CONQUEST

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

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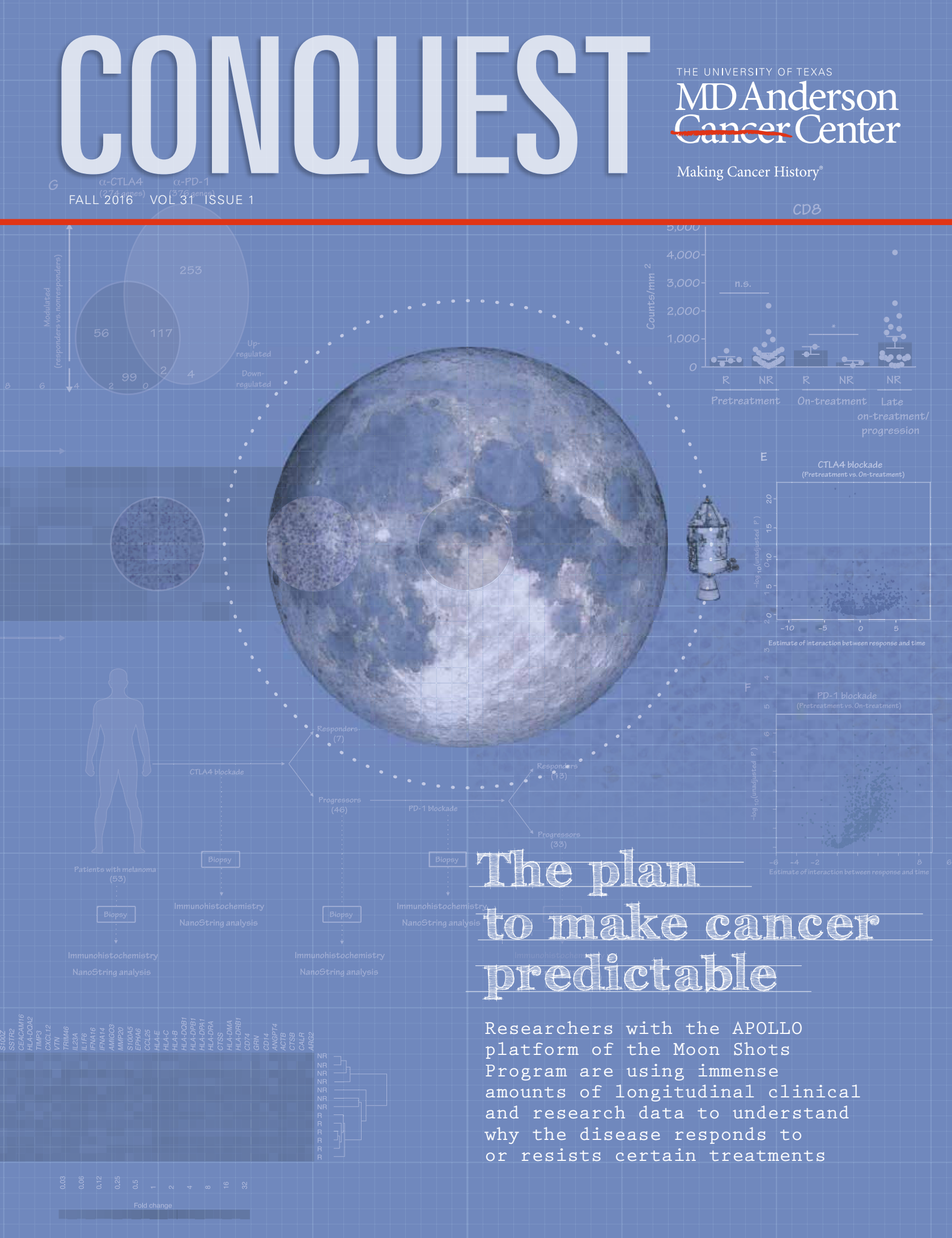


The plan to make cancer predictable

Researchers with the APOLLO platform of the Moon Shots Program are using immense amounts of longitudinal clinical and research data to understand why the disease responds to or resists certain treatments

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

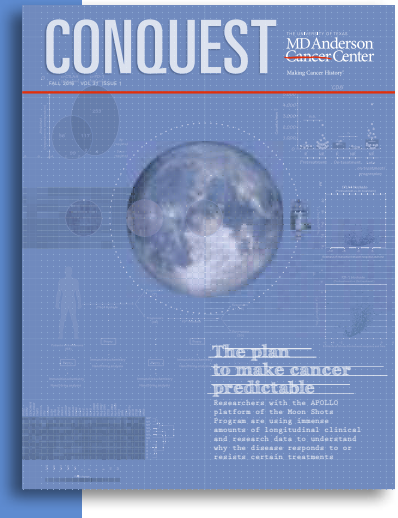
By our words and actions, we create a caring environment for everyone.

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: ***Getting a firm scientific grip on the extreme survival skills of advanced cancer is the mission of MD Anderson's APOLLO program, which stands for Adaptive Patient-Oriented Longitudinal Learning and Optimization. Through the program, researchers are collecting blood samples and biopsies before, during and after treatment, and conducting deep molecular and immune analysis of those tumor samples to understand why they respond to or resist a given treatment.***

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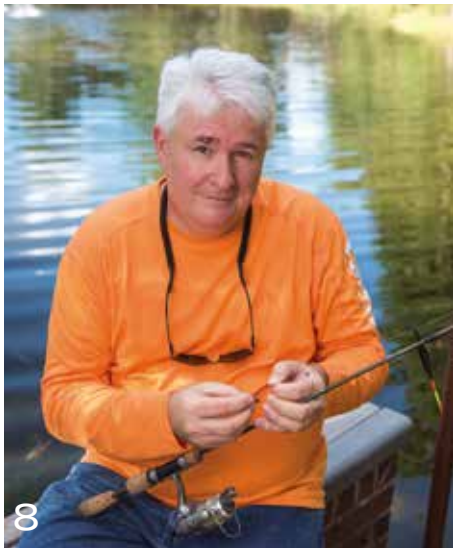


FEATURES

When the doctor becomes the patient

By Laura Sussman

Wyatt McSpadden

When researchers and physicians enter the field of medicine, they make a commitment to improve human life. It's been said that those who choose the field of cancer are inherently altruistic and sympathetic. Yet when faced with their own cancer diagnosis, their sympathy becomes empathy in its truest form. Here, five experts from MD Anderson offer their perspectives on living that transition.

OLIVER BOGLER, PH.D.,

professor and senior vice president, Academic Affairs

Diagnosis: Stage III invasive ductal carcinoma of the breast

Cancer induces a fundamental shift in your perspective, and how you feel about your life. In my experience, the hardest period of time was actually after Irene's intensive treatment was finished because I was very keen for life to return back to normal. But unless you've been through it yourself, it's very hard to understand what the other person in your life is going through and how it changes your outlook.

For that reason, I was in a sense relieved when I was diagnosed because it gave me a chance to understand the shift she went through years before. I understand it completely now. The perspective on your life — how you feel about your future, how you react, how you apportion your time, and how you prioritize what you do — all just shifts fundamentally. I wouldn't say I feel fortunate to have had cancer, but it certainly helps me understand what Irene went through and has brought us to a similar place at this time, so we can share our lives better together.

IRENE NEWSHAM, PH.D.,

assistant professor, School of Health Professions

Diagnosis: Stage II invasive ductal carcinoma of the breast

I was diagnosed in 2007. I found a lump three days before I had my annual physical exam, where I underwent a mammogram — and five years before Oliver's cancer diagnosis. For me as a survivor, it's as though I'm walking on a thin sheet of ice. Anytime that I have a pain or a cough, I feel like that ice is going to crack and my disease will recur. It's unfortunate that Oliver was also diagnosed with breast cancer, but I think that he understands my anxiety better and I have someone with that same perspective who can keep me level. At times, I find myself readjusting the way I see life. You can get lost in the details and stresses of everyday life — kids, house, work and flat tires — but you just have to stand back and say, "It's OK, it's a flat tire. It's not a recurrence. Life is good."

Irene Newsham, Ph.D., and Oliver Bogler, Ph.D., are faculty members, cancer survivors and spouses.

ALYSSA RIEBER, M.D.
Associate professor, General Oncology

Diagnosis: Hodgkin lymphoma

My first experience with cancer came during my first three months of medical school at age 21. I didn't enter medical school thinking that I wanted to go into oncology. Before my own diagnosis, I didn't know any cancer patients, and no one in my family had cancer. So just being in that waiting room influenced me to take a career path that has turned out pretty well. I feel like I get to do the best job every day with my patients.

By going through this experience, I'm able to have a different relationship and conversation with my patients. I know that shock of having a diagnosis. I know that sometimes you cannot have a meaningful conversation right after you first hear the word cancer. Your mind kind of goes blank and you have that earthquake experience. And then once you process it, you can move on toward the practical diagnostic and treatment discussion.

"I'm here today. Today is a good day."

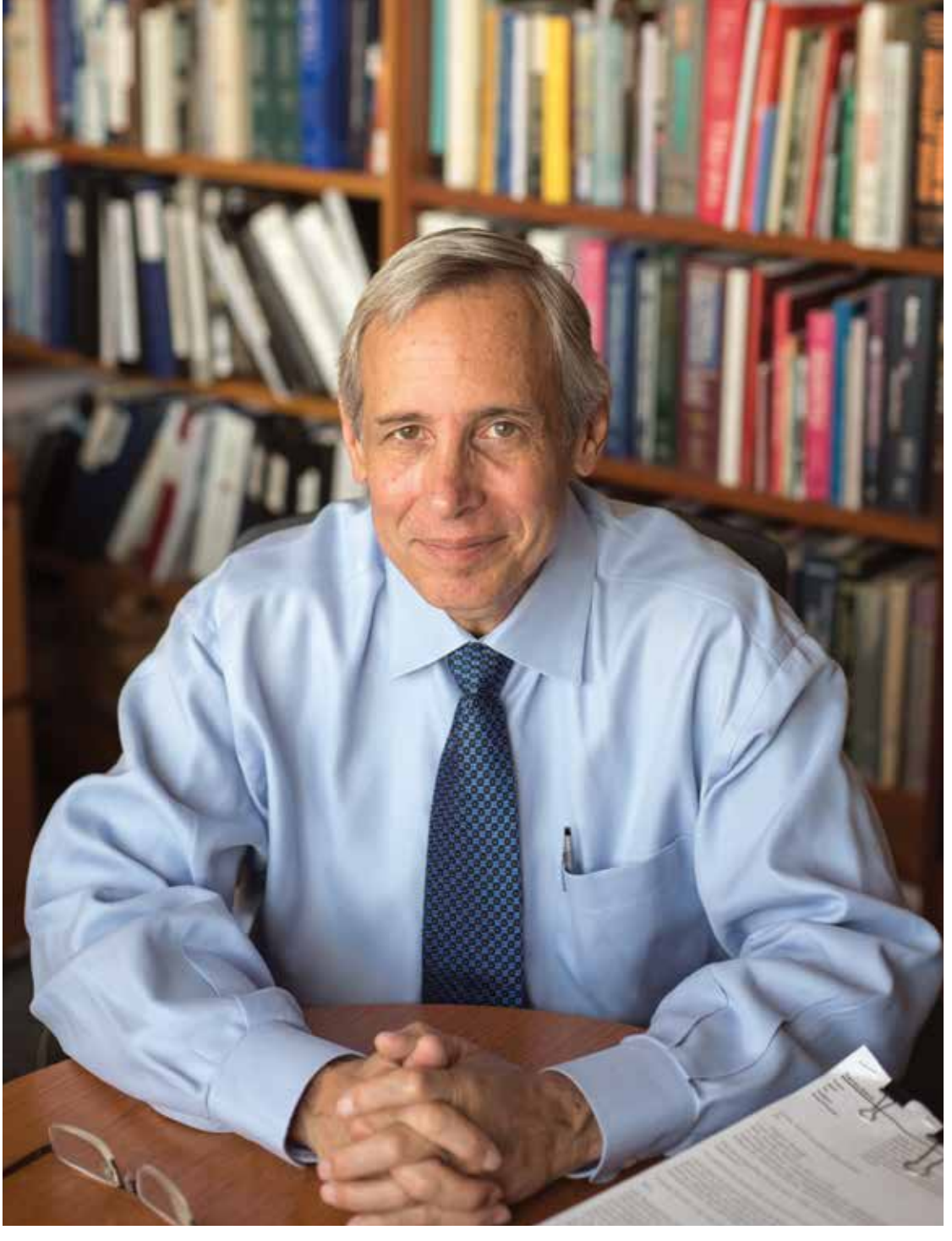
— Irene Newsham, Ph.D.

NAOTO UENO, M.D., PH.D.
Professor, Breast Medical Oncology

Diagnosis: Sarcoma

There's a significant anxiety and a lot complexity that come with a cancer diagnosis. Sometimes I strongly feel the emotions of my patients. So, for me, the difficult part as a physician is that I cannot show my illness or weakness in front of my patients, because I feel that may affect the confidence they have in me. At the same time, when my patients have a difficult time, I can relate.

Am I better person? I'm not quite sure. However, cancer has given me a different perspective, and I've had a lot more experience than someone who has not had cancer.



BURTON DICKEY, M.D.
Chair, Pulmonary Medicine

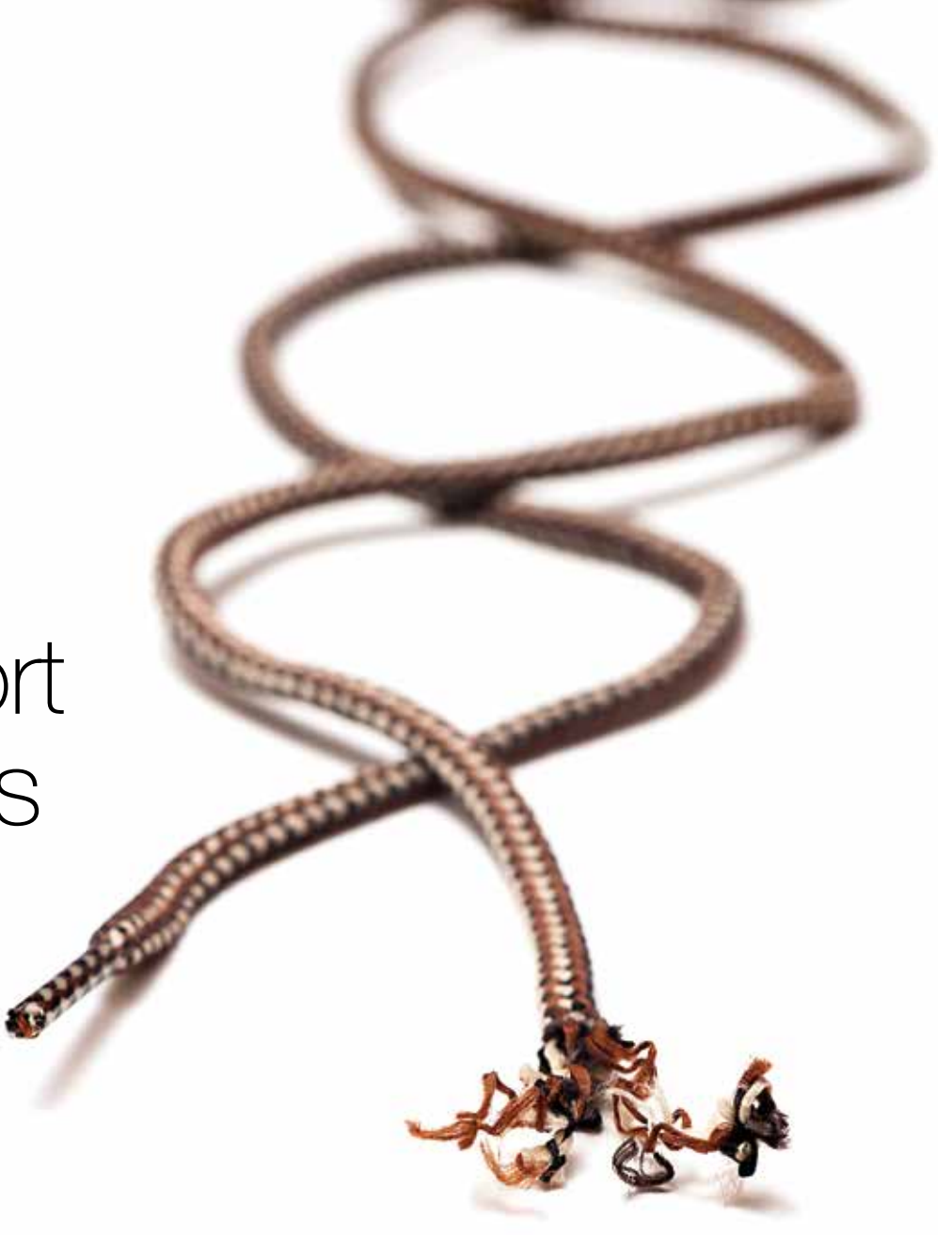
Diagnosis: Multiple myeloma

This is a shared human experience. If it's not cancer, it's dealing with some other life-threatening illness. It's dealing with mortality and that it could happen at any time, and that everything can change in a day. We all know that, but how do we deal with that emotionally and cognitively?

When I was first diagnosed, I didn't hear much of anything else. It's like one of those movies when something dramatic happens and they blur the periphery — and all you can see is this tunnel vision in the center. There's this whittling away of everything else in your life, and forcibly prioritizing and questioning things. If I have to give things up, what would it be that I would really focus on? How would I want to spend my time? Now, having been through my cancer experience, it's a little easier when I get very absorbed and things get hectic, for me to stand back and say, "OK, things should be prioritized a little bit differently." I think that's an important lesson for all of us.

The long and the short of telomeres

By Ron Gilmore



Adolfo Chavez III

Shoelaces only work well if they're capped at the ends by small plastic tips that prevent them from fraying. In much the same way, telomeres, the protective "caps" found at the ends of chromosomes, forestall the densely wrapped genetic material inside from unraveling.

Due to their unique function, telomeres have been tied to cancer development and are increasingly showing promise as targets for cancer therapy.

The secret is in their length. Every time a cell divides, the chromosomes inside shorten. But because telomeres protect the ends of the chromosomes, the only parts of the chromosomes that are lost are the telomeres.

"The valuable DNA within the chromosomes is preserved," says Courtney DiNardo, M.D., assistant professor of Leukemia.

After a cell divides, usually between 50 and 70 times, its telomeres become too short and can no longer provide protection. This impacts a cell's ability to divide, allows chromosome ends to fuse together, and creates genetic havoc that can lead to cancer.

Telomeres were first recognized in the 1970s for their ability to protect chromosomes. Since then, researchers have gained new insight into the role they and a related enzyme known as telomerase play in cancer.

Telltale enzyme

"Telomerase is detected across all stages and grades in nearly 90 percent of cancers," DiNardo says. "This suggests that telomerase mutations are generally an early event in cancer progression."

DiNardo heads an MD Anderson program on hereditary hematological malignancies that includes a group of diseases known as telomere syndromes. People with these syndromes inherit gene mutations involved in telomere maintenance, putting them at higher risk of developing certain cancers. Many also share unique symptoms such as unusual skin and hair discoloration, nail disease and white patches in the mouth.

"Patients with a telomere syndrome known as Dyskeratosis Congenita (DC), have very short telomeres and are at increased risk for bone marrow failure and acute myeloid leukemia (AML) and a group of bone marrow disorders known as myelodysplastic syndromes (MDS). They also have an increased risk of developing solid tumors and pulmonary fibrosis, a respiratory disease in which scars form in lung tissues and lead to serious breathing problems," DiNardo says.

Those diagnosed with DC at an early age are monitored for their susceptibility to AML or MDS later in life since both diseases tend to strike well into adulthood. Scientists hope that by measuring telomere length, they may be able to detect cancer or susceptibility to cancer earlier and offer improved treatments based on current telomere-based research.

In the June 2016 issue of the International Journal of Molecular Science, DiNardo wrote about the likelihood for recognizing susceptibility to MDS earlier:

Among sporadic primary MDS in young adults, or those with familial clustering of MDS, an underlying susceptibility to MDS is likely more common than previously considered. Recognizing patients with potential hereditary syndromes and referring them for genetic evaluation and counseling not only can provide valuable insights for treatment, but also for education, risk assessment, and psychosocial support for patients and their families."

As many as 10% of people with hematologic malignancies may have an underlying predisposition to cancer that's linked to telomere syndromes — much higher than previously thought, DiNardo says.

Courtney DiNardo, M.D., assistant professor of Leukemia Wyatt McSpadden

Therapeutic targets

Telomerase is a prime target for cancer therapeutics because it's found in a majority of tumor types. Several anti-telomerase agents including imetelstat and vaccines are under investigation.

"Telomerase-based immunotherapy is another attractive cancer approach," DiNardo says. "This is being studied as a possibility because telomerase degradation by cancer cells results in protein fragments and peptides that are exposed on the tumor surface — potential targets for therapy."

Simona Colla, Ph.D., an assistant professor of Leukemia, is studying how telomeres and telomerase impact cancers like AML and MDS, which fall into a group of disorders linked to defects in telomere maintenance genes, known as telomeropathies.

Colla, along with Derrick Ong, Ph.D., postdoctoral fellow of Cancer Biology, and Ronald DePinho, M.D., professor of Cancer Biology and MD Anderson president, discovered a direct link between telomere dysfunction and MDS. Their findings were published last year in Cancer Cell.

"MDS risks include advancing age, therapy-induced DNA damage, and/or shorter telomeres, but whether telomere erosion directly causes MDS was unknown," says Colla. "Our study provided evidence that DNA damage caused by telomere loss is linked to this disorder."

Colla added that their findings were consistent with long-standing observations that poor prognosis in MDS correlates strongly with short telomeres and elevated DNA damage in stem cells. She believes this improved understanding should provide highly specific risk biomarkers for preventing and treating MDS, which today is considered an incurable disease without stem cell transplantation, an option usually not available to most MDS patients due to additional existing illnesses at the time of diagnosis.

The researchers also are studying how stem cells carrying inherited mutations affecting the telomere maintenance pathway can restore telomere function during cancer development.

Stacey Hanks raises quarter horses in the coastal town of Rockport, Texas. Wyatt McSpadden

The evolution of chemo: From a brutal beginning to a tolerable today

By Ronda Wendler

When Stacey Hanks was diagnosed with breast cancer, her doctor recommended the standard treatment — surgery to cut out the tumor, followed by chemotherapy and radiation.

"I was on board for everything but the chemo," Hanks says. "My cousin went through chemo 15 years ago, and it was rough."

After a heart-to-heart talk with her family, Hanks finally said yes to her doctor's plan.

"I wanted the cancer gone, and to raise the odds that it would never come back," she says. "Chemotherapy gave me added assurance."

To her surprise, the treatment was much easier than she anticipated.

"Other than losing my hair and feeling exhausted for a few days after each session, I had virtually no side effects, says the 50-year-old Hanks.

Today, her previously long hair has grown back thicker than before, and she's wearing it in a short new "do."

"I can feel the ocean breeze on my neck. It's nice," says Hanks, who raises quarter horses in the coastal town of Rockport, Texas.

Inflated fears

For most people, the word "chemotherapy" calls to mind crippling nausea, debilitating fatigue and hair loss.

That's understandable, says Michael Keating, M.D., professor of Leukemia.

"A lot of people have inflated fears about how bad chemo is going to be," he says. "They've heard horror stories from friends or relatives who've had it in the past. We've come a long way — the treatment is much easier to tolerate today. But people still remember yesterday's chemo when the drugs could be as brutal on the patient as they were on the tumor."

Michael Keating, M.D., professor of Leukemia
Adolfo Chavez III

Keating, who's been a cancer doctor for more than 40 years, has some vivid memories of his own.

"In the 1970s and '80s, patients waited outside MD Anderson to be picked up and driven home after chemotherapy. They held turquoise-colored, kidney-shaped basins because their nausea was so bad. Some required sedation. It was that distressing."

Those days are gone, but Keating says some people are frightened enough to actually decline chemo, even when he tells them doing so decreases their chances of a cure.

"I assure them that we have tricks today — like anti-nausea medications, alternative therapies such as acupuncture, meditation and yoga, and new ways of delivering chemo drugs — that make them much easier to tolerate."

How chemo works

When a normal cell becomes worn out or damaged, it divides to create a copy of itself. The old cell dies, and the new one takes its place.

"At this very second, cells in your body are replacing themselves in an orderly and organized way," says William Plunkett Jr., Ph.D., professor of Experimental Therapeutics.

But when a normal cell mutates and becomes cancerous, its division and growth spin out of control.

"Most cancer cells replicate rapidly and often," Plunkett explains. "More and more of them are produced until they form a tumor that intrudes upon and starves normal tissues."

To win this "battle of the cells," doctors prescribe chemotherapy, with "chemo" meaning chemicals, and "therapy" meaning "treatment" — the use of chemicals to treat cancer. Some chemo drugs kill cancer cells outright. Others keep cancer cells from dividing and reproducing. But chemo drugs can't distinguish between healthy cells and cancer cells, so they attack both.

"Healthy cells become 'collateral damage' in the fight to destroy cancerous ones," Plunkett says. "That's why patients become sick and have side effects like vomiting, diarrhea, fatigue, hair loss, mouth ulcers, nerve damage and more. The drugs disrupt normal cells in virtually every area of the body.

"Each time chemo is given," Plunkett says, "doctors must strike a balance between killing cancer cells and sparing normal cells."

An accidental discovery

Chemotherapy owes its unlikely origin to a World War II naval tragedy.

On the night of Dec. 2, 1943, Germany launched a devastating air attack on the Italian port of Bari, sinking or damaging 40 ships. One of these, the U.S. ship SS John Harvey, was carrying a secret cargo of mustard gas shells that exploded on impact. Military personnel forced to swim through the resulting toxic mess ended up with severe and fatal burns.

Autopsies revealed that the mustard gas killed the soldiers' rapidly dividing white blood cells, prompting doctors to wonder if it could do the same for cancer cells, which also divide and grow quickly.

The military hired pharmacologists to study the use of mustard gas chemicals, and from these trials the first chemotherapy drug, mechlorethamine, was created to treat lymphoma. Patients showed a remarkable improvement and more drugs followed.

Anti-nausea breakthrough

Today, more than 100 chemotherapy medications are available to tame most tumors. Most are far easier to take than the chemo drugs of yesteryear. Advances in anti-nausea medicines, along with new ways of delivering chemo drugs — such as encasing them in fat bubbles to cushion absorption, or latching them onto proteins that seek out tumors and avoid healthy cells — are helping patients undergo chemo with fewer side effects.

"You may not feel great all the time," says Laura Michaud, Pharm.D., manager of Clinical Pharmacy Services. "But you can keep going. And that's a big improvement on what chemo used to be like."

Laura Michaud, Pharm.D., manager of Clinical Pharmacy Services, says more than 100 chemotherapy drugs are available to combat cancer today. Wyatt McSpadden

A big breakthrough, Michaud says, came in the early 1990s when a new class of drugs called serotonin antagonists were introduced. These medications, whose trade names include Zofran, Aloxi, Kytril and others, block stimulation of the nausea receptors in the brain.

"Before serotonin antagonists came along, the drugs we had to control nausea just weren't that effective," Michaud says. "Some people had to be hospitalized during chemotherapy — the nausea and vomiting were that bad. The only way to get patients through it was to sedate them."

Today, most chemo is given in outpatient clinics, and patients are home in time for dinner.

"People getting chemo are living full lives," Michaud says. "Many can still hold down jobs and care for their families."

Jim Nudo's story

Jim Nudo stayed "on the job" throughout his one-year course of chemo for lung cancer.

"I assumed I'd need to take a leave of absence, but it wasn't as bad as I imagined," says Nudo, whose company makes safety shut-down systems for refineries and chemical production facilities.

Jim Nudo is once again enjoying his favorite hobby, saltwater and freshwater fishing, after completing a year of chemotherapy that he says, "wasn't as bad as I imagined." Wyatt McSpadden

He needed anti-nausea medicine only once, when a tainted meal from a restaurant — not chemo — made him sick.

That's a stark contrast to what Nudo's father experienced 15 years ago when he, too, battled lung cancer.

"My dad had a much harder time," says Nudo, who developed the disease despite having never been a smoker. "My treatment wasn't a walk in the park, either — I'd sometimes get fatigued and lose my appetite — but my experience was far less grueling than my dad's."

Chemo helped slow down Nudo's cancer, but his disease was advanced when detected and has spread beyond his lungs.

Now he's on to the next phase of treatment, and is trying a new-generation immunotherapy drug. Rather than attacking the cancer directly, as chemo does, immunotherapy rallies a patient's own immune system to fight the disease. The immune cells seek out and destroy cancer in the same way they destroy bacteria, viruses and other invaders. Immunotherapy drugs are a recent breakthrough in the war against cancer, and are credited with curing former President Jimmy Carter's metastatic melanoma.

But the drugs don't work for everybody, and researchers are working to understand why. (See story on page 12.) When they do work, as they did for President Carter, the results have been particularly impressive.

"Immunotherapies are pretty well tolerated," Michaud says. "Unlike chemo, they don't contain toxins that poison cells, so there's no hair loss or blood cell abnormalities. But they have a different set of potential side effects."

The surging immune response brought on by this new generation of drugs can overshoot its target and attack healthy tissues and organs, similar to an autoimmune disorder.

"Fortunately, the vast majority of such reactions are not severe and can be reversed when the medication is stopped," Michaud says.

So far, Nudo has had no problems with the therapy.

"I'm feeling great," he marvels. "It's as though I'm on zero medications."

He's back to enjoying his favorite hobby, saltwater and freshwater fishing, and is helping his daughter and son remodel their condominiums.

"Life is wonderful," he says.

A practical partnership

Immunotherapy is an extremely important new weapon in the cancer doctor's arsenal, but it doesn't replace chemotherapy, Keating says.

He envisions the two working synergistically to cure more cancers.

"Chemo can wipe out a tumor, but if you have just one cell left, the tumor can come back. Today, we can use chemo to shrink the tumor, and then follow up with the immune drug. Pairing both therapies could make each more effective."

Whether used alone or in combination with next-generation treatments, Keating says one thing is certain: "Chemotherapy will remain a mainstay of cancer therapy for the foreseeable future."

Removing cancer's unpredictable advantage

By Scott Merville

The Moon Shots Program's APOLLO platform applies deep molecular and immune analysis to biopsies taken over time to freeze the moving target

When the ever-growing arsenal of new cancer therapies meets the ever-changing target of advanced cancer, the outcome often is unpredictable.

Immunotherapies, which free the immune system to attack tumors, result in long-term remissions, even cures, for a significant but small number of patients across several cancer types. But for most, they have little or no impact.

Right now, there's no reliable way to predict who will benefit from immunotherapy treatment. Or to envisage what the next best step should be after a treatment of any type — immunotherapy, targeted therapy, chemotherapy, radiation — fails.

Getting a firm scientific grip on the extreme survival skills of advanced cancer is the mission of MD Anderson's APOLLO program, which stands for Adaptive Patient-Oriented Longitudinal Learning and Optimization.

"Cancers are exceptionally adaptive in the face of treatment pressure," says Andrew Futreal, Ph.D., interim chair of Genomic Medicine and co-leader of APOLLO. "We know a tumor after therapy is likely to be different than before, but we haven't done a good job of tackling this from a research perspective until now," says Futreal, who also co-leads MD Anderson's Moon Shots Program.

GET TO KNOW APOLLO

APOLLO stands for Adaptive Patient-Oriented Longitudinal Learning and Optimization. It's a platform for MD Anderson's Moon Shots Program, which was created to save more lives by accelerating the development of new approaches based on scientific discoveries.

APOLLO addresses advanced cancers' tenacious ability to survive by changing in response to treatment by systematically:

- Gathering high-quality biopsies and blood samples before, during and after treatment.
- Preparing samples for deep genomic and immune response analysis by expert platforms.
- Depositing analytical results, with clinical information and other data, in the Translational Research Accelerator (TRA), a comprehensive and secure big data platform.

MD Anderson researchers will be able to search the TRA to develop new hypotheses and science-based therapies.

By the way: In Greek mythology, Apollo was the god of healing and medicine, light and truth.

APOLLO is a systematic approach that relies on taking blood samples and biopsies before, during and after treatment, and conducting deep molecular and immune analysis of those tumor samples to understand what causes them to respond to or resist a given treatment.

In the next two years, APOLLO is scheduled to conduct such analyses in 2,100 patients enrolled in 28 high-priority clinical trials for melanoma, multiple myeloma, glioblastoma, lymphoma, sarcoma, lung, breast, colorectal, pancreas and ovarian cancers, and cancers caused by the human papillomavirus.

Beyond the initial biopsy

Research with serial biopsies is important to understanding what is happening with cancer on a molecular level and building a knowledge base leading to the routine use of repeat biopsies in the clinic.

"If you don't get a biopsy after treatment, you're not going to learn about tumor evolution and how tumors resist treatment," says Ignacio Wistuba, M.D., APOLLO co-leader and chair of Translational Molecular Pathology.

APOLLO uses computer technology to combine large volumes of patient data with findings from the latest research studies. This allows clinicians to generate better-informed treatment decisions for patients.

Andrew Futreal, Ph.D., interim chair of Genomic Medicine and co-leader of APOLLO F. Carter Smith

Cancer patients generally undergo an initial biopsy to guide treatment, with shrinkage or progression measured afterward by CT or MRI scans for size and volume, and PET scans for metabolic activity.

Biopsies may be taken surgically, through endoscopy, or with radiologically guided core needles or fine needles that extract small samples from less accessible tumors and, potentially, from circulating blood. Interventional radiologists take image-guided core-needle biopsies in difficult-to-access tumors.

"MD Anderson's interventional radiology group is one of the best in the nation and they'll play a key role in APOLLO," Wistuba says.

While taking biopsies after treatment makes scientific sense, there are risks with the procedures, and the clinical benefit of doing so hasn't been proven, which means insurers and other payers don't currently cover the cost.

"We have to build the evidence first," Futreal says. "You can't just go full bore into clinical implementation of this until we generate and analyze the data in the research setting."

Patients enrolled in clinical trials under the APOLLO protocol are asked to consent to repeat biopsies and multiple blood draws at no additional cost. They may also refuse to have biopsies at any time during the study.

The development of liquid biopsies — blood tests that allow less-invasive analysis of tumors before and after treatment — will be a perfect fit for this approach, Futreal notes.

Gathering all the data

Results of these analyses, plus clinical information, will be added to the Translational Research Accelerator (TRA), which is a big data platform that integrates longitudinal clinical and research data — the same sample tracked at different points in time — to support translational research throughout the institution.

Information from approximately 250,000 patients treated at MD Anderson since 2012 has been loaded into the secure database. Research data from Moon Shots Platforms is being added, with the full platform being available in fall 2016.

The TRA will provide MD Anderson researchers with an unprecedented capacity to more quickly and efficiently generate science-based inquiries in the pursuit of better cancer treatment.

"APOLLO, with its pipeline of comprehensive data feeding the Translational Research Accelerator, drives our vision of every patient contributing to, and potentially benefiting from, research," says Futreal.

APOLLO pilot:
Biopsies during treatment tell new tale for melanoma

Immune response measured in tumor biopsies during the course of early treatment predicts which melanoma patients will benefit from specific immune checkpoint blockade drugs — drugs that release a molecular brake on the immune system, freeing it to fight cancer — MD Anderson researchers reported in the journal Cancer Discovery.

Analysis of biopsies before treatment did not indicate who would respond in this unique longitudinal study of 53 melanoma patients treated with two immune checkpoint inhibitors between October 2011 and March 2015.

"Before treatment, analyzing samples with a 12-marker immune panel or a 795-gene expression panel, you can't tell who will respond with any degree of certainty. During treatment, there were night-and-day differences between responders and nonresponders," says study senior author Jennifer Wargo, M.D., associate professor of Genomic Medicine and Surgical Oncology. She is also the co-leader of the clinical aspects of APOLLO.

Response rates ranged from 8 to 44% of patients given the drugs separately, with many responders having complete responses that last for years. Identifying biomarkers to help determine who should receive these drugs has been the subject of much research, but biomarkers have not strongly or exclusively predicted response before treatment.

The team's findings suggest that assessment of immune responses should be considered in biopsies taken shortly after treatment begins, Wargo says. This is because they may provide far more value than analysis of pretreatment samples, at least until better pretreatment biomarkers are identified.

Their findings could also help guide treatment with drugs that block protein receptors on T cells known as PD-1 and CTLA-4. Both of these receptors shut down the immune system's attack on tumors.

Jennifer Wargo, M.D., associate professor of Genomic Medicine and Surgical Oncology and co-leader of the Melanoma Moon Shot Wyatt McSpadden

Serial biopsies identify signature of success

"Profound and highly statistically significant" differences between responders and nonresponders to anti-PD1 therapy were found in nearly all of the 12 immune markers in the early on-treatment biopsies. These included the density in the tumor of killer T cells, other T cells that assist the killers, and the presence of immune checkpoint molecules.

The team's findings have implications for treatment and further research to understand how melanoma responds to or resists treatment.

"We could start by treating with anti-PD1, do an early on-treatment biopsy and, based on that, either continue or add another agent," Wargo says.

Tumor samples were collected at various times when it was technically feasible and safe to do so. For example, of the 46 patients undergoing anti-PD1 treatment, 24 had pretreatment biopsies (seven responders, 17 nonresponders), 11 had biopsies during treatment (five responders, six nonresponders) and 12 provided tumor samples at progression.

"We should be incorporating analysis of longitudinal tumor and blood samples into clinical trials, and, ultimately, we may even incorporate this into treatment with standard-of-care therapy," Wargo says. "This effort is critical to guiding patient care in this era of precision medicine."

From hepatitis C to hepatitis free

MD Anderson's one-of-a-kind clinic treats the virus and cancer

By Ronda Wendler

Norman Hart's roughened hands and sturdy frame tell of decades spent outdoors working construction in the hot Oklahoma sun.

"I've always been active and rarely sick," says the now-retired 66-year-old carpenter and bricklayer.

But several years ago, Hart got the flu twice in three months.

"It hit me hard the first time, and even harder the second," he says.

After failing to get better, Hart made a rare visit to his hometown doctor in Tulsa, Oklahoma. Bloodwork revealed a puzzling surprise — he had leukemia *and* hepatitis C.

"I was stunned and devastated," Hart says. "Suddenly I went from being a healthy, hard-working guy to a seriously sick guy. I had no clue how this happened."

Though no one can say with certainty, doctors believe Hart got hepatitis C when he underwent open-heart surgery as a child in 1958. The operation fixed a dime-sized hole in his heart — a condition he'd had since birth. The surgery also required Hart to receive five pints of donated blood.

"The nation's blood supply wasn't screened for hepatitis C until 1992, when a highly sensitive test to detect the virus was developed," says Harrys Torres, M.D., associate professor of Infectious Diseases. "People like Mr. Hart, who received a transfusion prior to that time, are at risk because hepatitis C is transmitted by blood-to-blood contact."

Three-fourths of reported cases can be traced to people who had blood transfusions before the blood supply was screened, or who shared needles while injecting illegal drugs, Torres says. The virus can also be spread through improperly sanitized tattoo and body-piercing equipment.

"If there's infected blood on the needle," Torres says, "it's transmissible."

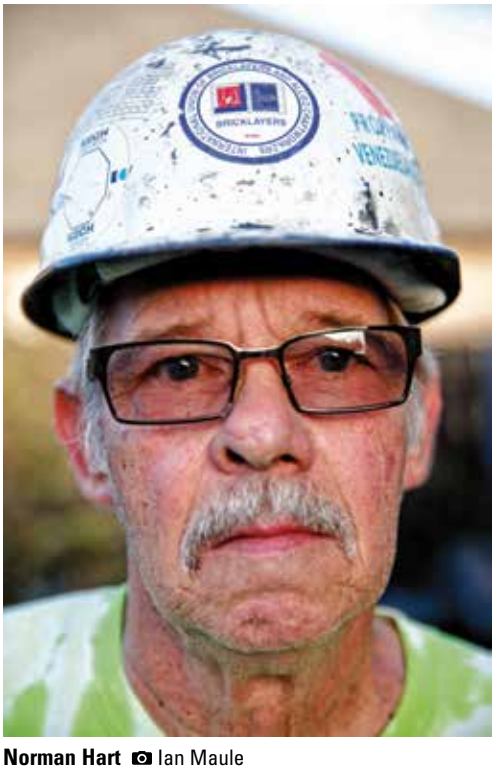
Turning lives around

To help the increasing number of patients like Hart, who are battling both cancer and hepatitis C, Torres established a new clinic at MD Anderson in 2009. It's the only one of its kind in the country.

"No other cancer center has a clinic solely devoted to managing patients with both diseases," says Torres.

Hart came to MD Anderson after his hepatitis C treatment in Oklahoma failed. Doctors there had administered a very powerful drug called interferon, which at the time was the "go-to" remedy for battling hepatitis C. Hart couldn't tolerate its side effects.

"I thought the treatment would kill me faster than the disease," he says.



Norman Hart Ian Maule

After each interferon injection, he became dizzy, fatigued and out of breath. Eating caused nausea and diarrhea. A restful night's sleep — so important to Hart's recovery — eluded him.

"I was miserable," he says. "My quality of life hit rock bottom."

With his immune system growing weaker, Hart took his doctor's advice and headed south to MD Anderson's one-of-a-kind clinic. Shortly after he arrived, the Food and Drug Administration approved a new class of drugs for hepatitis C called direct-acting antivirals, or DAAs.

"That's when my life turned around," says Hart, one of MD Anderson's first patients to be cured with the treatment.

Patients take one pill each day for 12 weeks. Side effects are virtually nonexistent, and the cure rate is 95%. Treating cancer patients with interferon, by comparison, takes up to 48 weeks, can cause debilitating side effects, and offers a less-than-50% cure rate.

"These new drugs have changed the face of hepatitis C treatment," Torres says. "Three months, one pill a day, and you're cured. The virus is completely eradicated."

To date, more than 600 patients have been seen in MD Anderson's hepatitis C clinic, and that number is growing.

Epidemic in the making

Roughly 4 million people in the U.S. are infected with hepatitis C, and 100 million worldwide.

"In truth, the number may be much higher," Torres says, "because many people are walking around undiagnosed. Thousands of cases are unreported."

A slow-acting, lethargic virus, hepatitis C silently attacks the liver over the course of 20 to 30 years. It replaces healthy liver tissue with fibrous scar tissue — a condition known as cirrhosis. Eventually the liver may stop functioning properly, and liver failure or cancer may occur.

"The liver tries to heal itself by replacing the scars with new cells it generates," Torres explains. "But the more new cells your liver creates, the higher the chances that a change, or mutation, will take place. That's how liver cancer develops in people who have hepatitis C, which is a leading cause of liver cancer in America."

Patients have no clue they're infected because the virus causes no symptoms as it does its damage over decades. Most people find out they have the disease through bloodwork collected during a routine medical exam, or while visiting the doctor for an unrelated problem.

"Most people with hepatitis C are going about their everyday business," Torres says, "unaware they carry the virus."

The good news, he says, is there's an increased awareness today of the need for hepatitis C screening. The bad news is the number of newly diagnosed patients is skyrocketing as the virus, contracted years ago, surfaces. About 17,000 new cases are diagnosed in the U.S. each year.

"It's an epidemic in the making," Torres says. "Given the prevalence of recreational drug use in the '60s and '70s, the absence of blood supply screening before 1992, and the two- to three-decade course of the virus, the Centers for Disease Control and Prevention anticipates a major spike in liver disease," he says. "An overwhelming number of people will be needing medical care, including liver transplants and cancer care, over the next two decades."

Links to more cancers

Liver cancer isn't the only disease linked to hepatitis C. Doctors have long realized the virus increases the risk for non-Hodgkin lymphoma, a type of cancer that originates in the lymphatic system — the disease-fighting network of lymph nodes and vessels that help the body fight infections.

And this year, a study led by Torres found a link between hepatitis C and head and neck cancers.

"We were seeing all these head and neck cancer patients at MD Anderson who tested positive for hepatitis C, so we began to wonder if there was a connection," he explains.

After studying more than 34,500 patients, his research confirmed that those with hepatitis C have more than twice the risk of mouth and throat cancer and nearly five times the risk for larynx cancer. The findings were published in the Journal of the National Cancer Institute.

Torres believes the disease will continue to be associated with more cancers as knowledge of the virus grows.

Hart was found to have lung cancer two years after being diagnosed with leukemia. Hepatitis C may have played a role, Torres believes.

"The virus changes our blood chemistry," he says, "so it may contribute to the development of other cancers."

Hart is now cured of hepatitis C, and both his leukemia and lung cancer are in remission.

"It matters less to me how I got sick," he says, "compared to the fact that I'm doing well now."

BABY BOOMERS ARE AT RISK

Baby boomers — Americans born between 1945 and 1965 — are five times more likely to have hepatitis C. To detect the disease in this high-risk group, the Centers for Disease Control and Prevention set forth guidelines in 2012 for a one-time hepatitis C screening for everyone in this age group.

Torres is taking this a step further and is spearheading an initiative endorsed by MD Anderson leaders to screen all new patients admitted to the cancer center, regardless of their age. So far, leukemia, lymphoma and bone marrow transplant patients are tested for the virus, but Torres wants everyone to be screened.

"Hepatitis C can cause cancer, so if we detect the virus early enough, we may spare our patients additional cancers that are associated with the virus," he says. "Studies have shown that eliminating hepatitis C in some non-Hodgkin lymphoma patients can cause their cancer to disappear. Wouldn't it be great if we learn this is true for other cancers as well?"

No national guidelines exist on how to treat patients who bear the double burden of cancer and hepatitis C, so Torres and experts from around the nation are writing them.

"I feel we're writing history," he says. "The recommendations we generate here will affect patients all over the United States and the world."

Harrys Torres, M.D., and clinical nurse Ruth Roach helped cure Jan Barbo, center, of hepatitis C. Adolfo Chavez III

A master gardner is back at work

Like Hart, Jan Barbo likely got hepatitis C from a blood transfusion. Almost 50 years ago, she suffered an ectopic pregnancy when a fertilized egg attached itself in her fallopian tube instead of her uterus. Barbo needed emergency surgery and two pints of blood after her fallopian tube, unable to accommodate the growing embryo, ruptured.

Her transfusion was in 1968 but her hepatitis C symptoms, true to the disease's course, didn't become apparent until 1982.

"My skin was jaundiced, my eyes were yellow, and I was very sick," recalls Barbo, who lives in New Mexico.

Her doctor in Sante Fe diagnosed Barbo with hepatitis, but recommended she wait for better drugs to come along before seeking treatment.

"The only therapy available at that time would take one year to complete," Barbo recalls. "My doctor said the remedy would cause me to feel as though I had influenza every day and I'd likely become depressed. The success rate averaged only 25%."

So Barbo waited. Instead of undergoing treatment, she focused on a healthy lifestyle. She exercised every day, ate a balanced diet and abstained from alcohol, which could further damage her liver.

Years later, she began experiencing severe abdominal pain caused by pancreatic cysts that sometimes lead to cancer.

"I knew pancreatic cancer was serious, so I wasn't about to mess around," she says. "I headed straight to MD Anderson."

Doctors continue to keep a close eye on Barbo, who remains cancer free. She's also an "alumnus" of the hepatitis C clinic. Torres treated her with the same FDA-approved drugs that cured Hart, and now Barbo, too, is free from hepatitis.

"There are no words to describe how my life has changed," says the 80-year-old master gardener who for many years published a gardening column in the Santa Fe New Mexican newspaper.

She's back to tending her 6-acre mountain-area homestead with its 300 apple, cherry and pear trees and 30-plus varieties of flowering plants. Located halfway between the picturesque communities of Taos and Santa Fe, the property offers majestic views of the Sangre de Cristo and Jemez mountains.

"I'm grateful for each beautiful day," says Barbo as she surveys the landscape from her front porch. "Hepatitis C could have killed me, but thanks to MD Anderson, I'm here today, enjoying life in this magnificent place."

‘We should be doing more to protect our children’

By Laura Sussman

The stats that support being vaccinated against the human papillomavirus (HPV) are staggering.

According to the Centers for Disease Control and Prevention (CDC), 80 million people in the United States are currently infected with the virus, which is linked to six cancers. There are 39,000 men and women diagnosed with HPV-related cancer every year.

Despite the evidence, a number of parents still choose not to have their children vaccinated — or don’t have them receive the full series of the vaccine.

The CDC recommends boys and girls be vaccinated at age 11 or 12 to give them time to build up protection before they’re exposed to the virus. It recommends that preteens and teens between the ages of 11 and 14 receive two doses of the vaccine. Three doses are recommended for those who begin the vaccine at 15. Though the body assimilates the vaccine best in the preteen years, it’s effective and approved for men and women up to age 26.

Nationally, only 42% of eligible girls and 28% of eligible boys have completed their vaccine series, with only Rhode Island, Virginia and Washington D.C. mandating it for teenagers.

In stark contrast, other countries have government-supported vaccination programs, with national averages as high as 99%.

“As a society, we shouldn’t have to see these cancers anymore, and yet every week I meet and diagnose young women with advanced, and sometimes deadly, cervical cancer,” says Lois Ramondetta, M.D., professor of Gynecologic Oncology and Reproductive Services, and a co-lead on the HPV-Related Cancers Moon Shot. “We have a safe and effective vaccine that could prevent the majority of these cases that’s tragically still being underused. We should be doing more to protect our children.”

Cancer is prevalent in Yvonne and John Cosgrove’s families, so the decision to vaccinate their children Phoebe, 13, and Jake, 14, against the HPV virus was an easy one. Nick de la Torre

HPV is a common threat

The human papillomavirus (HPV), a group of more than 150 related viruses, is widespread and dangerous. The CDC reported the following statistics:

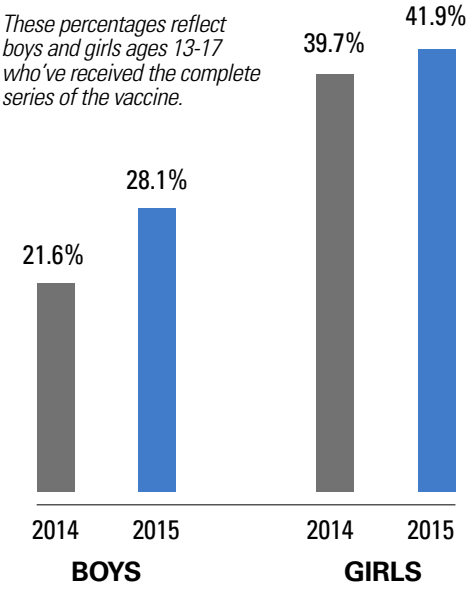
Six:
The number of cancers the vaccine can protect against, including cervical, anal, oropharyngeal, vulvar, penile and vaginal cancers.

14 Million:
The number of new HPV infections diagnosed in the country each year.

39,000:
The number of men and women diagnosed with an HPV-related cancer every year.

U.S. vaccination rates continue to rise

These percentages reflect boys and girls ages 13-17 who've received the complete series of the vaccine.



A very personal decision to vaccinate

For Linda Ryan, the decision to have her sons Matthew, 18, and Ethan, 14, vaccinated against the virus was deeply personal. She currently is receiving treatment for her second recurrence of HPV-positive cervical cancer. Ryan says there's almost no therapy she hasn't endured.

However, having to tell her family that her cancer was back was far more excruciating than any therapy, she says.

"These are the people who love you and can't imagine living without you. Knowing you have cancer makes the thought of living without you more of a reality than any parent or young child should have to face.

"With the HPV vaccine my children likely won't have to tell me or their children they have cancer," Ryan says. "As a parent, I couldn't ask for much more."

They've seen too much cancer

Both Yvonne and John Cosgrove have felt the impact of cancer. The disease runs deep in Yvonne's family, with a history of myeloma, lung, BRCA-associated breast and ovarian cancers and melanoma. John's father died of lung cancer and his grandmother died of breast cancer.

With this collective history, as parents, Yvonne says they are "extremely plugged into health, awareness and prevention, while trying to maintain a healthy balance of fun."

Given their vigilance, the decision to vaccinate their children, Phoebe, 13, and Jake, 14, was an easy one. Fortunately, says Yvonne, her family's pediatrician did an outstanding job of educating her about the importance of the vaccine.

When Yvonne and Phoebe were asked to participate in MD Anderson's marketing campaign to encourage HPV vaccination, they were more than willing. The institution's inaugural marketing/educational campaign featured parents, their children and HPV-associated cancer survivors.

"Among our peers, there's a lot of awareness around the vaccine itself, but there doesn't seem to be the understanding of what HPV truly is and all of the cancers the virus is associated with," says Yvonne. "It's important for people to understand just how prevalent the virus is, and that there is a way to prevent so many cancers."

Cervical cancer survivor Linda Ryan decided to vaccinate her sons Ethan, 14, and Matthew, 18, against HPV "so they likely won't have to tell me or their children they have cancer." Adolfo Chavez III

John, in particular, appreciated learning more about the virus and the vaccine.

"Generally, moms take their kids to pediatric appointments — we're no exception, so I never had a conversation with my kids' pediatrician about the vaccine," he admits. "I think this campaign and my family's participation helped get the message out to a broader audience, and gave me a better understanding of just how necessary the vaccine is."

Practicing what they preach

As the program manager for the HPV-Related Cancers Moon Shot, it's Lori Stevens' responsibility to educate the general public about the virus's impact.

MD Anderson surveyed its employees to better understand their HPV knowledge and awareness, and received more than 4,000 responses. Half said they had a child within the appropriate vaccination age range, and said they'd be interested in having their child inoculated at MD Anderson.

Armed with those responses, Ramondetta, Stevens and others pushed for MD Anderson to begin a Saturday vaccination clinic for eligible employees and their children. The clinic is open to employees ages 26 and under, and employees' children ages 9 to 26. The vaccine is 100% covered by insurance, with no co-pay or deductible for the employee.

When the monthly clinic opened in June, Stevens' 11-year-old son, Kirby, was first in line.

"Obviously, as an institution, we've been advocating for the vaccine, but it was really important for MD Anderson to be able to provide it for our employee family," Stevens says. "A diagnosis of cancer is just so scary, and I feel fortunate that I have the opportunity to protect my child."

A stem cell transplant helped Bindu Chakravarty battle acute myeloid leukemia. Nick de la Torre

After a stem cell transplant, professor returns to the classroom

By Ronda Wendler

Chemistry professor Bindu Chakravarty rarely missed a day teaching at Houston Community College. So when she called in sick one morning, it was with good reason.

"I had a 101-degree fever and was so exhausted, I could barely get out of bed," she remembers. "Something was very wrong."

For several weeks, Chakravarty, 59, had been fatigued and running a low-grade fever. But she took aspirin and kept on going.

"I thought whatever illness I was fighting would run its course," she says. "I didn't want to let my students down."

When aspirin ceased to work and her fever spiked, Chakravarty's worried husband insisted she visit a doctor. Instead of going to class, she headed to her family physician's office.

A blood test revealed her platelets — cells in the blood that help it clot — were low. The doctor explained that this can cause excessive bruising and bleeding.

"Now I understood why my gums bled when I brushed my teeth," Chakravarty recalls, "and why I was covered in bruises."

Because a low platelet count can be a red flag for leukemia, Chakravarty's doctor referred her to an oncologist at MD Anderson, where tests revealed she had a cancer of the blood called acute myeloid leukemia, or AML.

"I was admitted to the hospital the next day," Chakravarty says, "and my cancer journey began."

Out of control

AML starts in the soft, spongy bone marrow, where blood is made. Immature, primitive stem cells inside the marrow evolve over time into three types of mature, healthy blood cells — white to fight infections, red to carry oxygen throughout the body, and platelets to help the blood clot. But in AML, the marrow produces too many immature white blood cells, called leukemic blasts. Because they fail to develop properly, the leukemic blasts can't fight infections. And because so many are being produced, they crowd the bone marrow and prevent it from making the normal platelets and red and white blood cells the body needs.

"Though AML starts in the bone marrow, it can quickly move into the blood and sometimes spread to other parts of the body, including the lymph nodes, liver, brain and spinal fluid," says Elizabeth Shpall, M.D., deputy chair of Stem Cell Transplantation and Cellular Therapy at MD Anderson. "It's important to start treatment soon after diagnosis."

The treatment plan

Early tests at MD Anderson revealed Chakravarty had a form of AML that's linked to a genetic mutation and is particularly aggressive.

Treatment began immediately. First, doctors in the Leukemia Department prescribed several rounds of intense chemotherapy to wipe out the cancer cells in her bone marrow.

The treatment can be effective, but it has an unwanted side effect: Healthy red and white blood cells and platelets become "collateral damage" and are killed along with the cancer cells by the chemo. This makes the body vulnerable to infection and uncontrolled bleeding.

For her own protection, Chakravarty spent 27 days in isolation until tests showed no remaining signs of cancer. Next came the second phase of treatment — a stem cell transplant to replenish her bone marrow with healthy stem cells from a matching donor.

To test whether a donor is a suitable match for a recipient, doctors examine genes in the human leukocyte antigen, or HLA System — the part of the immune system that recognizes self and not self. In a full match, eight or more of the HLA genes need to match between donor and recipient. When stem cells are derived from another source — donated umbilical cord blood — a match in four of six HLA markers is considered acceptable for most patients.

None of Chakravarty's family members qualified as a match, nor did any of the 28 million people who signed up as donors with various registries. So Shpall recommended using blood collected

from an umbilical cord immediately following the delivery of a baby. After the umbilical cord is cut, a needle is inserted into the vein of the cord, and the blood in the cord and placenta is collected and frozen until it's needed for a transplant.

This infant blood is rich in new stem cells that haven't yet been educated against foreign invaders, reducing the chances they'll attack a recipient's tissues.

"The nice thing about cord blood is it contains a large number of stem cells that are naïve," Shpall explains. "So they're less likely to cause complications in recipients. For this reason, we don't need a full match when we use cord blood."

The number of stem cells in one unit of umbilical cord blood, however, is not enough to repopulate the bone marrow of an adult. So after more mild chemo and radiation to kill any straggling cancer cells, Chakravarty underwent a double cord transplant, in which blood from two umbilical cords is combined to provide a sufficient number of stem cells.

The procedure is essentially painless, Shpall says, and is similar to a blood transfusion. The donated stem cells are thawed and infused into the recipient's vein through an IV. The stem cells then naturally migrate into the bone marrow. The restored bone marrow begins producing normal blood cells within several days to several weeks.

"In some cases, the transplant can have an added benefit," Shpall says. "The new blood cells also attack and destroy any cancer cells that survived the chemo and radiation."

Age isn't everything

While stem cell transplants may be lifesaving, not everyone is a candidate.

When approving a transplant, doctors take into account the patient's overall physical condition, diagnosis, stage of disease and previous treatments. Tests are conducted to make sure the patient is healthy enough to undergo the procedure.

Stem cell transplants traditionally have been offered to children and young adults, though, ironically, blood cancers most often affect older patients.

"In the past, older adults had more complications with stem cell transplants, mainly due to the high levels of chemo and radiation required before the procedure," Shpall explains. "Today, we've reduced the toxicity of these pre-treatment regimens."

Doctors now are more likely to evaluate older patients on an individual basis, Shpall says, and to consider physiological age instead of chronological age when deciding who's eligible for a transplant.

Taking it slowly

One month after receiving her donated stem cells, Chakravarty was released from the hospital.

Tests continue to show no signs of AML, but she knows her immune system may take months or even years to fully recover, so she's "taking it slowly."

This semester she's teaching a full course load, but online and hybrid classes only, where some traditional face-to-face "seat time" is replaced with online learning.

Chakravarty regularly returns to MD Anderson where doctors monitor her progress. She credits her family and friends, co-workers, MD Anderson caregivers, and devout Hindu faith with seeing her through.

"I view my cancer journey as a test," she says. "This experience has deepened my belief in the goodness of humanity. Everyone supported me when I needed it most."

STEM CELL TRANSPLANT OPTIONS

Different types of stem cell transplants are used to treat cancer. Their names are based on who donates the stem cells.

AUTOLOGOUS ("AUTO")

This type of transplant uses a patient's own stem cells, which are removed from their blood and frozen. When the patient is ready for transplant, the cells are thawed and given back to them.

Upside: *Because the cells are a patient's own, there's less risk of rejection or graft-versus-host disease, which occurs when a donor's cells think the recipient's cells are foreign and attacks them.*

Downside: *Some original cancer cells may remain in a patient's donated supply.*

TANDEM (DOUBLE AUTOLOGOUS)

This is an autologous transplant performed twice instead of once, with a three- to six-month break in between. All the stem cells needed are collected beforehand, and half of them are used for each transplant.

Upside: *Studies have shown improved survival rates and quality of life with tandem transplants compared to a single transplant.*

Downside: *Because two transplants are performed, the risk of complications is higher than for a single transplant.*

ALLOGENEIC ("ALLO")

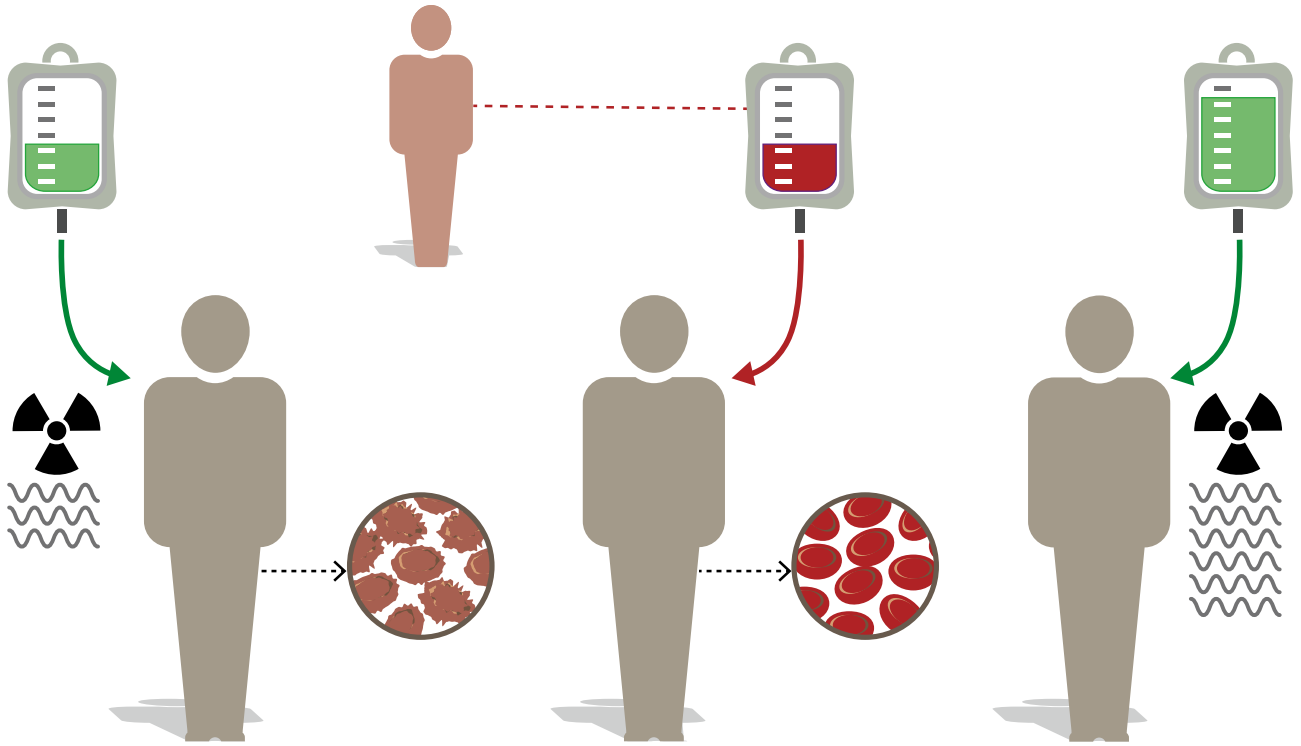
Instead of using a patient's own stem cells, those used in allogeneic transplants come from a donor. Stem cells from relatives or unrelated donors whose tissue type closely matches the patient's may be used. Donors can be located through bone marrow registries such as the National Marrow Donor Program, and through umbilical cord blood banks.

Upside: *The transplanted stem cells are cancer-free. Donor stem cells create a new immune system and may launch an attack against cancer cells remaining in the patient's body.*

Downside: *A recipient's body may see the donor stem cells as foreign and reject them, or the immune cells from the donor may attack not only cancer cells, but also healthy cells in the recipient's body.*

HOW A STEM CELL TRANSPLANT WORKS

Certain cancers that affect the blood or immune system can devastate a person's bone marrow, which is further destroyed by chemotherapy and radiation during treatment. When this happens, a stem cell transplant becomes necessary to replace the bone marrow. Here's a basic breakdown of the process:



A patient receives high doses of chemotherapy and radiation to wipe out the cancer cells in the bone marrow. However, healthy red and white blood cells and platelets become collateral damage, leaving the patient vulnerable to infection and uncontrolled bleeding.

Stem cells taken from a donor are given to the patient though an IV. These new cells replenish the bone marrow by growing into healthy blood cells.

Following a transplant, the donated stem cells can attack and kill remaining cancer cells, or they can allow a patient to undergo higher doses of chemo to kill the disease.

MINI (REDUCED INTENSITY)

Patients receive less chemo and radiation before a mini-transplant than a standard transplant. The goal is to kill some, but not all, of the cancer cells and suppress the immune system just enough to allow donor stem cells to settle into the recipient's bone marrow, take over, and launch an attack against the remaining cancer cells.

Upside: *In the past, older patients and those who are too sick or frail to withstand the intense levels of chemo and radiation used in standard transplants were denied transplants. With the advent of mini-transplants, age and medical frailty are no longer "deal-breakers."*

Downside: *Mini-transplants have only been performed since the late 1990s, so long-term patient outcomes are not yet clear. Though the procedure lowers the risk of some complications, cancer may be more likely to return.*

SYNGENEIC (IDENTICAL TWIN)

This type of allogeneic transplant can only be used if a patient has an identical sibling with the exact same tissue type.

Upside: *Graft-versus-host disease will not be a problem.*

Downside: *Because a recipient's new immune system is so much like their original, it can't effectively fight the remaining cancer cells. Every effort must be made to destroy all the cancer cells before the transplant is done in order to help keep the cancer from coming back.*

HALF-MATCHED

A half-matched donor is someone whose tissues are only half identical to the patient's, but they're close enough to allow him or her to move ahead with a transplant. Parents are always a half-match for their children, and vice versa. Siblings have a 50% chance of being a half-match for each other.

Upside: *This procedure greatly expands the potential donor pool, making virtually all patients eligible for transplants.*

Downside: *Because the match between donor and recipient is only half, the donor's immune system may generate a stronger attack against the recipient's tissues.*

CANCER PREVENTION RESEARCH IS BEING REDEFINED

By Clayton Boldt, Ph.D.

"Pay for this month's chemo or rent? It's a terrible choice."

That's how Kelly McGauhey kicked off her "elevator speech," a 90-second summation of her experience this past summer in MD Anderson's Cancer Prevention Research Training Program.

"As the costs of cancer drugs rise, there's been an explosion of interest in financial toxicity," explained McGauhey. "But we don't really know who it affects or if researchers are measuring it in a way that can be compared."

To more accurately compare studies, McGauhey spent the summer analyzing the different measurements used to describe the consequences that can come from the high cost of cancer treatment. These consequences include patients forgoing or delaying drugs or care, and mental and physical health problems brought on by the stress of this financial burden. McGauhey's ultimate goal is to help patients understand and learn to navigate this complicated financial landscape.

"Everything I learned while a trainee informs and influences the way I think about and create career development programming for our postdocs. It is the unique blend of research, scholarship and professional development acquired through the program that ultimately allows the trainees to be successful on their career path."

Tracy Costello, Ph.D., program manager, Postdoctoral Affairs and Development

But how does researching financial toxicity fit within a cancer prevention training program? Very well, as it turns out.

Cancer prevention is an evolving field, expanding beyond lifestyles that lower cancer risk. Understanding health disparities, improving survivorship and informing public policy are just a few more examples of its larger scope, all with the goal of reducing the burden of cancer in the world.

With one of the oldest and largest prevention research training programs in the country, MD Anderson continues to drive that evolution through an innovative, multidisciplinary curriculum that includes the Cancer Prevention Research Training Program.

"We're working toward expanding the field and making new connections, particularly in people who are early in their careers," says Shine Chang, Ph.D., a professor of Epidemiology and director of the program, which was founded in 1992 by Robert Chamberlain, Ph.D., professor emeritus of Epidemiology. "We want to encourage them to consider a place for prevention in whatever they do for their careers."

"I would not have had a career had I not started under the auspices of the prevention research training program as a postdoctoral fellow. Drs. Chamberlain and Chang's passion and leadership have directly impacted many lives."

Eileen Shinn, Ph.D., assistant professor, Behavioral Science

McGauhey, a former patient navigator with the American Cancer Society, is currently pursuing a master's degree in public health. Though she didn't plan on a cancer prevention career, this summer has made her think twice.

"I think it opens your eyes to a lot of different possibilities," she says. "It's really neat to be able to work so closely with people you wouldn't normally meet otherwise."

Opportunities in the program include short-term summer experiences, such as McGauhey's, as well as pre- and post-doctoral fellowships, which last up to two years.

"Our goal is to have an interdisciplinary training program where trainees can get a broad view of the entire landscape for cancer prevention," explains Carrie Cameron, Ph.D., assistant professor of Epidemiology and the program's associate director. "A lot of people are surprised to find out there are so many opportunities in cancer prevention."

Michelle Fingeret, Ph.D., an associate professor of Behavioral Science who holds joint appointments in Head and Neck Surgery and Plastic Surgery, initially was unsure of her place in this field, but her experiences as a postdoctoral trainee helped launch her career.

Kelly McGauhey's goal is to help patients understand and navigate the cost of cancer care. Nick de la Torre

"My postdoctoral fellowship through the Cancer Prevention Research Training Program allowed me to obtain top-notch training and mentorship in the areas of tobacco cessation, health disparities, and cancer prevention research. These experiences were critical in helping me to become an independent researcher committed to reducing tobacco-related cancer disparities for the underserved."

Diana Hoover, Ph.D., assistant professor, Health Disparities Research

"As someone who conducts research on managing the psychological and social effects of cancer and its treatments, it was a real challenge to know where I fit in this cancer prevention landscape," says Fingeret. "I began to think of it in terms of the vital need to prevent psychosocial impairments caused by cancer."

Fingeret, a clinical psychologist, is now director of MD Anderson's Body Image Research and Therapy Program, which works with patients to address concerns about their self-image and helps them adjust to changes to their bodies caused by treatment. She attributes much of her program's success to meaningful collaborations with her former training program mentors.

"I was so glad they had a focus on multidisciplinary research because there's no way I would be successful in my career without having that as a foundation," says Fingeret. "I wouldn't be where I am today if I hadn't had that postdoctoral fellowship."

The program's success has made it a national model for cancer prevention research training. Despite discontinuation by the National Cancer Institute of funding dedicated to cancer prevention research training, Chang and Cameron will continue to improve the curriculum and strive to make cancer prevention a priority among future scientists.

"When we've prevented every last cancer that can be prevented, and we help every survivor learn how to protect themselves against future cancers, then we'll be done," says Chang.

"The cancer prevention research training fellowships were invaluable for my career because they provided excellent mentorship and career-development training. There's a certain pride in being a trainee because you know that you belong to a special program that is really invested in your success."

Mala Pande, Ph.D., assistant professor, Gastroenterology

“Without this program, my cancer would not have been discovered.”

Thanks to the FIT-Flu screening program, an uninsured man’s colorectal cancer was caught early and his life was saved

By Clayton Boldt, Ph.D.

Three years ago, Stephen Cadmus faced a dilemma. He needed to see a doctor, but he had no health insurance.

Cadmus was financially wiped out five years earlier when the tech consulting business he owned fell victim to the Stanford Financial Group’s $7 billion Ponzi scheme. Some 28,000 investors bought certificates of deposit from Stanford International Bank in Antigua, which was owned by Houston financier R. Allen Stanford. But most of the clients’ money financed Stanford’s lavish lifestyle instead of the securities it was supposed to.

“My company had been buying investments from Stanford for more than five years,” Cadmus says. “We lost it all — every last penny.”

To get the medical attention he needed but couldn’t afford, Cadmus visited a local clinic that offered reduced-fee services. He shared his concerns about seeing blood in his stool, and doctors gave him a take-home test called FIT, or fecal immunochemical test. Test takers swab a small amount of stool on a stick, place the stick in a plastic container and mail it to a lab for analysis.

Within days, the results of Cadmus’ test showed blood in his stool — a possible indicator of colorectal cancer — so he underwent a colonoscopy. Results showed he had stage II colorectal cancer.

“I had absolutely no other symptoms that would have led me to believe anything was wrong,” he says. “My worst fears were realized.”

Cadmus’ FIT test and colonoscopy were provided free through the FIT-Flu program. Designed by colorectal cancer experts at the University of California, San Francisco, the program offers free FIT tests, along with annual flu shots, to low-income, uninsured, Medicaid-eligible adults ages 50 to 75. FIT-Flu is underway at various sites throughout the country, including MD Anderson. The American Cancer Society recommends the program and helps clinics implement it.

“Without this program, my cancer would not have been discovered,” Cadmus says. “On so many levels, I am very fortunate.”

Since 2013, MD Anderson has partnered with federally qualified health centers in nine Texas counties to provide cancer screening and prevention services, including FIT-Flu. These centers receive enhanced reimbursement from the Centers for Medicare and Medicaid Services (CMS) in exchange for providing care to those covered by Medicaid, the joint federal and state program that helps those with limited income and resources get medical care.

Kavon Young, M.D., is medical director of a clinic in Houston's historic East End where uninsured patients get cancer screenings through a partnership with MD Anderson. Wyatt McSpadden

"MD Anderson's programs have leveled the playing field by allowing us to provide our patients with screenings they couldn't easily get," says Kavon Young, M.D., medical director of El Centro de Corazon, a partner clinic in Houston's historic East End that primarily serves uninsured Hispanic patients.

According to the Texas Medical Association, more than 5 million Texans are without health insurance.

"There's been a need for cancer control efforts for the low-income and uninsured in our community for a long time that we've been unable to address because of lack of funding," says Lewis Foxhall, M.D., vice president for MD Anderson's Office of Health Policy, which spearheads the cancer center's initiatives for the underserved.

But thanks to funding from the CMS, Foxhall says MD Anderson can now offer many vital programs to this population, including mobile mammography, skin and colorectal cancer screenings, tobacco prevention and cessation, and childhood obesity prevention.

More than 400 people have received skin screenings and more than 4,500 have had mammograms. Of the 7,500 who've received the take-home FIT test, 300 have received follow-up colonoscopies, 110 had precancerous polyps removed to prevent cancer from developing, and 21 have been diagnosed with cancer and referred for further care.

These programs are made possible in part by funding from the Medicaid 1115 Transformation Waiver, which allows Texas to expand Medicaid managed care and funding to hospitals and clinics that serve large numbers of uninsured patients. A grant from the Cancer Prevention and Research Institute of Texas also helps pay for the programs and recently expanded FIT-Flu to an additional 19 counties. While screening and diagnostic procedures are funded, treatment is not. However, patients who need additional follow-up are connected with program navigators who steer them to treatment they can afford.

"It's very refreshing as a provider to talk with patients about the next steps, and to reassure them that MD Anderson is going to take that next step with them," Young says.

Despite their successes, these programs face an uncertain future. The Medicaid 1115 Transformation Waiver has been extended through 2017, but ongoing discussions between Texas and CMS will determine the status of future funding.

Although the support of CMS may not be constant, MD Anderson intends to find a way to continue providing these services, says Foxhall.

"It's been very exciting to see the reception in the primary care community to these programs," he says. "Our partner clinics have really taken advantage of these potentially lifesaving interventions, and we are very appreciative of all the work that they're doing with us to help address these needs."

Cadmus, whose company has recovered from its losses and is doing well, also appreciates the partnerships.

"I know how very lucky I am. The doctor, the clinic and the MD Anderson screening program literally saved my life."

Dylan Harrell, 12, is a patient in MD Anderson's Pediatric Brain Tumor Program, which is led by Soumen Khatua, M.D. Nick de la Torre

For pediatric brain tumors, age is only a number

By Katrina Burton

When a 4-year-old Dylan Harrell began experiencing headaches, his family never would have guessed a brain tumor was the cause.

But a scan at a hospital in their hometown of Dallas revealed a golf-ball-size tumor lodged in a difficult-to-reach part of Dylan's brain. In 2008, he was diagnosed with pleomorphic xanthoastrocytoma (PXA) — a rare brain tumor.

"Other than headaches, Dylan had no symptoms," says his mom, Jennifer Harrell. "The diagnosis brought quite a shock to our family, but it spurred us to act quickly."

Doctors in Dallas surgically removed most of the tumor, but three months later a scan revealed it was growing back. Dylan transferred to the Children's Cancer Hospital at MD Anderson and enrolled in the Pediatric Brain Tumor Program — a collaborative effort that brings together experts from MD Anderson Children's Cancer Hospital and Children's Memorial Hermann Hospital to deliver treatments tailored to children.

Approximately 3,000 children and adolescents are diagnosed with brain tumors in the United States each year. These tumors can differ greatly from those in adults in cell type, presentation and how they respond to treatment. Therefore, it's important that physicians who specialize in pediatric brain tumors treat them.

"Health care providers at both hospitals, along with affiliated physicians at UTHealth Medical School in Houston, work together to give pediatric brain tumor patients a second chance at life," explains Soumen Khatua, M.D., associate professor of Pediatrics and director of the program. "An array of neurospecialists treat the most complicated brain and spinal tumors in very delicate areas of the body." Every case is different, Khatua says.

Ashley Cipolla, 21, enrolled when headaches, blurred vision, sensitivity to bright lights and noises revealed she had a fast-growing brain tumor called a medulloblastoma.

"One day my father found me passed out on the restroom floor," Ashley says, recalling the events that led to her emergency room visit and surgery at Baylor St. Luke's Medical Center. Her surgeon, Ashwin Viswanathan, M.D., clinical assistant professor of Neurosurgery, has a shared appointment at MD Anderson.

Patients have access to a number of treatment options at MD Anderson, including clinical trials, the Proton Therapy Center and the BrainSUITE — an operating room that includes a magnetic resonance imaging machine, which allows neurosurgeons to have a real-time view of their patients' tumors during surgery.

Four years after chemotherapy and proton therapy — a highly targeted type of radiation that zaps tumors without damaging surrounding tissue — Cipolla is back in school, working and participating in her favorite activities: dancing, running and swimming.

Dylan was found to have a gene mutation that qualified him for an MD Anderson clinical trial in which he's receiving multi-targeted therapy. On the cusp of turning 13, he plays soccer, is on his school's swim team and is doing well in his classes.

"He's very active, and shows no outward signs of having a tumor," says his mom.

LOCATIONS

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

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- MD Anderson Cancer Center at Cooper (Camden, New Jersey)
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