Fall 2014 VOL 29 ISSUE 1 CONNOUEST



HPV causes 99% of all cervical cancer. A vaccine protects against the virus. So why don't more people get it?

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On the cover: Close to 80 million people in America are currently infected with the human papillomavirus, more commonly known as HPV. The virus causes almost all cases of cervical cancer and is linked to other forms of the disease. However, there's a vaccine available to stop it.



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CONTENTS CONQUEST FALL 2014





FEATURES

- 2 CANCER FRONTLINE A renewed effort in the breast cancer battle, expanding MD Anderson's reach in Houston and a visit to the Healthy Living Garden.
- 4 NO SILENT NIGHT The annual Camp AOK prom gives teen patients a chance to dress up and get down.
- 6 THE BIG PROBLEM WITH HPV The human papillomavirus and the cancers it causes can be prevented with a vaccine. Unfortunately, not enough kids are getting it.

14 MISSION UPDATE

Since being announced in 2012, the Moon Shots Program has launched new approaches in surgery, targeted therapies, drug combinations and more. Get up to speed on the progress in accelerating the end of cancer.

20 PILOT PROGRAM

Dan Minton was blindsided by his lymphoma diagnosis, which grounded the part-time aviator. But a clinical trial helped him tackle the disease without chemo.

22 MAJOR MINERS

Scientific "treasure hunters" dig deep into mountains of data to better understand how and why cancers form.

25 THE PRECISIONISTS

The doctors of the Skull Base Tumor Program are going where no surgeons would go before.

28 **GIVING HIS TIME AND HIS ALL** Volunteer Ervin Grice is proud to put on the blue jacket as a patient advocate.

30 NURSING GIANTS

Meet four winners of the Arceneaux Award, MD Anderson's highest nursing honor.





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

Want to combine the design of the print version with the convenience of your tablet? The iPad version is for you. It's filled with multimedia extras and features sleek, user-friendly navigation. The Free app can be downloaded from Newsstand or the iTunes App store by searching "Conquest Magazine."

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



CANCER FRONTLINE

BIG PLANS FOR MD ANDERSON'S BREAST CANCER PROGRAM

MD Anderson's Breast Medical Oncology Department recently announced news of two significant recruitments, starting at the top with Debasish Tripathy, M.D., an enthusiastic new chair with an optimistic view of his department's role in improving care and expanding treatment options for breast cancer patients. Another addition made headlines in late July when it was revealed that V. Craig Jordan, Ph.D., the developer of several cancer-fighting drugs, would join the institution this fall.

Jordan is best known for his key role in transforming a once-failed contraceptive medication into a valuable breast cancer treatment that has saved many lives. The drug, later named tamoxifen, originally was created to prevent pregnancy by blocking estrogen. Jordan developed the strategy of long-term adjuvant tamoxifen therapy, in which breast cancer patients take tamoxifen after their primary treatment to lower the risk of recurrence. He also described and deciphered the properties of a new group of medicines called selective estrogen receptor modulators (SERMs). Jordan was the first to discover the preventive abilities of tamoxifen and the drug raloxifene, which are now approved by the Food and Drug Administration to reduce breast cancer incidence in high-risk women.

Tripathy comes from the Norris Comprehensive Cancer Center at the University of Southern California. The New Orleans native recently spoke about his future



Debasish Tripathy, M.D., is the new chair of Breast Medical Oncology.
Aldolfo Chavez III

vision for breast cancer care and research at MD Anderson, and more.

Tell us a little about your work.

I'm interested in understanding why breast cancer cells become resistant to drugs that initially work. Overcoming resistance could make many of our drugs much more effective for a longer period of time, or more able to cure advanced breast cancer, which is a goal we have yet to attain. My research has focused on resistance mechanisms to available drugs that block the function of a growth-promoting gene called HER2. We've discovered certain proteins that may cause resistance, and we're testing strategies to reverse their actions in the hopes it can prolong remissions or even lead to cures in patients with advanced HER2-positive breast cancer, which account for about a fifth of all breast cancers.

What drew you to MD Anderson?

MD Anderson's rare combination of history, scientific excellence and unparalleled scope has made it the leading cancer research and care institution. We all want to make the largest impact we can in the lives of those with cancer. I feel that I can best do that here.



V. Craig Jordan, Ph.D., is known as the "father of tamoxifen." F. Carter Smith

What's your vision for Breast Medical Oncology? Where do you see the department heading under your leadership?

I would like to move toward a more patient-centered approach to breast cancer care and research. This approach reflects our growing understanding that the genomics and genetics of each person results in a unique type of cancer for which we need to personalize therapy. This is an amazing time of technological and biological advances, making breast cancer a more survivable disease. We're also in the midst of changes in health care delivery that aim to make the fruits of progress available as broadly as possible. We want to make sure that our services are available to those in Houston and the surrounding area, but that our impact continues to be worldwide.

What are some of the most exciting recent advancements in the field?

MD Anderson has been a leader in the identification of altered genes that drive cancer growth and other characteristics. This can now be addressed by an array of drugs that are more focused and, therefore, have fewer side effects. This year we witnessed a boom in new biologically targeted cancer drug approvals and we expect that trend to continue due to sustained research efforts. We have newer tools at our disposal to address fundamentally new scientific theories as to why some cancers may be difficult to eradicate. I believe that the coming years will be a triumph for "team science," where research groups collaborate to use population-based information and detailed testing on genes and proteins of each tumor to develop new personalized cancer therapies and diagnostic tests.

- Jim Newman

EXPANDING ACCESS TO MD ANDERSON CARE

Teaming up with Memorial Hermann

MD Anderson and Memorial Hermann Health System are bringing a new level of breast screening and diagnostic services to Memorial Hermann's community breast care centers.

Starting in late November, MD Anderson will become the exclusive provider of breast radiology services for five of Memorial Hermann's 10 breast care centers — those in Memorial City, The Woodlands, Sugar Land and Northeast and Southwest Houston.

In the next year, the network will expand to Memorial Hermann's breast care centers in Katy, Pearland, Pasadena, Upper Kirby and Northwest Houston. The collaboration may eventually expand to Cypress, South Katy and Spring.

In Memorial Hermann facilities, supported by Memorial Hermann equipment and staff, MD Anderson breast radiologists will interpret diagnostic images, perform biopsies and consult with patients and physicians.

"Prevention, early detection, risk reduction, education and outreach are key components of our mission," says MD Anderson President Ron DePinho, M.D. "This collaboration allows us to offer our screening expertise to a greater number of women. They can take comfort in knowing their imaging will be provided by radiologists who have dedicated their careers to caring for patients with cancer."

Dan Wolterman, president and CEO of Memorial Hermann Health System, says the partnership will give patients the flexibility and convenience of staying close to home while receiving the highest level of care.

"Our partnership will combine the convenience and advanced technologies of Memorial Hermann's breast imaging centers with interpretation and consultation from the world-renowned cancer expertise of MD Anderson."

.....

— La Chanda Ricks

Making imaging more accessible to West Houston

MD Anderson Diagnostic Imaging Center in West Houston is now open, bringing cancer care services closer to home for residents of West Houston and the surrounding area. The center is available to patients who have a confirmed cancer diagnosis or whose primary care physician suspects cancer. Women who would like to have their screening mammograms performed and read at the new location may call directly to make an appointment.

The facility offers a full array of cancer imaging and lab services, including Magnetic Resonance Imaging (MRI), Computed Tomography (CT), Positron Emission Tomography (PET), digital X-ray and general and Doppler ultrasound for diagnostics and biopsies.

A separate women's imaging center offers ultrasound, 3-D digital breast tomosynthesis, ultrasound-guided biopsies and other technologies that will allow MD Anderson radiologists and staff to return a same-day diagnosis. Digital mammography for screening and diagnostics also is available.

In addition to breast imaging services, the center provides pelvic ultrasound and MRI, as well as sonohysterography, an advanced uterine imaging technique using ultrasound and fluid.

MD Anderson radiologists will be at the West Houston center to review and interpret all images, and also consult with physicians who referred their patients for tests. The radiologists are MD Anderson faculty subspecialized and fellowship-trained in oncologic radiology. Because of new digital technologies, they can securely share images with colleagues at the Texas Medical Center campus for additional opinions on especially rare or unusual cancers or tumors.

Center Medical Director Monica Huang, M.D., and a team of MD Anderson radiologists, imaging nurses, technologists and administrative employees staff the new 35,000-square-foot center.

— Julie Penne



🖸 Gini Reed

REAPING THE BENEFITS OF GARDENING

Before you head outdoors to plant perfect rows of squash, pick plump tomatoes or prune purple eggplant, know that backyard gardening is almost as good for your health as it is for your taste buds. All that digging, lifting and bending provides a workout for the respiratory and cardiovascular systems and can improve strength, endurance and flexibility.

Besides promoting exercise, studies have shown that simply spending time in a garden alleviates stress, lowers blood pressure, encourages healthier eating and improves sleep.

And then there's the cancer-fighting component.

"One way to reduce our risk of cancer and other diseases is to eat five servings of vegetables and fruits daily," says Claire McKindley, a dietitian in Clinical Nutrition. "Growing your own garden can be motivation to eat a more plant-based diet."

To provide patients, caregivers, employees and volunteers with the healing benefits of "horticulture therapy," MD Anderson staff, led by a retired horticulture professor from Texas A&M University, has created the Healthy Living Garden on the grounds of the cancer center's Mays Clinic.

Nestled between towering buildings and busy intersections, the peaceful garden provides quiet space away from the stress of everyday living. Roses, pansies and peonies bloom alongside arugula, basil, tomatoes and squash.

Tended by MD Anderson groundskeepers and volunteers, the garden's produce is used in "Cooking for Optimal Health" classes taught by the institution's dietitians.

David Renninger, project manager for the Healthy Living Garden, hopes it'll inspire people to plant their own gardens.

"Gardening provides the opportunity to connect with nature and offers numerous physical and emotional benefits," Renninger says. "Why not get your exercise while being rewarded with tasty and nutritious produce?"

- Katrina Burton

FORGETTING CANCER ON A NIGHT TO REMEMBER

By Ronda Wendler Dr. Carter Smith

The sophisticated dresses and sleek tuxedos. The curling irons and makeup. The flashing cameras.

No, this wasn't a typical day at MD Anderson Children's Cancer Hospital. It was a "prom prep center" for teens affected by cancer. They dressed to the nines for an unforgettable night of dancing and dining at The Woodlands Resort and Conference Center, a 45-minute drive north of Houston.

The hospital's prom, held each August as part of Camp AOK — a weeklong summer camp for "Anderson's Older Kids" — gives cancer patients and their siblings a chance to let loose and have fun.

"Teens with cancer sometimes have to miss their high school proms," says Hilary Bagwell, 30, who attended prom twice — at ages 14 and 15 — when she was battling lymphoma. "They may feel self-conscious about their hair loss or weight loss or having to walk with crutches. But here, none of that matters."

Today, Hilary is a third-grade teacher, a new mom and a cancer survivor.

A couple of months ago, Hilary was back — this time as a volunteer. During prom preparations, she and her sister Jaime, a professional stylist who has done hair and makeup for the Miss Texas, Miss USA and Miss Universe pageants, made sure every partygoer got the full beauty treatment.

For a few hours, it was all about the dresses, jewelry, shoes, hair and lip gloss. The excitement in the air was almost as thick as the hair spray.

Zachary Mortus, Mia Sharpe











Chloe Tillman, Dr. Michael Rytting, Morinsola Keshinro, Lauren Shinn, Carra Hartley











TOO MANY CASES OF PREVENTABLE CANCER

MD ANDERSON DOCTORS ARE WORKING TO STOP HPV-RELATED DISEASES BY INCREASING AWARENESS AND ACCESSIBILITY TO THE CACER PREVENTION VACCINE

> arissa Meyer, M.D., stares out her office window at the vast landscape of the Texas Medical Center. She's sad, angry and, above all, frustrated.

> > Meyer, a gynecologist, has just informed a 30-year-old woman with cervical cancer that her disease is terminal. The patient's main worry is how her two young children will fare without her.

> > "This is so heartbreaking and so unnecessary," Meyer says. "Unlike some other female cancers, cervical cancer is almost always 100 percent preventable." Yet Meyer sees this scenario over and over again.

> > Women in their 20s and 30s, many who have small children and are the pillars of their families, arrive in her office complaining of pelvic pain and abnormal bleeding. By the time symptoms appear, the cancer often has progressed and spread to other parts of the body.

> > "It's tragic that women are still diagnosed with this disease," says Meyer, an assistant professor in Gynecologic Oncology and Reproductive Medicine at MD Anderson. "Cervical cancer should be obsolete by now."

> > Obsolete because since the 1940s, Pap tests have been successfully detecting cervical cancer in its early stages, before it has a chance to spread. When caught early, the disease is highly curable.

Thanks to the Pap test, cervical cancer rates have gone down overall, but among the poor and uninsured who have difficulty accessing care, the disease continues to take a toll.

"Lack of insurance, lack of transportation, lack of information — whatever the reason, some women don't avail themselves to this simple and lifesaving test," Meyer says.



Human papillomavirus

(HPV) is the most common

the United States. Almost

will acquire HPV at some

point in their lives.

sexually transmitted virus in

every sexually active person

First Anti-Cancer Vaccine

Today, yet another weapon has been added to the cervical-cancer fighting arsenal, and Meyer is determined to make sure everyone knows about it.

A vaccine that blocks transmission of the human papillomavirus (HPV) — the virus that causes almost all cervical cancer cases — promises to prevent most occurrences altogether. In extoling the vaccine's benefits, American Academy of Pediatrics president Thomas McInerny, M.D., dubbed it "the first anticancer vaccine."

"How groundbreaking is that?" asks Lois Ramondetta, M.D., a gynecologist and professor in Gynecologic Oncology and Reproductive Medicine.

Like Meyer, Ramondetta is on a mission to wipe out cervical cancer.

"We've got the Pap test, now we've got the HPV vaccine. There's absolutely no justification for this disease to exist today. Every time I see another case,

> I think, 'this is inexcusable,'" says Ramondetta.

But like the Pap test, the HPV vaccine, which was introduced in 2006, has been slow to be embraced.

"That's a dangerous mistake," says Ramondetta. "If you think you won't contract HPV, think again."

Had sex? You've probably had HPV

The human papillomavirus holds the dubious distinction of being the most common sexually transmitted infection in the United States.

"Eighty percent of women and men — pretty much anyone who's had sex — have been infected at one time or another," Ramondetta says.

Through sexual activity, more than 40 strains of HPV can be passed along. These strains are split into two categories: those that cause cervical and other forms of cancer, and those that cause genital warts.

Two strains — HPV 16 and 18 — are blamed for the majority of cervical cancer cases, as well as most anal cancers and a large share of vaginal, vulvar and penile cancers. The strains can also cause cancers in the back of the throat, most commonly at the base of the tongue and in the tonsils, in an area known as the oropharynx. These are called oropharyngeal cancers.

Two other strains — HPV 6 and 11 — cause most genital warts. Though unsightly and contagious, warts won't turn into cancer, even if they remain untreated. Without treatment, warts can multiply, stay the same or disappear altogether.

Most people infected with HPV will never get cancer or warts. Their bodies will clear the virus, usually over the course of two years, and they'll never realize they were infected. During this phase of unawareness, those infected may unknowingly pass the virus along to others.



But in a small number of people, the virus persists and remains in the cells.

The longer the virus lingers, the more likely it is to cause cancer by doing what it does best — slowly and silently causing cells to grow abnormally. Ramondetta says progression from time of HPV infection to fullblown cancer can take five to 10 years, or even longer.

"This means your actions as a youth can have consequences in adulthood," she warns. "About the time you get married or start a family or new career, you can be diagnosed with an HPV-related cancer."

When HPV invades the cervix and causes cells to become precancerous, Pap tests can flag the abnormal cells before cancer develops, and doctors can intervene to return a woman to health. A second test, approved by the Food and Drug Administration (FDA) in 2011, detects the presence of the HPV virus that *causes* the cells in the cervix to change. This test, when performed in conjunction with the Pap test, provides a powerful one-two punch in the war against cancer.

"Cervical cancer would be virtually unheard of if these two tests were used in tandem with the vaccine," Ramondetta says.

The other HPV-linked cancers

While cervical cancer can be detected with screening, no effective screening tests exist yet for the other cancers linked to HPV: vaginal, vulvar, penile, anal and oropharyngeal cancers.

Cathy Eng, M.D., has seen a steady increase in anal cancer cases nationwide, up from 3,500 to 7,000 per year. And that number is rising.

"A number of these patients are living with HIV/ AIDS. Their compromised immune systems prevented them from fighting off the HPV virus," says Eng, associate professor in Gastrointestinal Medical Oncology. "Despite the use of drugs that suppress the HIV virus, the risk of anal cancer has not declined."

Furthermore, Eng says many patients with HIV/

Nearly 80 million people in America (one in four) are currently infected with HPV.

many patients with HIV/ AIDS are older than 26, the FDA's cutoff for those with weakened immune systems to receive the HPV vaccination.

Given that patients with HIV/AIDS are living longer today than in years past, Eng believes there may be an association

between longevity and the increase in anal cancer cases.

Meanwhile, oropharyngeal cancers that affect the back of the throat are also dramatically increasing in numbers, says Erich Sturgis, M.D., associate professor in Head and Neck Surgery. Since the late 1980s, cases are up by 225%, with heterosexual middle-aged men accounting for the lion's share of cases. Researchers



associate this rise with the sexual revolution of the late 1960s and '70s, and the increase in oral sex among heterosexual couples.

"Until this millennium, most oropharyngeal cancers were caused by smoking and alcohol use," Sturgis says. "But now, more than 70 percent of these cancers have been shown to be HPV related."

"These are serious cancers," Sturgis says. "Treatments are typically painful, difficult and have many long-term side effects.

"It's scary that there are no routine screening tests for these cancers," he says, "which are on the rise." Lois Ramondetta, M.D., whose daughter Jessica left home for college earlier this fall, wants all parents to know that the HPV vaccine is not about sex — it's about protecting their children from cancer.



Cervical cancer isn't the only cancer tied to HPV. Erich Sturgis, M.D., says the number of oropharyngeal cancers, which affect the back of the throat, are rising sharply.

> Each year, about 21,000 cases of HPV-related cancers could be prevented by getting the HPV vaccine.

Thank you, Michael Douglas

If you own a TV, radio or computer, you probably heard the furor over actor Michael Douglas' statements to a British newspaper in June 2013 about his throat cancer. (It was later revealed to be oropharyngeal cancer affecting the base of his tongue.) The Guardian reported

> that when he was asked if he regretted his "years of smoking and drinking, usually thought to be the cause of the disease, Douglas replied, 'No, because without wanting to get too specific, this particular cancer is caused by HPV"

"Michael Douglas did us all a favor by raising awareness about human papillomavirus," Sturgis says.

Although HPV-related cancers are on the rise, they're still rare compared to breast, prostate and lung cancers. But experts say more could be done to prevent them — including boosting vaccination rates among young people. "We have a vaccine that's safe and effective," Sturgis says. "And it's being underused, especially in boys."

Only about 14% of boys under age 18 are getting the complete three-dose vaccination, compared to 38% of girls, Sturgis says. This is in part because the Centers for Disease Control and Prevention (CDC) only updated its guidelines in favor of immunizing boys in 2011, while recommendations to vaccinate girls have been in place since 2006.

Vaccinating boys for HPV is also likely to benefit girls, Sturgis adds, by reducing the spread of the virus.

Though the Affordable Care Act requires insurers to cover the vaccine and the uninsured can get the vaccine at no cost through the federal Vaccines for Children program, the majority of Americans remain unvaccinated.

Why don't people take this simple precaution that can save their lives? According to Ramondetta, several reasons exist.

Getting through to parents

The HPV vaccine doesn't cure HPV, it only prevents it. So to be effective, the vaccine needs to be given before a person becomes sexually active.

The CDC recommends vaccinating boys and girls at the age of 11 or 12 to give them time to build up immunity against the virus before they begin sexual activity.

That makes some parents squeamish. They fear that saying "yes" to the HPV vaccine will also encourage their children to say "yes" to sex at an early age.

"This is not to say that your preteen is ready to have sex," Ramondetta says. "In fact, it's just the opposite — it's important to get your child protected from a cancer that may occur later in life before he or she ever thinks about sex. This is about protecting your child against cancer."

She also points to a recent study in the journal Pediatrics that shows adolescent girls who receive the HPV vaccine are no more likely to show signs of sexual activity than girls who aren't vaccinated.

"The HPV vaccine doesn't open the door to sex," Ramondetta assures reluctant parents. "It closes the door to cancer."

There's one more upside to getting the vaccine at a young age, Ramondetta says. Studies show the body assimilates the vaccine best in the preteen years, when the immune system is "revved up."

Though 11 and 12 are the ideal inoculation ages, the vaccine is available to males and females as young as age 9. And it's offered to males through age 21 and females up to age 26.

The CDC also advises men and women with weakened immune systems, including those with HIV/ AIDS, as well as gay and bisexual men, to get vaccinated through age 26, providing they didn't get fully vaccinated when they were younger.

"Even if you've already had sex, remember, the vaccine protects against more than one strain of HPV," Ramondetta says. "You may be infected with one strain



only, so the vaccine will protect you against the additional strains. Cover your bases, get vaccinated."

Not a one-shot proposition

The HPV vaccine isn't a one-and-done process. It's administered in three doses over six months. After the first shot, a second is required one or two months later. After the second shot, a third is required four to five months after that.

"To develop maximum immunity, it's important to receive all three doses," Ramondetta stresses.

Yet doctors report they're finding it difficult to finish out the series for most children.

"It's shameful that in the U.S., the richest country in the world, we can't vaccinate against cancer," says Meyer, who teams with Ramondetta to promote vaccinations for "patients, patients' children, employees, family members and anyone who will listen."

She says the required time lapse between shots is a major culprit behind the failure to finish out the three-shot series.

"Parents get busy at work, kids get busy at school and everyone forgets it's time to return to the doctor's office."

To counter this, Meyer is piloting a reminder program in which pediatricians at The University of Texas Medical School in Houston send postcards, text messages and emails to alert parents that their children's shots are due. A public education campaign using social media channels like Facebook and Twitter also is in the works.

Lately, she's been giving parents refrigerator magnets equipped with built-in timers that "count down" the days between inoculations and flash conspicuously when it's time for another shot.

Messages and magnets help, but to make a significant dent in America's dismally low HPV vaccination rate, Meyer says shots should be given to children at school. In Australia, where this model is used, more than 70% of girls have completed the three-dose course. Not surprisingly, Australia's HPV infection rate has dropped significantly. In 2013, the country extended the program to include boys.

Schools and pharmacies are convenient alternatives to doctors' offices for the HPV vaccine, according to a recommendation this year from the President's Cancer Council. And Meyer wholeheartedly agrees. She hopes to pilot an HPV vaccination program in a Houston school soon.

"Make it convenient. If people won't come to the vaccine (in the doctor's office), bring the vaccine to people. Whatever it takes, just do it."

Image problem

The HPV vaccine has an image problem, Meyer says.

"It should've been introduced from the beginning as a cancer-fighting vaccine, not a sexually transmitted diseases vaccine."

Meyer points out that gynecologists were the first to receive shipments of the vaccine to give to their patients, when in fact, pediatricians should've been first in line.

"Remember," she says, "the target audience is 11and 12-year-olds."

When the vaccine eventually arrived at pediatricians' offices, the pediatricians received virtually no guidance on how to talk to parents about why their children should be vaccinated. Because HPV is usually diagnosed in adults, pediatricians' experience with it may be limited, Meyer says. Consequently, they may unknowingly be giving the vaccine the "short shrift."

Meyer and Ramondetta joined a CDC speakers bureau that educates pediatric societies about HPV and helps pediatricians develop talking points to use in their discussions with parents.

"It's disheartening," Meyer says. "I've been a member of the bureau for more than a year, and not once have I been asked to give a talk."

Compared to other countries, the U.S. does a stellar job administering neonatal vaccines, Meyer contends. Parents and providers are engaged and "on board" to get babies vaccinated. But when children become preteens, the commitment levels drop off.

Meyer recommends bundling the HPV vaccine with the two vaccines that are required at age 11 before kids can enter middle school — Tdap, which protects against tetanus, diphtheria and pertussis, and the meningococcal vaccine, which protects against meningitis.

To date, only Washington, D.C., and Virginia have enacted legislation requiring students entering the sixth grade to be vaccinated against HPV.

Wake-up call

"Even though the U.S. is doing an inadequate job of vaccinating kids for HPV," Meyer says, "our efforts still make a difference."

A Journal of Infectious Diseases study published in June 2013 revealed that since the HPV vaccine was introduced in 2006, infections have dropped 56% among U.S. girls ages 14 to 19, even though only slightly more than one-third are fully vaccinated.

This report provides irrefutable evidence that the HPV vaccine works, Meyer says.

"The report should serve as a wake-up call to our nation to protect the next generation from cancer by improving HPV vaccination rates," she says. "We have the vaccine, we know it works, the science has been done. Now we just need to get it out there." The HPV vaccine comes in two brands: Gardasil, manufactured by Merck and approved by the FDA in 2006, and Cervarix, manufactured by GlaxoSmithKline and approved by the FDA in 2009. Both protect against cervical, anal, vulvar, vaginal, penile and oral cancers. Only Gardasil, the most widely used vaccine, offers added protection against the HPV strains most likely to cause genital warts, and only Gardasil is approved for females and males.

Gardasil manufacturer Merck is working on a future vaccine that will prevent transmission of nine strains of HPV — five more than its current vaccine. However, Lois Ramondetta, M.D., warns against waiting.

Serving the underserved MD Anderson is taking care to where the cancer burden is heaviest By La Chanda Ricks

"Is it possible to make cancer history?"

That's a question Ethiopian President Mulatu Teshome asked during a recent visit to MD Anderson. "We believe so," answered President Ron DePinho,

M.D., before adding, "but we're not there yet."

Getting there will require waging a global war against cancer, DePinho explained, with a focus not only on treatment, but also on prevention and early detection.

During an August trip to the United States, Teshome made a point to visit the leading cancer center, where he introduced the idea of collaboration.

The World Health Organization (WHO) predicts Africa, where infectious diseases such as malaria, HIV and, more recently, ebola have garnered the biggest slice of attention and resources, will have more cancer cases than any other country in the world by 2020. Sixty percent of global cancer cases will be in Africa, Asia and Central and South America, with the majority in Africa.

Therefore, the continent's leaders are turning their attention to the looming epidemic, which their health systems currently can't handle. And MD Anderson stands ready to help, according to Oliver Bogler, Ph.D., senior vice president for academic affairs.

"Our mission is to end cancer in Texas and the world. We take that very seriously," says Bogler, who also heads the cancer center's Global Academic Programs (GAP).

GAP manages the Sister Institution Network, a consortium of researchers at 29 premier academic cancer institutions in 22 countries.



Kathleen Schmeler, M.D., associate professor in Gynecologic Oncology and Reproductive Medicine (right), is helping OB/GYN medical residents in Central American countries such as Nicaragua learn to better prevent, diagnose and treat gynecologic cancers through the Central American Gynecologic Oncology Education Program.

In May 2012, in a small hotel conference room overlooking Stavanger, Norway, the network's directors assembled for their annual meeting. For the first time, the leadership made a commitment to pool their resources and expertise to address the cancer burden in Africa.

The GAP team then began identifying other U.S.based organizations already working with African institutions and governments.

"Instead of doing it alone and learning as we go, it's more realistic and more useful for us to partner with organizations that are already engaging with Africa. They have the experience, are familiar with the territory and know how best to put all of our resources together to make an impact," says GAP project director Shubhra Ghosh, M.D.

Sharing knowledge

In 2013, MD Anderson signed a memorandum of understanding with the Union for International Cancer Control (UICC), a membership-based, nongovernmental organization headquartered in Switzerland. UICC is made up of 760 organizations across 155 countries that join together to help the global health community accelerate the fight against cancer.

The memorandum called for MD Anderson to help increase cancer care in sub-Saharan Africa and develop care models that can be implemented across the continent.

The initial focus is on educating and training doctors and other health care workers, who are in extremely short supply.

For instance, Zambia has a population of about 13.8 million, but only 15 gynecologists to treat women with cervical cancer.

MD Anderson is working with the UICC to host two training workshops for clinicians in Zambia and Mozambique. These workshops will include "train-thetrainer" programs, in which local physicians teach what they learn to other health care workers and create a "passit-along" knowledge chain. After workshops conclude, providers in Africa will participate in Project ECHO (Extension for Community Healthcare Outcomes), a telementoring initiative developed by the University of New Mexico to make knowledge and expert-level care more accessible to underserved communities. Through Project ECHO, local providers present cases and get feedback from MD Anderson specialists through biweekly video conferencing. This initiative is modeled after a current project that's using ECHO for cervical cancer prevention in a community along the Texas-Mexico border.

A preventable cancer

One disease where education will have a dramatic impact is cervical cancer. In the U.S., the Pap test, introduced in the 1940s, has dropped cervical cancer rates by 70% (No. 14 on the list of most common female cancers). The HPV vaccine and HPV detection test are expected to further reduce the disease over time. (See story on Page 7)

But in Africa, Latin America and the Caribbean, cervical cancer is at or near the top of the list of cancers in women. The highest incidence is in Africa.

"It's terrible that your chance of getting cervical cancer depends on where you live and if you have access to screening," says Kathleen Schmeler, M.D., associate professor in Gynecologic Oncology and Reproductive Medicine. "We have a responsibility to share our expertise and knowledge with the rest of the world."

Streamlining screening

Last year, MD Anderson signed a memorandum of understanding with the newly formed African Cancer Institute (ACI) at Stellenbosch University in Stellenbosch, South Africa — the institution's first African research partner — to advance the prevention, diagnosis and management of cancer across the continent. The first collaborative initiative, led by Schmeler, will study the use of high-resolution microendoscopy (HRME) to diagnose and prevent cervical cancer.

This innovative technique, developed by researchers at Rice University, uses a fiber optic probe, placed on a patient's cervix, to transmit cervical images to a cell phone. Immediately, clinicians can detect whether the patient has precancer and needs treatment. This method potentially can be used in areas where no gynecologist, pathologist or lab is available.

"The idea is that someone, like a primary doctor, nurse or community health worker, could go out into an underserved area and perform a cervical cancer screening and precancer treatment in one visit, close to the patient's home," Schmeler explains. "Then, the few people who need cancer treatment can travel for care. It gives them an option where there wasn't one."



Latin America

Many of the cervical cancer prevention measures planned for Africa were first launched and tested in underserved areas of Latin America.

For example, the HRME technique currently is being studied in Latin American trials.

The initial pilot studies were made possible by a grant from the Sister Institution Network Fund. Large studies of more than 10,000 women will begin soon in Brazil, El Salvador and Houston with grants from the National Cancer Institute.

Ripple effect

OB/GYN medical residents in Central America are learning how to better prevent, diagnose and treat gynecologic cancers through the Central American Gynecologic Oncology Education Program (CONEP).

Two gynecologic oncologists — volunteers from MD Anderson and other institutions — travel to Guatemala, Honduras, El Salvador, Nicaragua, Panama and Costa Rica for three to five days every six to 12 months. During each visit, physicians lecture, teach, make patient rounds and provide hands-on surgical training to medical residents.

Since CONEP's launch in 2009, about 100 Central American medical residents and faculty have participated in each of the visits. Some of the residents then visit MD Anderson for one- to three-month observerships. Ethiopian President Mulatu Teshome and Ron DePinho, M.D., president of MD Anderson, discussed the institution's worldwide cancer-fighting collaborations during Teshome's visit to Houston in August.

TRACKING THE TRACKING THE

By Scott Merville

Two years after launching the Moon Shots Program, researchers and clinicians are reporting on gains in their mission

In operating rooms, clinics, research labs and even the Texas State Capitol in Austin, innovation driven by the MD Anderson program is already impacting cancer treatment and prevention.

With a name inspired by President John F. Kennedy's goal to put a man on the moon by the end of the 1960s, the program was launched two years ago with the goal of saving as many lives as possible, as quickly as possible. In that time, teams of researchers and clinicians have focused on six moon shots targeting eight cancers: acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), chronic lymphocytic leukemia (CLL), melanoma, lung cancer, prostate cancer, and triple-negative breast and ovarian cancers — two cancers linked at the molecular level.

Giulio Draetta, M.D., Ph.D., a professor in Molecular and Cellular Oncology and co-director of the Moon Shots Program, divides the ideas underpinning the program's efforts into two themes: "Execution and rocket science."

"This first wave of accomplishments reflects the moon shots' emphasis on execution," says Draetta. "It's a matter of more efficiently applying what we already know about cancer to help our patients."

Execution

Since receiving initial funding of \$1 million each, the six moon shots teams' accomplishments include:

• Creation of an MD Anderson algorithm for deciding when ovarian cancer patients should have surgery. This systematic approach has more than doubled the rate of complete surgical removal of patients' tumors from 25% to more than 80% of the time.

• Leadership in developing targeted therapies for CLL has cut the use of debilitating chemo combinations from 51% of new patients in 2011 to 15% today.

• The first "intent to cure" clinical trial for prostate cancer, based on clinical and scientific research at MD Anderson, aims to convert periodic hormone therapy for a subset of patients into a single-episode curative regimen. • Identification by the Lung Cancer Moon Shot's drug discovery program of two leukemia drugs with potential to treat certain lung cancer patients. A clinical trial of one of those drugs is underway.

• In an important prevention milestone, the Melanoma Moon Shot provided expert information to the Texas Legislature, which led to a successful effort by a coalition of groups to persuade lawmakers to pass a statewide ban on the use of tanning beds by those under age 18.

• Two new clinical trials, based on research findings at MD Anderson, aim to overcome resistance to standard-of-care therapy for myelodysplastic syndromes. One trial is the first to deploy the rising therapy of immune checkpoint blockade against leukemia.

Rocket science

The second concept of the Moon Shots Program, what Draetta calls "rocket science," is establishing supportive platforms to provide new or additional expertise and cutting-edge technological resources.

"Rocket science enables our clinicians and scientists to make discoveries and clinical advances that really turn the world around," he says. "Achieving that will require inventions yet to come — it will take awhile."

Moon shots research already is benefiting from new "rocket science" innovations in the fields of immunotherapy, genomics, proteomics, prevention and big data — the capacity to systematically compile and analyze massive amounts of information. The program also benefits from MD Anderson's drug discovery and development platforms, including the Institute for Applied Cancer Science.

Learning from each patient

"A central theme of the Moon Shots Program is to learn as much as we can from every single patient," says Andy Futreal, Ph.D., the program's co-leader with Draetta. "We need to think longitudinally — how patients' conditions, treatments and tumors change over time

- and be smarter about how we collect and use that information."

"You need to build an engine to learn," Futreal says.

To do this, he leads APOLLO, short for Adaptive Patient-Oriented and Longitudinal Learning and Optimization. The technology-driven program creates a more cohesive system for standardizing long-term collection of patients' medical history, high-quality tissue and blood samples, and genomic and molecular analyses of those samples. It's coupled with research data and aggregated in a centralized big data warehouse.

The resulting information is available both to clinicians and researchers using advanced analytic tools such as MD Anderson's Oncology Expert Advisor[™] (OEA) powered by IBM Watson — the world's smartest computer. Under development in the Moon Shots Program, OEA will tap MD Anderson databases and external sources of information such as scientific publications and clinical trial results at unimaginable speeds to deliver treatment recommendations in the clinic.

By seamlessly blending patient data with the latest research insights and best practices in clinical care, and analyzing it over time, APOLLO will help researchers improve patient care by understanding factors that determine treatment response, resistance, toxicity and survival.

APOLLO was piloted in Leukemia this year and is expanding to the Lung and Melanoma moon shots.

"The current model is that a scientist forms a hypothesis and writes a protocol to collect biospecimens, which come from tissue that may or may not represent exactly the same point in cancer progression for each patient or speak best to the question being asked. Next, the scientist generates molecular data from these samples, analyzes the data and eventually publishes the results," Futreal notes. "What we're talking about here is an effort to standardize the process and expand it to many more patients. This would mean that more traditional, hypothesis-driven investigation is significantly empowered and we move into an era of data-driven hypothesis generation around key clinical questions.

"We're building an engine to accelerate the translational process," Futreal says. "Every cancer research institution on the planet is struggling with this right now. Raising the quality of our information is going to benefit everyone.

"MD Anderson has an opportunity to lead."

In its first full year of operations, MD Anderson's Moon Shots Program has launched new approaches to ovarian cancer surgery and melanoma prevention, as well as targeted therapies and drug combinations for leukemia, prostate and lung cancer. And there's more to come. Here are some updates.

Ovarian and breast cancer Improving surgery, preventing disease

plishment that improves survival.

Investigators in the Breast and Ovarian Cancer Moon Shot have developed a new surgical protocol that's dramatically increasing the rate of complete tumor removal in ovarian cancer patients, an accom-

Under the new protocol, all patients receive a laparoscopic evaluation during which two surgeons independently rank the distribution and spread of the disease to other organs. If the resultant score is less than 8, patients proceed to surgery. If it's greater, they receive chemo before going to surgery.

"Our new surgical algorithm allows us to be much smarter about whom we operate on upfront," says moon shot co-leader Anil Sood, M.D., professor in Gynecologic Oncology & Reproductive Medicine.

In the first 78 cases involving the protocol, complete tumor removal was achieved 88% of the time. The protocol is now standard practice at MD Anderson.

Previously, virtually all new patients had surgery to explore the extent of disease and to remove as much of it as possible. Worldwide, this practice results in 20 to 30% of these patients achieving "complete gross resection," or removal, of all of their visible tumor, Sood says. At MD Anderson, the rate was about 25%.

"One focus of moon shots is achieving the greatest clinical impact with current knowledge," Sood says. "A great deal of effort went into this algorithm, but it was all based on existing knowledge."

Reaching out to families

The moon shot focuses on high-grade serous ovarian cancer (the most malignant form of the disease) and triple-negative breast cancer (a particularly aggressive form more likely to spread and recur than other forms of breast cancer). All such patients now are offered genetic screening for mutations in the BRCA 1 and 2 genes, which elevate a person's risk for either cancer. If the patient has these inherited mutations, that raises the possibility that sisters, daughters and other relatives might have the same risk-increasing mutations.

"We encourage patients to communicate their results with other family members, offer our help in facilitating that communication and also offer them genetic screening," says moon shot co-leader Banu Arun, M.D., professor in Breast Medical Oncology.

When BRCA mutations are found, and other risk factors are considered, the moon shot offers preventive options, including mastectomy, removal of the ovaries, or both.

Eighty of the first 1,346 breast cancer patients and 34 of 298 ovarian patients tested positive for BRCA mutations. Of those 114 patients, 45 have enrolled in the outreach program, which was launched in April. As a result, women with elevated cancer risk have been identified.

Giulio Draetta, M.D., Ph.D. Professor in Molecular and Cellular Oncology

Draetta arrived at MD Anderson in 2011 to direct the Institute for Applied Cancer Science. He oversees the moon shots platforms, which provide expertise, infrastructure and technology to support the program, and will focus on opportunities to develop new diagnostic tools and therapies. Draetta's focus has been on drug discovery and development. In Eric Kayne

AML/MDS

Overcoming drug resistance

The Acute Myeloid Leukemia (AML)/ Myelodysplastic Syndromes (MDS) Moon Shot has opened two clinical trials to address a crucial problem for MDS patients: swift progression when their disease resists a crucial class of drugs called hypomethylating agents. Both trials are based on research into resistant MDS by physician-scientist and moon shot leader Guillermo Garcia-Manero, M.D., professor in Leukemia.

One trial is the first conducted in leukemia of a rising type of cancer immunotherapy called immune checkpoint blockade.

Garcia-Manero and colleagues implicated several immune checkpoint molecules, which stop the immune system's natural attack on cancer cells, in the development of MDS resistance. In solid tumors, these checkpoints have been successfully blocked by antibody-based drugs, unleashing the immune system to attack, an approach invented by James Allison, Ph.D., executive director of the immunotherapy platform and chair of immunology.

The clinical trial tests a drug that blocks the PD1 checkpoint.

The team also identified the receptor 2 protein (TLR2) as a potential target and connected with an Irish biotech company to test an antibody to TLR2 in the second clinical trial.

Tracking down the details

Intensive research continues to identify other sources of resistance, Garcia-Manero says. Three pairs of drug-resistant and drug-sensitive MDS cell lines have been generated, as well as the first mouse model of MDS.

Moon shots investigators have also identified faulty molecular signaling pathways that lead to drug resistance in some MDS patients.

In molecular signaling, a group of molecules in a cell work together to control one or more cell functions. After the first molecule in a pathway receives a signal, it activates another molecule. This process is repeated until the last molecule is activated and the cell function is carried out. Abnormal activation of signaling pathways can cause cancer, drug resistance or other problems. Parallel DNA and RNA sequencing, which reduces costs and speeds results by sequencing both at the same time, and DNA methylation analyses, which identify a common signaling tool that cells use to turn off genes that suppress cancer cells, are also underway.

There are also similar research efforts targeting AML cell lines resistant to hypomethylating agents.

Under the auspices of the APOLLO platform (Adaptive Patient-Oriented Longitudinal Learning Optimization), more than 3,500 AML and MDS samples gathered repeatedly from patients over time have been genomically sequenced.

"We expect to achieve full genomic and proteomic understanding of AML and MDS within five years," Garcia-Manero says. Andy Futreal, Ph.D. Professor in Genomic Medicine

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Futreal holds the Robert A. Welch **Distinguished University Chair and remains** on the honorary faculty of the Wellcome **Trust Sanger Institute in the United** Kingdom, where he was co-director of the **Cancer Genome Project before coming to** MD Anderson in 2012. He's in charge of integrating genomic and molecular data with clinical research. While at Sanger, Futreal led a team that identified cancerdriving mutations in the BRAF gene. This led to the development of targeted therapies for patients with the mutations, as well as ERBB2 mutations active in nonsmall cell lung cancer and genes active in kidney cancer. 🖸 Eric Kayne

Chronic lymphocytic leukemia Easing out chemo

-odewe

The Chronic Lymphocytic Leukemia (CLL) Moon Shot is accelerating the transition from chemotherapy combinations for most patients to new targeted therapies and immunotherapy approaches.

MD Anderson CLL experts were instrumental in developing the targeted therapies ibrutinib and idelalisib, both approved in 2014 for CLL by the Food and Drug Administration (FDA). These and other drugs such as the antibody rituximab are inducing long-term responses in CLL patients with fewer and less harsh side effects than chemo.

Only 15% of new CLL patients at MD Anderson are treated with chemo, down from 48% two years ago. And that's by design, says moon shot co-leader Michael Keating, M.D., professor in Leukemia. "We hope to double the cure rate to 70 percent of patients by using these new approaches," Keating says.

While chemo combinations cure about 35% of patients, they also are unfit for elderly or frail patients, work poorly against CLL with specific mutations, cause development of additional cancers such as AML and MDS, and severely suppress the immune system.

Jan Burger, M.D., Ph.D., leads a 208-patient clinical trial of ibrutinib or ibrutinib plus rituximab. In it, each patient's CLL is genomically analyzed before and after treatment, as well as after the disease becomes drug-resistant, should that occur. Such specific genomic information will help investigators understand how resistance develops and how to counter it.

The randomized trial opened in December of 2013 and has now enrolled more than 110 patients.

Burger says the hope is the trial will address a puzzle about ibrutinib resistance.

"Ibrutinib generally kills 90 to 95% of CLL cells, leaving detectable levels of the disease in the blood and bone marrow a year or more after treatment, yet the patients have no clinical problems," he says. There's a concern that the residual disease will seed a recurrence later.

Other patients respond well initially to ibrutinib and then become fully resistant. "We don't know if the same mechanisms are involved in both cases," Burger says.

Additional studies are underway to better illuminate how ibrutinib works and its relation to white blood cells called T cells, the attack dogs of the immune system.

Melanoma

Getting minors out of tanning beds

Like all of the moon shots, the melanoma effort is deeply involved in learning from patients by analyzing tumors and blood samples and developing creative clinical trials to treat the disease.

But the first accomplishment came in prevention.

Surgical and medical oncologists, scientists, behavioral scientists and governmental relations experts were among those who worked together to achieve a state ban on tanning bed use by minors, which took effect September 2013.

"We've embraced and fostered multidisciplinary planning and practice in our clinics for decades," says Melanoma Moon Shot coleader Jeffrey Gershenwald, M.D., professor in Surgical Oncology. "Now some of our moon shots projects span well beyond clinical departments to academic departments, prevention and non-academic departments. That's a new approach, a supercharged version of MD Anderson's collaborative strengths."

The moon shot's crucial role was to provide information on melanoma, its connection to UV light exposure and the impact of indoor tanning on melanoma risk. MD Anderson teamed with a broad coalition of groups to support the legislation. Gershenwald, Ellen Gritz, Ph.D., chair of Behavioral Science, Mary Tripp, Ph.D., instructor in Behavioral Science, and Mark Moreno and Wesley Duncan of Governmental Relations were instrumental in the effort.

Texas became the fourth state to ban the use of tanning beds by those under the age of 18. Now, Gershenwald notes, 11 states have enacted similar laws, and the momentum continues to build.

In May, the FDA upgraded indoor tanning lamps and UV lights to moderate-risk devices, which require a black-box warning that the products should not be used by people under 18 years of age, and other regulatory measures.

"The time is now to double-down on our efforts to educate everyone, particularly our youth, about the dangers of UV exposure from the sun and from tanning beds," Gershenwald says.

Prostate cancer

Competing drugs team up

At first, the drugs abiraterone and enzalutamide were thought to be rivals, competing over how to best thwart androgen-receptor driven, castrate-resistant prostate cancer. But MD Anderson prostate cancer researchers found instead that they're powerful allies for some patients.

Based on earlier studies that showed certain patients treated with the two drugs achieved a pathological complete response, a phase II combination clinical trial was launched under the auspices of the Prostate Cancer Moon Shot. Christopher Logothetis, M.D., calls it "the first intent-to-cure clinical trial for prostate cancer."

The two drugs target the androgen receptor testosterone pathway in different ways to reduce levels of the male hormone, which fuels most prostate cancers. Both are approved by the FDA as single agents for prostate cancer, but cancers eventually become resistant to them.

So far, 128 eligible patients are enrolled in the 180-patient phase II study.

Logothetis, chair of Genitourinary Medical Oncology, and colleagues found that the drug combination stops the resistance that develops to either drug alone. Their findings inspired a national phase III clinical trial of the combination, even before the completion of the phase II trial.

The endpoint of the trial will be progression-free survival two years after patients' testosterone returns to normal levels.

It fits into a larger theme of identifying biomarkers to more effectively guide treatment with available drugs. In addition to pinpointing patients who need anti-hormonal drugs, the team also found that 30% of patients were resistant to these options and, therefore, are better treated with chemo.

"We now know how to select those who need each type of therapy, have markers and models to reflect that, and have designed and gained approval of a clinical trial to integrate those concepts," Logothetis says. "We've done that in a year."

Lung cancer

Leukemia drugs, lung cancer targets

The Lung Cancer Moon Shot has identified two drugs approved for leukemia that potentially hit lung cancer targets in some patients.

One, the targeted therapy ibrutinib, already is in a moon shot clinical trial for lung cancer patients with specific mutations in the epidermal growth factor receptor (EGFR) protein.

"We know there won't be one treatment for lung cancer because it's not one disease," says moon shot co-leader John Heymach, M.D., Ph.D., and chair of Thoracic/Head and Neck Medical Oncology. "We'll do better treating patients in subgroups based on genetic mutations that drive their disease."

The moon shot screened 30 drugs approved by the FDA for other cancers against 90 human non-small lung cancer cell lines to identify ibrutinib and another drug yet to go to trial.

"It costs hundreds of millions of dollars and takes 10 years to develop a new drug from scratch," Heymach notes. "When we identify approved drugs, we can move them right into a clinical trial."

Catching cancer early

Screening former and present heavy smokers with a low-dose CT scan catches enough treatable, early-stage lung cancer to reduce deaths from the disease by 20%.

"If you detect lung cancer early enough, 90% of those patients are cured," Heymach says. Most lung cancer is only found much later, when treatment is markedly less successful.

The problem with low-dose CT screening is that 96% of detected spots and growths are false positives. Sam Hanash, Ph.D., professor in Clinical Cancer Prevention and head of the moon shots proteomics platform, leads a project to reduce false positives and identify biomarkers that help determine who should be screened.

An MD Anderson study opened earlier this year to gather tissue from people who come in for screening, analyze it for telltale indicators of cancer and follow those screened over time.

Grounded by disease, a pilot flies again with the help of an immunotherapy drug combo

Beating lymphoma into remission with a one-two punch By Will Fitzgerald The Carter Suith

• F. Carter Smith

hen Dan Minton noticed a recurring swelling in his neck, he headed for the doctor's office. A biopsy revealed some unexpected news.

"I was devastated, to say the least, because I've always been very healthy and active," says Minton, 57, who lives in North Carolina. "Neither side of my family had a history of cancer, so hearing the word 'lymphoma' came as a complete shock."

Minton isn't alone. Nearly 80,000 in the U.S. will be diagnosed with the disease this year, according to the American Cancer Society.

Lymphoma is a cancer of the lymphatic system, which is a part of the immune system. Divided into two types, lymphomas are either Hodgkin's or non-Hodgkin's, with the latter accounting for more than 90% of cases.

Lymphomas begin when immune system cells called lymphocytes — white blood cells that help the body fight infection — begin multiplying uncontrollably. Left untreated, these cells can invade other parts of the body, including lymph nodes, and complicate a patient's prognosis.

Part of the shock Minton felt when hearing his diagnosis was not knowing the cause of his disease.

Minton's case is a snapshot of the rapid progress science is delivering. Others notably point to the development of ibrutinib, for which MD Anderson led the first in-human trials. "Our body's white blood cells mutate to recognize foreign invaders, and when this process goes wrong, the cells become malignant," says Nathan Fowler, M.D., associate professor in Lymphoma and Myeloma. "Unlike other diseases where we can point to smoking or sun exposure, we know of few risk factors that lead to lymphoma's development."

After conducting his own research, Minton, a father of four, decided to place his health in the hands of the experts and flew to Houston in late 2012. At MD Anderson, his diagnosis of a subtype of non-Hodgkin's lymphoma known as stage III follicular lymphoma was confirmed. Doctors told Minton about a promising clinical

trial involving two existing drugs that hadn't been used in combination before.

The two drugs, lenalidomide and rituximab, represent a growing shift away from using chemo for treating lymphoma, says Fowler, who is Minton's oncologist. Together the drugs work by stimulating the body's immune system to recognize cancer cells and destroy them, removing the need for chemo and its side effects. The combination is proving especially beneficial in follicular lymphoma, a disease known for high relapse rates. Led at MD Anderson, the initial pilot study of the two drugs in 2008 enrolled 30 patients. Researchers were astonished when they found 100% response rates in those with follicular lymphoma.

"Although the number of patients who responded was small, seven total, we became very interested in this combination and immediately expanded the trial to 110 patients," Fowler says. "As we hoped, the results of the larger group mirrored what we saw earlier with an overall response rate of 98 percent."

Since beginning treatments with the combination, Minton noticed the swelling in his neck reduced dramatically in a matter of weeks. Five months later, in the spring of 2013, he was in complete remission.

"My response to treatment has been great, without any relapses, and I currently come to MD Anderson every two months for maintenance therapy," he says. "I'm looking forward to completing the trial early next year, and I'm very hopeful about what the future holds."

Minton's case is a snapshot of the rapid progress science is delivering. Others notably point to the development of ibrutinib, for which MD Anderson led the first in-human trials. That drug has revolutionized care for two different types of disease, mantle cell lymphoma and chronic lymphocytic leukemia.

Before ibrutinib, the median survival of mantle cell lymphoma was three years, but some patients on the drug have remained in remission up to five years, Fowler says.

"It's such an exciting time for researchers and patients in many subtypes of lymphoma," he says. "For the first time in decades, these breakthroughs in our understanding of the disease are translating to clinical advances and literally changing survival patterns."

For Minton, the advances are somewhat simpler. Progress allows him to focus on the things that matter most, such as family. This includes two grandchildren, managing a real estate business and his favorite hobby, flying.



By Ron Gilmore 🖸 Wyatt McSpadden

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hese scientific "treasure hunters" are researchers in MD Anderson's Bioinformatics and Computational Biology department. They have the patience and the know-how to analyze mountains of information and locate that one precious vein of data that will contribute greatly to our understanding of cancer's inner workings. And they believe that "molecular profiling" may be the mother lode for developing new therapies.

They include Han Liang, Ph.D., who's confident the future of cancer medicine rests largely in molecular profiling. It's a technique scientists use to analyze individual patients' tumors to identify genetic characteristics and any unique biological markers. Biomarkers are molecules that can indicate the presence of a condition or disease, and are increasingly being used to measure how the body responds to therapies.

Liang, assistant professor in Bioinformatics and Computational Biology, purports that comprehensive molecular profiling could one day help identify patients who may resist certain therapies and may guide clinicians in tailoring treatment strategies to each patient's unique genetic makeup. Armed with information about a patient's distinct disease, physicians can tailor personalized treatment strategies designed for maximum effectiveness.

Liang conducted a multi-institutional study of data supplied by The Cancer Genome Atlas (TCGA), a program funded by the National Institutes of Health that's examining genomic changes in more than 20 different types of cancer. His team looked at 953 samples from four cancer types: lung, ovarian, brain and kidney. The study's findings, published in the journal Nature Biotechnology, revealed that molecular profiling, while still in its infancy, may eventually hold promise for cancer patient prognosis.

There are 3 billion DNA code letters in each human cell and 32 thousand billion cells in the body. So each person has 96 thousand billion billion DNA code letters. That's more than 10 times as many code letters as there are grains of sand in all of the beaches on Earth. And an unlucky mutation of any one of those code letters can initiate a cancer or make it resistant to our drugs. That defines our challenge — and our opportunity.

— John Weinstein, M.D., Ph.D., chair of Bioinformatics and Computational Biology "By analyzing data from multiple cancer types, we could evaluate prognostic models and identify gene alterations that led to tumor formation," he says. "This wouldn't have been obtained by looking at tumor data from just one cancer type."

PSEUDO (GENE) SCIENCE AND SUPERCLUSTERS

Liang also led an effort to study the quirky pseudogene — a misfit of a gene that's generally believed to have no purpose because it's lost its protein-coding abilities. His recent study in Nature Communications showed otherwise.

After reviewing more than 2,800 samples from patients with seven types of cancer, Liang concluded that the largely ignored pseudogenes may very well be the new targets for helping medical experts discover new biological markers. These markers will allow doctors to both personalize treatments for individual patients and better equip them to predict cancer survival rates.

Like Liang, Roeland Verhaak, Ph.D., an assistant professor with a dual appointment in the Bioinformatics and Computational Biology and Genomic Medicine departments, also conducted a large-scale study, which compared how genes are expressed in 12 tumor subtypes. His team's work, published in Oncogene this past August, identified eight cancer "superclusters" that shared similar disease pathways and gene expression.

In his study, Verhaak identified one particularly large supercluster of cancers, all which shared common genetic mutations and expressions, DNA changes and increased cell proliferation. In this supercluster, mutations in the protein TP53 led to cancer growth by refusing to let cells die, even though they had experienced DNA damage. TP53 normally suppresses tumor growth.





Han Liang, Ph.D., believes molecular profiling will guide the future of cancer medicine.



Roeland Verhaak, Ph.D., and his team have identified eight cancer "superclusters" that share similar disease pathways and gene expression.

DESIGNER DATA ANALYSIS

Like many MD Anderson scientists engaged in unraveling the mysteries of cancer's cellular causes, Verhaak relies on high-tech approaches to understanding the mountains of information that accrue in databases such as The Cancer Genome Atlas.

To process and analyze data on such a large scale in a systematic, automated manner, he and fellow scientists developed the Pipeline for RNA-Sequencing Data Analysis, or PRADA — an acronym suggested by Verhaak's fashionsavvy wife.

Unlike its fashion namesake, PRADA doesn't involve manipulation of fancy fragrances or exotic leathers. Rather, it involves a software program that provides multifaceted analysis of genetic information from gene expression levels to detect items only a scientist could identify or be passionate about, such as intragenic fusion variants and homology scores.

The software has been used extensively and successfully to better understand brain and kidney cancer through The Cancer Genome Atlas program.

THE WIRED WORLD OF POST-GENOMICS

As the chair of Bioinformatics and Computational Biology, John Weinstein, M.D., Ph.D., oversees a department that collaborates with many departments and people across MD Anderson. This includes Gordon Mills, M.D., Ph.D., chair of Systems Biology, Lauren Byers, M.D., assistant professor in Thoracic/ Head and Neck Medical Oncology, and Wei Zhang, Ph.D., professor in Pathology, who incorporate molecular data into their work to improve cancer prognosis. Centers such as the Institute for Personalized Cancer Therapy, the Center for Targeted Therapy and the Kleberg Center for Molecular Markers are also focusing on this area of study.

Weinstein is widely known for his introduction in the early 1990s of the Clustered Heat Map, which has been labeled by some as the "most common visual icon of the postgenomic era." The Heat Map was built upon work Weinstein completed while serving as head of the Genomics and Informatics Group at the National Cancer Institute, where he developed a collection of web-based bioinformatics software packages known as the "Miner Suite." The Clustered Heat Map graphically allows investigators to understand complex data and is today a commonly used bioinformatics software tool.

Weinstein currently leads a group that is on the forefront of discoveries in molecular profiling. His approach to research, for which he has coined the term "integromic," has been described as "part experimental, part computational."

Weinstein's group uses more than two dozen microarray platforms and other technologies to unscramble the tangled network of cellular processes that are believed to lead to cancer. When properly deciphered, these processes may offer exciting new options for prevention and treatment.

Former U.S. Secretary of the Interior Stewart Udall once wrote that "mining is like a search-and-destroy mission." The work of scientific investigators such as Liang, Verhaak and Weinstein — along with many of their MD Anderson colleagues — is very much a search mission for the essence of our genetic makeup. And delving into the depths of genetic mysteries for new solutions may one day destroy the cancer that robs us of our health.





Braving a surgical no man's land

The Skull Base Tumor Program is an all-pro team of surgeons and specialists tackling tumors in very hard-to-reach places.

By Julie Penne



Franco DeMonte, M.D., helped pioneer MD Anderson's Skull Base Tumor Program. Previous and facing pages: DeMonte during surgery.

ight miles in the air while piloting a flight from New Jersey to Houston, Gerald Ahrens' life took an unexpected turn.

"I got a nosebleed that just wouldn't stop," says Ahrens, who flies charter and corporate jets. "Something just wasn't right."

That nosebleed 10 years ago was the beginning of a whirlwind journey that brought Ahrens to MD Anderson. Here, doctors found he had squamous cell cancer in his sinus cavity — the hollow, air-filled spaces in the bones around the nose.

Now 68 and cancer free, Ahrens was one of the early patients to benefit from MD Anderson's Skull Base Tumor Program, which celebrates its 10th anniversary this year. Bringing together neurosurgeons, head and neck surgeons, radiation oncologists and other health care professionals, the program treats patients who develop tumors at the base or "floor" of the skull, where the brain sits. This region includes the area behind the eyes and nose.

Franco DeMonte, M.D., who helped pioneer the program, says not all skull base tumors are cancerous, but all are rare and complex.

"Treating skull base tumors is challenging because they are very close to critical nerves and blood vessels in the brain, head, neck and spinal cord," says DeMonte, professor in Neurosurgery. "Surgeons must carefully work around these delicate structures without damaging them." At MD Anderson, patients in the Skull Base Tumor Program are treated for a variety of cancers or noncancerous tumors that reside in the bones around the eyes or inner ear, in the roof of the nasal cavity, or in the sinus cavities. These include chordomas (cancerous bone tumors at the base of the skull), meningiomas (aggressive tumors that originate in the lining of the brain and are usually benign) and acoustic neuromas (noncancerous tumors that develop on the nerve that connects the inner ear with the brain).

Most patients undergo surgery,

Skull base tumor surgery can affect a patient's hearing, sight, smell, speech and appearance. Because of this, supportive services step in to provide balance therapy, physical therapy, audiology, speech therapy, plastic reconstructive surgery, dentistry and ophthalmology to patients.

"Supportive services bring another dimension of expertise to the program," says DeMonte. "And because these teams are so good at what they do, our patient outcomes and quality of life are very much improved. Everyone on this team contributes, and it's the patients who most benefit."

and at MD Anderson, many skull base tumor surgeries are performed endoscopically. Surgeons pass an endoscope — a long, thin tube equipped with a miniature light and a video camera through a natural opening such as the nose to peer into the skull and locate the tumor. Various tiny surgical instruments, which allow the surgeon to shear away bits of the tumor, are introduced alongside the endoscope.

Because many skull base tumors are rubbery or fibrous and hard to cut out, tools are designed to scrape, pick, grasp, cut and suction as the surgeon whittles away the tumor.

"These tumors often adhere to critical structures like nerves and blood vessels, so extreme precision is necessary during removal," says Ehab Hanna, M.D., professor in Head and Neck Surgery, who helped establish the program along with DeMonte.

In addition to leading-edge surgical techniques, MD Anderson patients have access to advanced radiation treatments such as proton therapy or gamma knife, as well as the latest chemo drugs.

"Surgery is the gateway for the majority of patients, but what makes our program truly multidisciplinary, and unlike any other program in the country, is what our colleagues in medical oncology, radiation oncology and other specialties offer," DeMonte says. "If we can see patients with these difficult cancers at the right time and leverage the team's full expertise, we can save lives."

A recent study conducted by DeMonte and Hanna showed that 80% of patients who had their first surgery for sinus cavity cancer at MD Anderson survived 10 years, which is well beyond the average of 60%. Another study showed that during a 50-year time span, the survival rate for patients with sinus cavity cancer has increased from 30% to 75%.

"Before 1990, skull base tumors were considered to be residing in no man's land, and often patients were told to go home and die," Hanna says. "Now, the future is exciting and hopeful, especially at MD Anderson."

The next step in the evolution of skull base surgery is to introduce robotics, which Hanna is exploring.



Mary Murrill came to MD Anderson in 2013 to be treated for an acoustic neuroma — a rare, noncancerous skull base tumor that develops on a nerve between the brain and inner ear. Patients often experience hearing loss, tinnitus or ringing in the ears, and dizziness.

"I thought I had a sinus infection, but antibiotics didn't help," says Murrill, who lives in Beaumont, Texas. "The pain in my ear was piercing, and the loud ringing noise kept me awake all night."

Murrill's doctor suggested she consult Paul Gidley, M.D., professor in Head and Neck Surgery. Gidley heads the Skull Base Tumor Program's acoustic neuroma service, where, with DeMonte, he performs about 30 acoustic neuroma surgeries a year.

Gidley and DeMonte removed Murrill's acoustic neuroma in an intricate 10-hour surgery that preserved her facial function and impacted both her hearing and balance. After working with an MD Anderson balance therapist to steady her equilibrium, Murrill is back on her feet.

"I felt so lucky knowing I was in the best of hands," she says.

Ehab Hanna, M.D., fresh from the operating room, is exploring robotics, the next step in the evolution of skull base surgery.



27



HETHER BARBECUING FOR A HUNGRY CROWD, MENTORING A YOUNGSTER WHO NEEDS A ROLE MODEL OR BRINGING A WARM BLANKET TO A GRATEFUL PATIENT, ERVIN GRICE'S LIFE IS ALL ABOUT SERVING OTHERS.

"I've always been community minded," says Grice, 69. "It's how my parents raised me and it's how I raised my kids."

For the past seven years, he has volunteered as a patient advocate in MD Anderson's Emergency Center, where patients receive after-hours critical care. His main role, he says, is to provide a calming and caring presence.

"Folks coming into the Emergency Center have an immediate medical issue. They're in pain, they're ill, and sometimes they're upset. I stay with them from the time they arrive until the doctor takes over."

"What can I do to make you more comfortable?" Grice greets patients warmly, though he's careful not to overdo it.

"You have to know when to insert yourself and when to back away," he explains. "Have you ever tried to enjoy a meal in a restaurant, and the waiter or waitress keeps interrupting? You don't want to be like that."

A good day in the Emergency Center is a slow day, Grice says.

"If you come to MD Anderson as a patient, I look forward to helping you," he says. "But I'd prefer to not see you here."

When Grice retired in 2005 after 41 years as a software engineer with NASA, he immediately began seeking chal-

lenging volunteer opportunities. Recalling his experience as a prostate cancer patient at MD Anderson years ago, the cancer center naturally came to mind.

"I still remember how impressed I was by those friendly volunteers in light blue jackets. They were always smiling and greeting me, keeping me company, and offering assistance. Now I'm proud to join their ranks," says Grice, briskly adjusting his own blue jacket with a self-assured tug.

Because of his proficiency in the Emergency Center, he has been selected to mentor and train new MD Anderson volunteers who shadow him for three weeks to learn the ropes.

"Ervin is an exceptional volunteer," says Susan French, executive director of Volunteer Services. "He's dedicated, he's enthusiastic and he makes everyone feel special and valued."

One of Grice's favorite volunteer roles at MD Anderson is mentoring children in the Health Adventures Program, which introduces youngsters to hospital careers. On Saturdays during the school year, 20 fifth-graders cheerfully hop off a bus and burst through the doors of the hospital, eager to learn something new.



"They could be home watching TV or playing video games, but they'd rather be here," says Grice, who guides the children on behind-the-scenes hospital tours. On a given weekend, the kids will don hospital scrubs, try out stethoscopes on a nursing unit or maneuver wheelchairs to learn about rehabilitation.

Children chosen for the program are academic high achievers from economically challenged households.

"They're dealing with tough times at home, but doing well in school, and we want them to continue doing well," Grice says. "We may be one of the few positive role models they have."

Several program graduates each year profess their desire to become a nurse, a scientist or a doctor.

"That's how powerful and gratifying this program is," says Grice, who preaches the benefits of keeping busy.

"Stay active," Grice says. "It's good for your health and your soul."

And active he is. On a recent weekend, Grice was up at 5 a.m., training to join 13,000 other runners in next January's Chevron Houston Marathon.

To "have some fun and relieve some stress," he runs 28 miles weekly, and especially likes to jog from Memorial Park

to the George R. Brown Convention Center in downtown Houston, then back again.

So far he's run 19 full marathons and three halfmarathons.

"Not bad for an old man," he quips.

Martha Joyce, Grice's wife of 45 years and a retired schoolteacher, prefers to exercise on the dance floor.

"When we Zumba and line dance at the senior center," says Grice, "we really kick up our heels."

On a Saturday this summer, Grice barbecued chicken, sausage and ribs basted in his legendary "secret sauce." A closely guarded combination of herbs, spices and other classified ingredients he concocted 30 years ago, the sauce regularly draws the entire family to the backyard. Relatives plead for the recipe. "Nope," says Grice.

The celebration commemorated a family milestone. Grice's 14-year-old grandson, Reid, joined MD Anderson as a teen volunteer. He mans the popcorn cart in the hospital's main lobby, where more than a thousand patients, caregivers and visitors enter each day.

"I just hope he can keep up with me," Grice says with a wink.

Taking care of the nurses

Meet four winners of the Arceneaux Award, MD Anderson's highest nursing honor

By Miriam Spradling

hen Debbie Houston came to MD Anderson in the late 1960s, cancer care was in its infancy. Back then, there were cigarette dispensers scattered throughout the Texas Medical Center campus and chemo treatment meant spending many weeks in the hospital.

Nursing was a natural career choice for Houston. Her mother, who's now 100, was a nurse for 50 years. Houston initially came to MD Anderson because it offered the most competitive salary to part-time nursing students. However, she stayed for more than four decades after she quickly realized making a difference in the lives of cancer patients was the biggest payoff of all.

"I worked with patients with lung and esophageal cancers as a clinical nurse specialist," she says. "Getting to know them and their families was my favorite part."

Her compassion for patients and dedication to oncology nursing earned Houston the inaugural Ethel Fleming Arceneaux Outstanding Nurse-Oncologist Award, first given in 1982.

Established by The Brown Foundation Inc. and named for a director of nursing who died of pancreatic cancer, the annual award is the institution's highest nursing honor. A committee representing MD Anderson's clinical faculty, patient care administration and nursing staff reviews nominations from peers and patients before selecting a recipient for the honor, which comes with a \$15,000 prize.

Arceneaux Award winners vary in ages, ethnicities and nursing specialties, but they have several things in common: a deep love for their patients, a passion for the nursing profession and a profound sense of humility.

"It was a shock and very humbling because I worked with so many deserving nurses, so I felt the pressure to prove my worth," Houston says. "It inspired me to improve my practice, get involved in oncology nursing organizations and be the best I could be because I was carrying the mantle of this award."

1982





Former winner is now the chair

Wenonah Ecung joined MD Anderson as a general oncology nurse in 1979 and has risen through the ranks, now serving as vice president for Clinical Administration. Along the way, she completed her master's degree and officially became a Ph.D. candidate. She's due to conduct her public defense at the end of this month. Ecung has overseen multiple departments and became chair of the Arceneaux Award selection committee — a role she still holds today.

"It's a pretty cool responsibility having been a recipient," says Ecung, who won the award in 1990. "It's reassuring to know we're passing the baton to worthy people who really are here to carry on the values of the Arceneaux Award."

Planning for the June award ceremony begins each fall. Once nominations are finalized, Ecung redacts all identifying information, including gender, area of employment and name of nominator.

"Anything that can create bias in the equation is removed," she explains. "The committee works blindly for a period of time, and I don't vote unless there's a tie."

Once the committee narrows it down to three finalists, everyone gathers for "speed Arceneaux," where nominees talk to committee members over lunch, switching tables every fifteen minutes until all have met.

Winning the Arceneaux Award was an honor and a privilege for Ecung. "It was tremendous recognition for a job I love doing, for people I love serving," she says.

Guarding the profession

Colleen Villamin was feeling the pressure of wearing many hats just before being nominated for the Arceneaux Award last year. Balancing motherhood with school and a full-time workload proved too much, so she put school on hold and began working part time. Winning the Arceneaux Award motivated her to complete her nursing education and return to the bedside.

"When I received this honor, I felt a huge obligation to fill the shoes of the nursing giants that walked before me," says Villamin, who worked in the Stem Cell Transplant unit at the time. "I decided to go back to school to complete the Clinical Nurse Leader program and then went back to work full time."

Since then, Villamin says doors have opened to her that she never thought possible. She's become a principal investigator of a nursing division study, and Advance for Nurses magazine invited her to write a standing feature, which she titled "Guarding the Profession."

"I picked that name because one of the roles of Clinical Nurse Leader is to do just that," she explains. "A lot of the brightest nurses become nurse practitioners, so it's up to Clinical Nurse Leaders to remain at the hospital and make sure nursing at the bedside is the best it can be."

Villamin, who now serves in the Thoracic and Cardiovascular Surgery unit, wears her Arceneaux pin with pride. She says patients ask her about it regularly.

"I tell them it's from people who donated money to recognize outstanding oncology nurses," she says. "We're very fortunate that they've been able to honor it and keep it going for so many years."



🖾 Wyatt McSpadden

As seen on TV

At age 10, Diane Barber, Ph.D., knew she would become a nurse someday. It was the late '60s, and Barber, living in southern Mississippi, religiously watched "Julia," a television series featuring Diahann Carroll in the titular leading role as an African-American nurse

"It was the most awesome thing at that time. I didn't have any family in the health care field," Barber says. "Julia was such a great role model. I watched her and told my grandmother, 'That's what I'm going to do when I grow up."

Now a nurse at MD Anderson for more than 16 years, Barber takes care of patients on phase I clinical trials. She says her patients' courage, spirit and hope motivate her daily.

"I can't get over how our patients leave their homes and support systems to participate in a phase I program with no guarantee they'll benefit from it," she says. "It's amazing. I think, 'if they can do this, I can go the extra mile for them."

Marrying young to a military officer who traveled the globe, Barber picked up a nursing degree along the way, enrolling in courses from Hawaii to Pennsylvania. Most recently, she obtained her Ph.D., a lifelong goal that she says ties with winning the Arceneaux Award as the proudest accomplishments of her career.

Barber, who currently teaches part time, plans to become a fulltime nursing instructor when she eventually retires from bedside nursing.

"I want to teach the next generation of nurses," she says. "They soak up everything you say. And it's rewarding to see the students get so excited."



F. Carter Smith

And the Arceneaux went to ...

The award carries a prize of \$15,000, which the winners have put to very good use over the years.

DEBBIE HOUSTON (1982)

With her award, she ... put a down payment on her house and finished her master's degree.

"Nurses are the unsung heroes of patient care. We're the ones who are with patients day and night. The fact that The Brown Foundation recognizes the people who are actually providing the care and comfort to patients is wonderful. It means a lot to me."

WENONAH ECUNG (1990)

With her award, she ... bought new bedroom furniture and a gold bracelet.

"I wanted to remember this feeling of what it meant to win the award and the responsibility that came with it. Every time I feel the bracelet around my wrist it's a reminder of my responsibility to give back."

COLLEEN VILLAMIN (2013)

With her award, she ... went back to school full time and treated her family to a vacation.

"I took my family on a Disney cruise since we hadn't gone anywhere in a long time. I thought about how patient my family had been with me while I was balancing work and school, so I wanted to give them my time."

DIANE BARBER, PH.D. (2014)

With her award, she ... plans to buy a blue Coach purse she's had her eye on for years and take a vacation with her husband.

"When I discovered I was nominated, I thought, 'there are so many wonderful nurses, I won't even come close.' Now I've gotten messages from people I don't even remember meeting telling me how much I deserve this. It's amazing the Arceneaux Award has so much recognition. The Brown Foundation really inspires so many."

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

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