen. They both thought about their 8-year-old twin sons, Beck and Elliott, back home in Katy, Texas, with supportive family members, who also were vital during Bree's treatment.

"After I completely lost it, I thought about how cancer teaches us the beauty of the world and how the Kilimanjaro experience reinvented that lesson," she says. "Oh, and I told everyone in the group that I loved them at least four times. It was glorious up there."

Back home in Katy, Bree and Stephen say they both think about the trip every day.

"It wasn't just about making it to the summit," says Stephen. "It was about personal growth, and proving that you have the strength to do something like this. I was so excited and proud to share this with Bree, and we certainly brought home many lessons to our boys, family members and community."

A new drug delivers renewed optimism

The FDA-approved lenvatinib is helping thyroid cancer patients who don't respond to standard treatment

By Ron Gilmore

Rafael Pantoja had all but lost hope. The thyroid cancer he had battled for 14 years was back and spreading.



Rafael Pantoja
 © F. Carter Smith

Then, earlier this year, he began taking lenvatinib, a drug that was tested at MD Anderson and approved by the Food and Drug Administration (FDA) in February. Lenvatinib treats patients such as Pantoja, whose thyroid cancer doesn't respond to the more traditional radioactive iodine therapy. It uses targeted radiation to destroy any thyroid tissue or cancer cells that remain after the thyroid is surgically removed.

"At this point in my treatment, lenvatinib was my only option," says Pantoja, a father of six and certified public accountant who lives in Caracas, Venezuela. "We went for it."

Pantoja, 62, is one of nearly 300,000 people diagnosed with thyroid cancer each year in the world.

For decades, the standard treatment was to administer repeated and often ineffective doses of radioactive iodine, and sometimes chemotherapy," says Steven Sherman, M.D., associate vice provost for Clinical Research. "About 10 years ago, with new scientific discoveries, we began recognizing the potential for treating patients with drugs that stop tumors from growing their own blood vessels."

That's exactly how lenvatinib works. A global study of the drug, also known as Lenvima, demonstrated a dramatic improvement in progression-free survival, with a 65% response rate.

"These are unprecedented results for thyroid cancer patients with such advanced disease," says Sherman, who led the study.

Results from the study were published this February in the *New England Journal of Medicine*, coinciding with the FDA's approval of the drug. Mouhammed Habra, M.D., associate professor of Endocrine Neoplasia and Hormonal Disorders, led the study's Phase III component at MD Anderson.

Pantoja, who has been under the care of Steven Waguespack, M.D., professor of Endocrine Neoplasia and Hormonal Disorders, directly benefited as a result of the clinical trials. So far, he hasn't experienced many of the side effects that sometimes accompany the drug, including diarrhea, fatigue, nausea and weight loss. He is, however, among the 40% of patients whose blood pressure rises after taking Lenvima. He's now on medication to keep his blood pressure in check.

"Lenvima appears to be working," says Pantoja, who underwent several surgeries to remove sections of his arm bone after the cancer spread. "I'm already seeing a 75% reduction in thyroglobulin."

The decline in thyroglobulin — a protein produced by both normal and cancerous thyroid tissue — is usually good news for patients being treated for advanced thyroid cancer.

Pantoja's grasp of the medical procedures that determine his fate are testament to the long road he's traveled. His journey began in 2000 when doctors removed a small nodule from his thyroid. Since then, his thyroid has been removed and he's undergone radioactive iodine treatments and arm surgeries, including one to implant a prosthetic bone that replaced much of his humerus.

This March, the cancer appeared to be moving into his chest.

"We were really getting worried," he says. "And then Dr. Waguespack said, 'You won't believe this, but there's this new drug, just approved, that might work for you.'"

Pantoja remains optimistic.

"It's been a long fight," he says. "But I think we've finally found a reason to be happy."



Steven Waguespack, M.D.
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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 patients at Lyndon B. Johnson 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

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