

THE UNIVERSITY OF TEXAS

DAnderson ancer Center

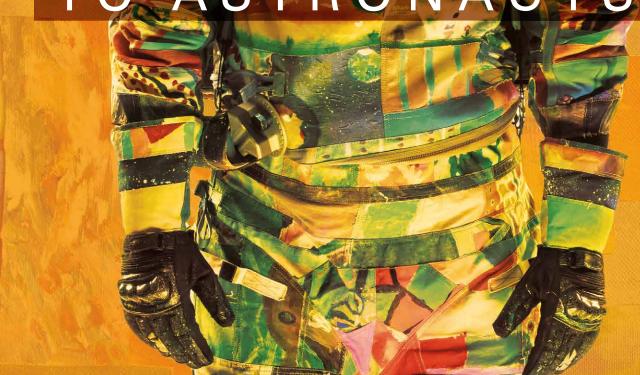
Making Cancer History®

SUMMER 2016 VOL 30 ISSUE 4



THE MISSION TO END CANCER:

FROM MOON SHOTS
TO ASTRONAUTS



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®.



Caring

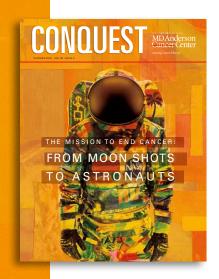
By our words and actions, we create a caring environment for everyone.

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: A unique collaboration between MD Anderson, ILC Dover, NASA and the International Space Station led to the Space Suit Art Project, which was developed through MD Anderson Children's Cancer Hospital's Arts in Medicine Program. Pediatric patients and their families, along with hospital staffers handpainted more than 600 decorative fabric swatches that were stitched together to create replica space suits named HOPE and UNITY. A third suit, COURAGE, is a hand-painted NASA-issue flight suit that was sent to the International Space Station.

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MEET THE SABIN FAMILY FELLOWS

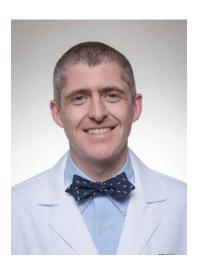
They are bold and creative scientists who aren't afraid to push the limits

ight of MD Anderson's top young researchers have been named Andrew Sabin Family Fellows and will receive \$100,000 each over two years to pursue creative, independent thinking and high-risk, high-impact research.

In 2015, Andrew Sabin, of East Hampton, New York, and the Andrew Sabin Family Foundation committed \$30 million to establish an endowment funding the Andrew Sabin Family Fellowship Program, which is designed to support the novel work of world-class cancer researchers in four categories: basic science, clinical, physician-scientist and population and quantitative science. Eight cancer research fellowships will be awarded each year.

"I wanted to provide a vehicle so that highly qualified researchers at the world's premier cancer center can focus on important work that can truly help people who suffer from cancer," says Sabin, who has served on the MD Anderson Cancer Center Board of Visitors since 2005. "I hope one of the fellows comes up with a cure. It would make me very proud to know that this gift made a difference."

The inaugural recipients, selected among 65 applicants through a rigorous peerreview process, shared with Conquest what the fellowship means for their research ...



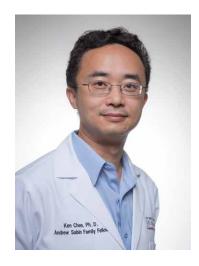
Benjamin Smith, M.D., associate professor, Radiation Oncology and Health Services Research

The Sabin Fellowship will allow me to expand my research in a novel direction by developing a project that will promote personalized decision-making for women with early breast cancer trying to decide between mastectomy and breast reconstruction or lumpectomy followed by whole-breast irradiation. This type of research is novel and would be difficult to fund via a more traditional method. The Sabin Fellowship is important because it will allow me to focus my time on conducting research — instead of writing grants — and generate data to expand this novel avenue of research.



Shannon Westin, M.D., assistant professor, Gynecologic Oncology and Reproductive Medicine

The Sabin Fellowship is providing the funding necessary to add novel endpoints to existing clinical trials. My colleagues and I are creating a platform to evaluate which patients may benefit most from therapies targeting p53, which is the most common molecular aberration in ovarian cancer and a number of other advanced solid tumors. The potential for practice-changing findings is great.



Ken Chen, Ph.D., assistant professor, Bioinformatics and Computational Biology

The Sabin Fellowship enables me to look more closely at the dark region of human genomes, to identify genetic variants such as structural variants and small insertions and deletions, which cannot be identified by current technologies, but are particularly important to tumor development.



Katharina Schlacher, Ph.D., assistant professor, Cancer Biology

I came to MD Anderson because it's an institution with a grand mission: eradicating cancer. To achieve that mission, we need research that pushes the envelope and changes how we think and how we treat patients. The Sabin Family Fellowship understands this need and supports such out-of-the-box thinking. The fellowship will further my study of DNA replication fork protection at in-depth molecular and biological levels in order to learn more about its potential as a cancer suppression mechanism across many different cancers.



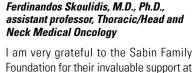
David Hui, M.D., assistant professor, Palliative, Rehabilitation and Integrative Medicine and General Oncology

The Sabin Fellowship is particularly important to my research because it enables me to conduct a high-risk, highyield project that examines the use of a highly innovative intervention — high flow oxygen and air — to relieve shortness of breath (or air hunger) in cancer patients. This symptom is common among cancer patients, and there are few treatment options available. I am grateful for the Andrew Sabin Family Fellowship Program because instead of having to spend a lot of time writing grants, this prestigious award allows my research team to jump right into the science. This preliminary study represents a critical step toward improving the quality of life of patients living with cancer.



Cullen Taniguchi, M.D., Ph.D., assistant professor, Radiation Oncology

I am incredibly humbled to be named a Sabin Fellow. This award will fund an exciting project that seeks to reduce toxicity from chemotherapy and radiation treatments to improve outcomes in our cancer patients.



Foundation for their invaluable support at an early stage in my independent research career. This fellowship will enable me to extend my work on the role of co-occurring genetic events in KRAS-mutant lung adenocarcinoma, a prevalent and difficultto-treat molecular subtype of non-small cell lung cancer. We will specifically focus on identifying novel molecular predictors of response of KRAS-mutant tumors to immunotherapy with immune checkpoint inhibitors.



Nicholas Navin, Ph.D., assistant professor, Genetics and Bioinformatics

The Sabin Fellowship has enabled me to pursue an exciting new, high-risk research project in my laboratory. This project will involve applying single-cell DNA sequencing technologies to breast cancer patients to understand how individual tumor cells evolve resistance to chemotherapy.

CANCER FRONTLINE

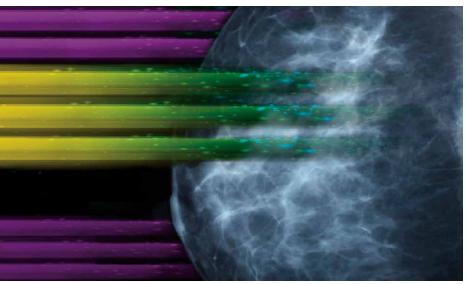


photo illustration by Kellye Sanford

SHORTER RADIATION COURSE RECOMMENDED FOR EARLY-STAGE BREAST CANCER PATIENTS

Early-stage breast cancer patients who received a shorter course of whole-breast radiation at higher doses reported equivalent cosmetic, functional and pain outcomes over time as those who received standard therapy consisting of a longer, lower-dose course of treatment, according to an MD Anderson study.

Published in the journal Cancer, the study found patient-reported functional status and breast pain improved significantly following both radiation schedules, and there were no significant differences in physician-reported cosmetic evaluations. With equivalent outcomes, the authors suggest the shorter course as the preferred option for patients because of a more convenient treatment schedule.

"In the United States, women historically have been treated with conventionally fractionated whole-breast irradiation (CF-WBI), given in smaller doses over a longer period of time, rather than hypofractionated whole-breast irradiation (HF-WBI), which consists of higher doses for a shorter treatment period," explains Benjamin Smith, M.D., associate professor of Radiation Oncology.

Large randomized trials from Canada and the United Kingdom have established HF-WBI as a safe and effective treatment for nearly all patients with early-stage breast cancer. In previously published research, the authors showed

patients receiving HF-WBI experienced less acute toxicity and post-radiation fatigue compared to those treated with CF-WBI. However, the adoption of HF-WBI has been limited in the U.S. In fact, researchers note only one-third of patients for whom HF-WBI is currently recommended by the American Society of Radiation Oncology (ASTRO) actually receive the shorter course of therapy.

"This trial is particularly important because there is still some hesitation among clinicians in the U.S. about adopting the hypofractionated schedule," says lead author Cameron Swanick, M.D, a resident in Radiation Oncology. "Because American patients tend to have a higher prevalence of obesity, and because prior trials excluded certain patients with high body mass index, there has been this concern that the shorter radiation treatment course may not be as safe for American patients."

The researchers continue to follow tumor control outcomes, though, to date, no meaningful difference in survival has been found. All outcomes will be reported once all patients have completed three-year follow-ups.

The results of this and previous studies further support the use of HF-WBI as the preferred radiation therapy for early-stage breast cancer patients, says Smith. "At MD Anderson, these shorter courses have become the standard of care."

AGGRESSIVE HPV-RELATED CANCER RESPONDS TO IMMUNOTHERAPY DRUG

Researchers have reported results of the first-ever Phase II clinical trial for treatment with the immunotherapy drug nivolumab on squamous cell carcinoma of the anal canal (SCCA), a rare malignancy that is on the rise.

The Phase II study was designed and led by researchers with MD Anderson's Human Papillomavirus-Related (HPV) Cancers moon shot. MD Anderson enrolled 18 patients who volunteered to provide both pre- and post-treatment tissue samples. The study revealed encouraging correlations between immunologic biomarkers and responses to treatment.

"There have been no standardized treatment options for metastatic SCCA patients," says Van Morris, M.D., assistant professor of Gastrointestinal Medical Oncology. "This study demonstrated responses in five of 18 patients treated at MD Anderson, and many of the patients had significant reductions in their tumor size."

The findings were presented at the American Association for Cancer Research's annual meeting in New Orleans.

"In this first prospective Phase II trial for refractory metastatic SCCA, our exploratory analysis of preand on-treatment tissue samples revealed potential correlations between immunologic biomarkers and clinical outcomes to nivolumab," says Cathy Eng, M.D., professor of Gastrointestinal Medical Oncology and national study principal investigator.

Metastatic SCCA, a cancer often associated with HPV infection, is normally treated with chemotherapy, although no trials have established a standard of care.

The study employed the monoclonal antibody nivolumab, one of the drugs represented among the growing arsenal of immunotherapies. The drug frees the immune system to attack cancer by disrupting a brake that halts immune response.

"This the first formal clinical trial completed with patients with previously treated metastatic SCCA," says Morris. "In this trial, patients received a biopsy just before being treated with nivolumab and then a second paired biopsy after two doses."

- Ron Gilmore



COST OF CHEMO FOR BREAST CANCER VARIES WIDELY

Costs associated with different breast cancer chemotherapy regimens can vary significantly. regardless of effectiveness, according to new MD Anderson research. Understanding cost differences should help guide informed discussions between patients and physicians when considering chemo options.

Sharon Giordano, M.D., chair of Health Services Research and professor of Breast Medical Oncology, presented the findings at the 2016 American Society of Clinical Oncology Annual Meeting in Chicago.

"The costs of cancer care have been increasing dramatically, both for the health care system and for patients. As physicians, we increasingly are recognizing the financial burden on our patients," says Giordano. "Both physicians and patients need greater access to information about the treatment costs so this critical issue can be discussed during a patient's decisionmaking process."

The American Cancer Society estimates 246,660 new cases of invasive breast cancer will be diagnosed this year in the United States. At least 35% of patients with breast cancer receive chemotherapy in addition to surgery or radiation. Therefore, choosing equally effective but less costly regimens could impact costs of breast cancer care nationally by \$1 billion every year, Giordano explains.

To calculate cost of care, the researchers analyzed claims from the MarketScan database of 14,643 adult women diagnosed with breast cancer between 2008 and 2012 in the U.S. To qualify for the study, women must have had full insurance coverage both six months before and 18 months after diagnosis, received chemotherapy within three months of diagnosis, and had no secondary malignancy within one year of diagnosis.

The researchers calculated adjusted average total and out-of-pocket cost using all claims within 18 months of diagnoses, normalized and 2013 dollars, with separate analyses conducted for regimens that did and did not include trastuzumab.

"In this study, we found substantial variation in the costs of breast cancer treatment for different chemotherapy regimens, even when comparing treatments of similar efficacy," says Giordano.

The largest variations were seen when comparing insurer costs. For patients who did not receive trastuzumab, median insurance payments were \$82,260, but varied by as much as \$20,354 relative to the most common regimen. Median out-of-pocket costs were \$2,727, but the largest variation was just \$382.

For those patients receiving trastuzumab-based therapies, median insurance payments were \$160,590, with a difference of as much as \$46,936 relative to the most common regimen. Median out-of-pocket costs were \$3,381, with relative differences as much as \$912.

The researchers plan to continue work with available and future data to better understand the relative value of cancer care options.

— Laura Sussman

MD ANDERSON ONCE AGAIN RANKED NO. 1 CANCER HOSPITAL

MD Anderson again has been ranked No. 1 for cancer care by U.S. News & World Report's annual "Best Hospitals" rankings. Since the rankings began in 1990, MD Anderson has been named one of the top two cancer hospitals in the nation, and has received the top position nine times in the past 10 years.

"It's an honor to once again be recognized as the nation's top hospital for cancer care, which we have earned through our unrelenting passion to serve patients and fulfill our mission to end cancer," says Ronald DePinho, M.D., president. "We thank our patients and their loved ones who entrust us with their care, and salute the 21,000 cancer fighters and 1.000 volunteers who make up our distinctive culture of exceptional care and compassionate caring."

Two subspecialties also were ranked in the survey's top 10. In Ear, Nose and Throat, MD Anderson's Head and Neck Surgery service ranked No. 9. The Gynecologic Oncology and Reproductive Medicine service ranked No. 9 in Gynecology. These subspecialties are especially notable since they include all major general hospitals in the nation, not just cancer centers. Both groups consistently have been high ranked since the early 1990s. Additionally, MD Anderson's Urology service tied for No. 36 in the national survey.

"This ranking reflects the extraordinary care delivered by our teams of highly subspecialized physicians, outstanding oncology nurses and dedicated supportive care professionals, all working together for the benefit of each patient who comes through our doors," says Thomas Buchholz, M.D., executive vice president and physician-in-chief.

The institution's commitment to patients, innovation, mission and outreach are among the hallmarks that have guided its rich 75-year history and that will direct its future. MD Anderson's diamond anniversary, to be celebrated in November, commemorates the year the Texas Legislature passed a bill to appropriate funding for a state cancer hospital. That same year, the MD Anderson Foundation agreed to match funds if the hospital would be built in Houston. Since that time, more than 1 million patients have sought care at MD Anderson.

— Julie Penne



Broadening the immunotherapy attack

Immune attack that began with melanoma is being extended to other cancers

By Scott Merville

he kidney tumor that snuck up on Philip Prichard was surprisingly large and aggressive by the time it clearly announced itself in the jarring voice of excruciating pain in his right side and leg during a 2012 business trip.

A physical exam and CT scan back home in Memphis revealed stage IV kidney cancer. Surgery removed a nearly 4-pound tumor, but by now the cancer had spread to other organs. Targeted therapy and an attempted second surgery didn't slow its growth.

"When I opened my eyes after the second surgery, my doctor came in and said 'we'll talk later," recalls Prichard, 48. "He had that look in his eyes that said, 'I don't know what to say right now.' Even on my morphine drip I could tell he was saddened by what was going on."

Prichard's wife, Susan, began researching where to turn next.

The couple arrived at MD Anderson in the spring of 2013 in search of hope and found it in a clinical trial for a drug that treats cancer by freeing the immune system to attack it.

At that time, the immunotherapy drug nivolumab was deep into clinical trials for melanoma, thought to be the cancer most vulnerable to immune approaches. However, newer studies had opened to test it against other cancers.

When doctors told Prichard he could join the trial, his response was, "Yeah, let's do this!"

Responding well

"Over the first three months, I began to feel a bit stronger and eat better," Prichard recalls. "Then the CT scans started to come in and they showed my tumors decreasing in size every time."

He didn't notice side effects, but given the discomfort and fatigue caused by the disease, he's not sure he would have noticed.

"I was pretty far down the path there," he says.

After three years of coming to Houston every other Tuesday for treatment, Prichard stopped taking nivolumab in March. He's back in good health and his fresh start inspired him to strike out from the family distillery business in a new venture with Susan: They're opening a whiskey bar back home in Memphis.

Prichard is among the 25% of metastatic kidney cancer patients who respond to nivolumab. About half of those have durable, long-term responses, says his oncologist, Nizar Tannir, M.D., professor and deputy chair of Genitourinary Medical Oncology.

"He's done really well. Nivolumab is the least toxic therapy we have for metastatic disease, and it comes with the chance of cure, or at least durable remissions for many years," Tannir notes. "That's not something you get with any other therapy."

Good news for metastatic cancer patients

The approach that helped Prichard, called immune checkpoint blockade, continues to have an increasing impact on solid tumors that have metastasized, or spread, to other organs. These cancers are the hardest to treat. Response rates to immonutherapy drugs on a variety of metastatic cancers range from 15 to 40% of patients, with many of these enjoying long-term remissions, some of which appear to be cures.

Not bad considering at one point many predicted these drugs might only work well for melanoma, the cancer with the highest rate of genetic mutations, thus providing the most targets for immune attack. It has long been thought to be the most "immunogenic" of cancers.

That's not surprising to Jim Allison, Ph.D., chair of Immunology and executive director of the immunotherapy platform at MD Anderson. Allison conceived checkpoint blockade out of his basic research on immune response.

"This approach treats the immune system, rather than focusing on the tumor, so there's really no reason that it shouldn't work in many human cancers," he says.

The drug developed from his research, ipilimumab (Yervoy), was approved by the Food and Drug Administration (FDA) in 2011 to treat inoperable or metastatic melanoma. Follow-up research of 5,000 patients who had advanced melanoma and were treated with the drug showed 22% surviving to 10 years and beyond — unprecedented results.

While news accounts of these drugs often refer to them as "only helping a fraction of patients," oncologists know that such results in metastatic cancers are incredibly rare.

"That immune checkpoint inhibitors work so well as single treatments against advanced, metastatic cancers is incredibly encouraging," says Padmanee Sharma, M.D., Ph.D., scientific director of MD Anderson's immunotherapy platform and a professor of Genitourinary Medical Oncology and Immunology.

"There's great opportunity to improve these early results by more precisely identifying patients who will benefit from immunotherapy and by understanding how to best combine immunotherapy with other types of treatment," Sharma says.

The immunotherapy platform addresses these issues by analyzing tumor biopsies before treatment, during treatment with immunotherapy, and then after treatment ends or the cancer worsens. It's an important part of the Moon Shots Program and its goal to reduce cancer deaths by cutting down on the time it takes to turn scientific discoveries into progress against these diseases.

In addition to studying the presence and strength of T cells — the immune system's targeted attack cells — in and around the tumor, the group looks for other immune cells, proteins and substances secreted by cells that foster or inhibit immune response. Understanding the complex interplay of these factors might help identify biomarkers — proteins, cells or molecules whose presence indicates that a drug will or won't work.

Since Philip Prichard entered the clinical trial in 2013, nivolumab (known as Opdivo), has been approved by the Food and Drug Administration for advanced melanoma. lung cancer, kidney cancer and Hodgkin lymphoma. Another immunotherapy that hits a related target was recently the first approved for bladder cancer.



Prichard's oncologist, Nizar Tannir, M.D., professor and deputy chair of Genitourinary Medical Oncology
■ Nick de la Torre

Immunotherapy drugs such as nivolumab work by blocking a protein called PD1 on T cells white blood cells that act as guided missiles against viruses, bacteria and abnormal cells identified by the immune system. Cancer cells can "turn off" an attacking T cell because they bear a protein called PD-L1 that acts like a key, connecting with PD1 to lock down the T cell. By blocking this connection, immunotherapy drugs allow the body's immune system to fight cancer.

Working on prostate cancer

One such biopsy study has opened a new door in prostate cancer — a tumor type that so far has stoutly resisted treatment by checkpoint blockade. Biopsy analyses by Sharma and her colleagues show that a particular combination of immunotherapy drugs might first draw T cells into these tumors, then free them to attack.

A national clinical trial of this concept, led by Sharma, will begin later this year.

"Companies with immunotherapy drugs had largely given up on prostate cancer, yet research has presented another opportunity," Sharma says.

They've also identified a third immune checkpoint that might be hindering immunotherapy for the disease.

There are about 165 clinical trials of various immunotherapies underway at MD Anderson, most of which involve some type of checkpoint blockade or immune-stimulating molecule. These trials generally focus on:

- Extending immunotherapy to other types of cancer such as leukemia, colorectal, pancreas, lymphoma, glioblastoma and cancers caused by the human papilloma virus (HPV).
- Testing immunotherapy drugs in combinations with each other or with targeted therapies, radiation, and surgery to broaden and deepen patient response and survival.
- Comparing these treatments, which are approved for late-stage disease, with standard of care at earlier disease stages to see if immunotherapy might be used earlier.

Pharmaceutical companies are bringing new drugs to trials that seek to stimulate or protect immune response in new ways.

Allison and Sharma, who also are director and co-director of the Parker Institute for Cancer Immunotherapy at MD Anderson, wrote reviews last year in the journals Science and Cell outlining how research can advance the field.

Well-thought-out combinations, they wrote, are the key to "development of new, safe treatments that may prove to be curative for many patients with many types of cancer."

Under an agreement reached this summer with Bristol-Myers Squibb, the developer of both nivolumab and ipilimumab, MD Anderson researchers will test new ways to treat lung cancer at all stages of the disease.

Currently, the standard of care for early-stage lung cancer is surgery. Clinical trials under the agreement will look at:

- Treating inoperable early-stage disease with immunotherapy, followed by targeted radiation.
- Giving patients whose disease is operable immunotherapy before and after surgery, seeking to cut the recurrence rate of lung cancer down from 50%.
- Providing immunotherapy followed by aggressive "consolidation therapy" either surgery or radiation for those with metastatic disease.

"These trials will allow us to integrate immunotherapy in innovative ways with other treatments, including surgery and radiation, to improve standard of care and expand treatment options for all patients, including those with early-stage disease," says John Heymach, M.D., Ph.D., chair of Thoracic/ Head and Neck Medical Oncology.

As a volunteer, brain cancer survivor offers coffee, tea and hope to patients and caregivers By Lany Kimmons

n 2005, Benjamin Chang had just graduated from Stanford University and was eager to start a career in mechanical engineering when he started to lose his vision.

It began slowly. First, his depth perception disappeared, which caused him to misjudge distances between objects and bump into furniture. As his condition worsened, he began tripping over curbs and could no longer go for a run or ride a bike — his two favorite activities — because he felt off-balance.

"I wasn't sure what was happening, but I knew something was wrong," recalls Chang.

After visiting his mother over the winter break, he made the decision to leave California and move back in with his family in Houston.

Chang immediately went to see an ophthalmologist and was diagnosed with a rare brain tumor that was pushing on his optic nerve, causing the vision loss. After undergoing surgery, his mother's best friend urged him to seek treatment at MD Anderson, where he received 28 days of radiation. He also went through six months of physical therapy and met with a counselor — both helped him cope with the physical and emotional stress of his vision loss.

As a young adult with cancer, it wasn't easy for Chang to move back in with his parents and come to grips with the loss of his sight and his independence.

"At first I was angry," he says. "Although it was frustrating, I tried to understand others' viewpoints and remain calm."

He also found it helpful to be upfront with people about his diagnosis, instead of allowing others to make assumptions about him and his abilities.

Though Chang thought everyone at MD Anderson was very kind, what really stood out to him were the volunteers. They came by each morning to offer magazines and conversation, which made him comfortable. They made him feel that he was not alone, and brightened his days in the hospital. This inspired him to become a volunteer himself.

Chang says "that he volunteers not for himself, but to give back." He says it's more rewarding for him than the people he serves.

Chang began volunteering in December 2011 after serving two years as a member of MD Anderson's Adolescent and Young Adult Advisory Council. Made up of for-

mer patients and employees, the council meets monthly to find new ways to enhance the experiences of young patients.

Today, he puts on his blue volunteer jacket every Thursday morning before his shift in the Mays Clinic Hospitality Center, where he offers patients and caregivers coffee, tea and refreshments. More importantly, he and his fellow volunteers offer hope, support, laughter and helpful information.

Chang now works for an environmental engineering firm. His condition is stable and he follows up with his MD Anderson team once a year. His outlook is bright and he continues to look ahead to the future.

"I tell patients to keep looking forward and have a positive attitude," he says. "I know that it can be hard, but I tell them to take things as they are."



Wyatt McSpadden

MD Anderson's first Hospitality Center opened in 1987. Today, its two hospitality centers average more than 114,500 visitors a year. Each weekday from 8 a.m.-3 p.m., myCancerConnection survivor and caregiver volunteers staff the centers and offer free coffee, tea, crackers or cookies to patients and caregivers.

To learn more about volunteering at MD Anderson, call 713-792-JOIN.

LOCATIONS

Main Building Floor 2, near The Sundial Mays Clinic Floor 2, near Elevator T, ACB 2.1002

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The origin of The Cancer Genome Atlas may be traced, in part, to John Weinstein, M.D., Ph.D., MD Anderson's chair of Bioinformatics and Computational Biology.

Nick de la Torre

hen President Barack Obama called for a \$1 billion National Moonshot Initiative to accelerate cancer research and "make America the country that cures cancer once and for all," he looked to Vice President Joe Biden to head the effort.

Biden's leadership — no doubt inspired by the death of his son Beau in 2015 from brain cancer — has involved attending key professional cancer research meetings and the formation of the Vice President's Exceptional Opportunities in Cancer Research Fund. The fund encourages scientists, physicians, advocates, philanthropic organizations and representatives of the biotechnology and pharmaceutical industries to work together and share data to generate new ideas and new breakthroughs.

How MD Anderson researchers are working with The Cancer Genome Atlas to unravel the mysteries of the disease

That sort of collaboration has been an important part of a program largely unknown to many Americans: The Cancer Genome Atlas (TCGA). Launched in 2005, and funded jointly by the National Cancer Institute and the National Human Genome Research Institute, TCGA makes cancer research data openly available to the research community to accelerate understanding of the molecular underpinnings of the disease and provide avenues to potential new

therapies. Although the program is in its final year of existence, it has been key to invaluable contributions to cancer science and laid the foundation for further exploration through new collaborative programs. MD Anderson has played an integral role in TCGA — from its formation to the present — through leadership and participation in TCGA-related studies.

Data from the Cancer Genome Atlas and other studies "has clarified that cancer is a disease of the genome," wrote Douglas Lowy, M.D., acting director of the National Cancer Institute (NCI), and Francis Collins, M.D., Ph.D., director of the National Institutes of Health (NIH) in the May 19, 2016, issue of the New England Journal of Medicine. "It has become increasingly apparent that knowing what driver mutations are present in a particular tumor is often more important than knowing which organ system it arose from. Genomic technology has also shown that although each tumor is molecularly unique, certain pathways are repeatedly affected — findings that have informed the design and use of a new generation of drugs targeting those pathways."

Data tsunami

The origin of TCGA may, in part, be traced to John Weinstein, M.D., Ph.D., chair of Bioinformatics and Computational Biology at MD Anderson. But it almost didn't happen.

It began back in 1991 when Weinstein, who was then working at the NCI, was planning to take the day off. Then he remembered his boss was

speaking at Grand Rounds that day. Going to work was a fortuitous decision that would lead Weinstein to pursue the development of vital data-related programs that would ultimately influence the creation of TCGA.

"During his talk, I had an idea that led to my laboratory group spearheading a comprehensive molecular profiling of the NCI-60, a set of 60 human cancer cell lines used by the NCI to screen more than 100,000 chemical compounds, plus natural products, for anti-cancer activity," says Weinstein.

He calls the supernova explosion of data resulting from these earlier efforts a "data tsunami," and likens the TCGA to a "12,000-square chess board of patient samples."

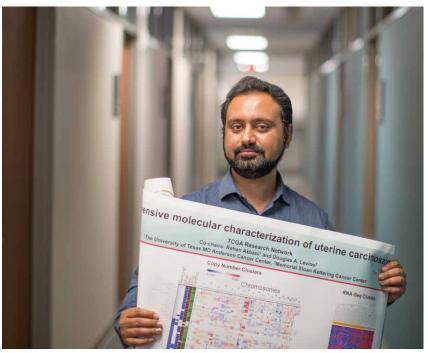
"It provides us a context within which to work out the rules of the genomic game and generate useful, potentially significant results, benefiting cancer patients and their families," he says.

Those results can provide researchers with a fresh look at how tumors are developing, and point the way to new therapies. Weinstein often is referred to as a "pioneer of postgenomic biology" in part for another one of his inventions: clustered heat maps. These maps allow researchers to visualize patterns in the huge masses of data and more quickly take advantage of them. Clustered heat maps have appeared in many thousands of publications, and Weinstein's group has now developed "Next-Generation Clustered Heat Maps (NG-CHMs)," which can be zoomed in on and navigated like a Google map. NG-CHMs are routinely used for data from many different cancer types in TCGA.

Today, TCGA is a massive effort that is studying genomic changes in more than 30 different cancer types and, according to Rehan Akbani, Ph.D., assistant professor of Bioinformatics and Computational Biology, MD Anderson is a "heavy hitter and proud participant in every one of TCGA's disease working groups."

"The MD Anderson Genome Data Analysis Center (GDAC) has established itself as the premiere provider of reverse-phase protein array (RPPA)-based TCGA proteomics data and analysis as well as batch effects analysis and data quality control," says Akbani.

Batch effects are the findings and results that occur due to technical artifacts when aggregating data from multiple institutions with varied computer systems, lab procedures and data collection methods. MD Anderson's work with assessing batch effects has helped assure that the data being studied by research institutions worldwide via TCGA are accurate and consistent. RPPAs involve performing protein assays on thousands of samples simultaneously, allowing measurements of protein expression, as well as protein modifications such as phosphorylation, which turn protein enzymes on and off.



Rehan Akbani, Ph.D., assistant professor of Bioinformatics and Computational Biology

Nick de la Torre

"What motivates me every day is the thought that somewhere in these datasets the answer to how to improve patient outcomes might be buried," says Roeland Verhaak, Ph.D. "And that is what it is all about in the end."

Finding the treasure

Sifting through enormous amounts of data has often been referred to as "mining," and scientists are the treasure-seekers in search of valuable nuggets that will lead to a better understanding of cancer's molecular workings.

MD Anderson investigators have had significant success in mining TCGA data and, working with multiple partners at cancer research institutions globally, have made important discoveries about the molecular nuances of cancer cells.

"MD Anderson researchers not only have contributed at a leadership level to The Cancer Genome Atlas, helping to ensure its success, but we also have participated in and served as lead investigators for TCGA-based studies that have opened up new possibilities for cancer diagnosis and treatment," says MD Anderson President Ronald DePinho, M.D. "I am proud of the effort that has gone into this pioneering program, and I know we will continue to benefit from the data for many years to come."

Revelations about two aggressive cancers

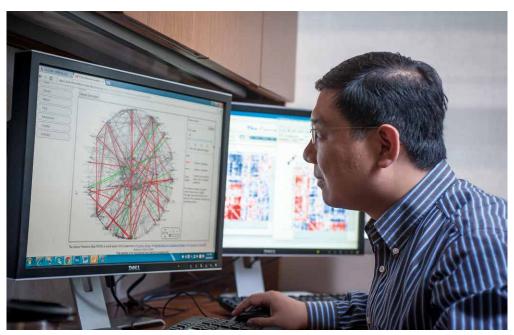
Roeland Verhaak, Ph.D., associate professor of Bioinformatics and Computational Biology, has led research investigations based on TCGA data that have revealed startling findings for two aggressive forms of cancer.

Earlier this year, Verhaak published findings from a study co-led by the University of São Paulo's Ribeirão Preto Medical School and Columbia University that revealed new information about diffuse glioma, which is found in some adult brain cancer patients.

Analyzing TCGA data, the team defined a complete set of glioma-associated genes from patient samples and used molecular profiling to improve disease classification. They were able to identify molecular correlations and provide insight into disease progression from low to high grades.

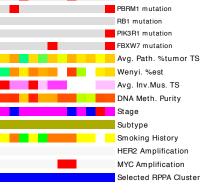
Another study, led by Verhaak and colleagues at the University of Michigan, revealed significant new findings about adrenocortical carcinoma (ACC), a rare cancer typically associated with poor prognosis.

The researchers — including those from 39 international institutions — examined 91 ACC tumor specimens from four continents and observed "massive" DNA loss followed by whole genome doubling (WGD). WGD occurs when tumor cells acquire an extra copy of their entire genome. The researchers found that WGD was associated with an aggressive clinical course, suggesting that it could be a hallmark of disease progression. They speculated that tumor growth could be slowed if they could prohibit WGD in future pre-clinical studies. "The true value of TCGA will probably not be recognized until years from now," says Rehan Akbani, Ph.D. "As John Weinstein said so eloquently, 'It is the work of a generation to mine all of this information, and although the project is concluding, it is really just the beginning.'"



Data from The Cancer Genome Atlas plays a vital role in the research of Han Liang, Ph.D., associate professor of Bioinformatics & Computational Biology.

Wyatt McSpadden



After TCGA comes to a close in early 2017, new NCI genomics initiatives run through the NCI's Center for Cancer Genomics (CCG) will continue to build upon TCGA's success by using the same model of collaboration for large-scale genomic analysis and by making the genomics data publicly available.

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The effects of RNA editing and gender on cancer

Han Liang, Ph.D., associate professor of Bioinformatics & Computational Biology, also has relied on TCGA data in his research.

The Cancer Genome Atlas glossary

Genome: The complete set of DNA (genetic material) in an organism. Almost every cell in the human body contains a complete copy of the genome. The genome contains all of the information needed for a person to develop and grow. Studying the genome may help researchers understand how different types of cancer form and respond to treatment. This may lead to new ways to diagnose, treat and prevent cancer.

The Cancer Genome Atlas has generated comprehensive, multidimensional maps of the key genomic changes in 33 types of cancer.

The TCGA dataset is 2.5 petabytes of data describing tumor tissue and matched normal tissues from more than 11,000 patients. It's available to the public and has been used widely by the research community.

How big is a petabyte? One petabyte is equal to 900 billion pages of plain text. According to a New York Times story on science and data, it's roughly equivalent to 799 million copies of "Moby Dick."

GENOME DATA ANALYSIS CENTERS (GDACS)

Immense amounts of data from array and second-generation sequencing technologies must be integrated across thousands of samples. These centers provide novel informatics tools to the entire research community to facilitate broader use of TCGA data. MD Anderson is home to two GDACs.

Genome Characterization Centers (GCCs) are responsible for characterizing all of the genomic changes found in the tumors studied as part of the TCGA program. The GCCs use state-of-the-art technologies to analyze genomic changes involved in cancer and provide this data to the cancer research community.

MD ANDERSON'S ROLE IN THE CANCER GENOME ATLAS

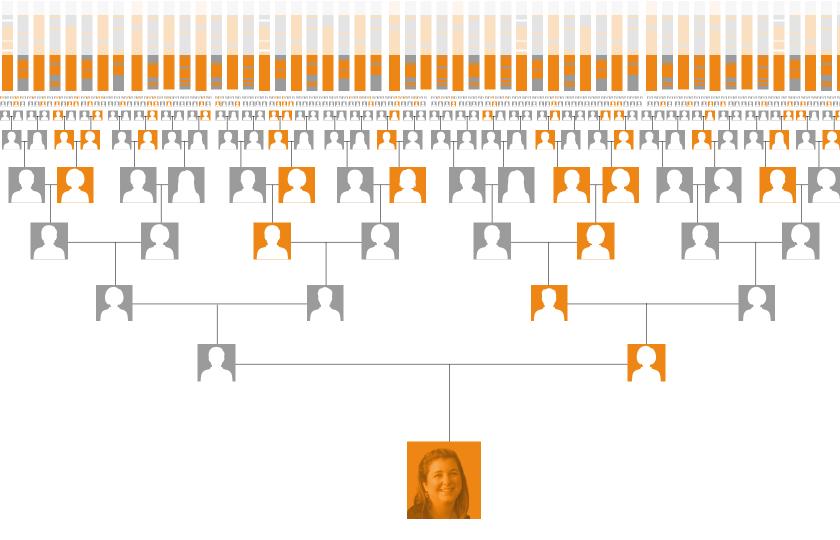
MD Anderson has played a leading role in establishing TCGA's Genome Characterization Centers. Gordon Mills, M.D., Ph.D., chair of Systems Biology, heads up the Proteomics GCC, which is aimed at improved analysis of cancer cell proteins with the goal of identifying proteins that could be used as drug targets or biomarkers for screening and diagnosis.

MD Anderson also leads two of TCGA's seven Genome Data Analysis Centers, which work with the GCCs to develop tools that help researchers process and integrate vast amounts of data analyses from across the entire genome.

MD Anderson principal investigators and co-PIs for two of the GDACs are Weinstein, Akbani, Mills and Al Yung, M.D., professor of Neuro-Oncology.



INHERITING A GREATER RISK FOR CANCER



More than 50 hereditary cancer syndromes have been identified to date. Genetic testing can lead to early detection and prevention of cancer.

By Clayton Boldt, Ph.D.

hen Nonnie Arriola was diagnosed with breast cancer at age 37, her first question was, "Why?" No one in her family had cancer, and Arriola was surprised to be diagnosed with the disease at such a young age.



After her breast cancer diagnosis, Nonnie Arriola, left, learned she had a BRCA1 mutation. The inherited mutation raises the risk for breast and ovarian cancers. Genetic testing also revealed her mother, Becky Carson, and her daughter, Brianna, carry the mutation.

Wyatt McSpadden

"I thought it might be genetic," she says. "I worried about my family and my children."

Hereditary cancers are caused by genetic mutations passed down from parents to children. The National Cancer Institute estimates these genetic "mistakes" play a role in about 5 to 10% of all cancers. More than 50 hereditary cancer syndromes have been identified, and genetic tests have been developed to detect many of these.

"New patients want to know, 'Why did I get this disease and is my daughter at risk?" says Karen Lu, M.D., chair of Gynecologic Oncology and Reproductive Medicine. "In some cases, we can actually give them that answer."

Knowing that a particular cancer is hereditary is extremely powerful, not only for patients but also for their families, says Banu Arun, M.D., professor of Breast Medical Oncology.

Lu and Arun are co-medical directors of MD Anderson's Clinical Cancer Genetics program. Launched in 2002, the program employs 13 counselors in multiple MD Anderson clinics to advise patients diagnosed with inherited forms of cancer.

"Physicians in those clinics are aware of the importance of genetic testing and champion the program," says Arun. "The process is simple."

Counselors first meet with patients to discuss family history and determine if testing is necessary. Patients who decide to proceed undergo

a simple blood draw. Results are back within weeks. Counselors and patients discuss the results and potential next steps.

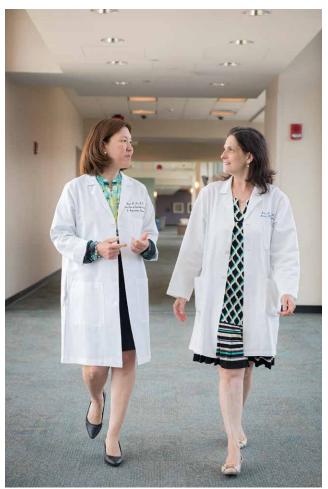
After undergoing genetic testing, Arriola learned she had a BRCA1 mutation, which significantly increases the risk of developing breast and ovarian cancers. After completing treatment, she had a double mastectomy to reduce the risk of the cancer recurring. Earlier this year, she completed reconstructive surgery and is doing well.

First-degree relatives — parents, siblings or children — of people with cancer-causing genetic mutations have a 50% chance of inheriting the same mutation, which dramatically raises their own cancer risk. They're treated in MD Anderson's high-risk clinics, where they may undergo more stringent cancer screenings, take anti-cancer drugs, are encouraged to adopt healthier lifestyles, or even have surgery to remove ovaries, fallopian tubes and/or breasts — an option known as preventive or prophylactic surgery.

"It's a positive ripple effect for the family," says Arun. "We've found when relatives are tested and take preventive measures, they can avoid the devastating cancers that run in their families."

After undergoing genetic testing, Arriola's mother and daughter discovered they carry her same BRCA1 mutation. They're taking action.

"My mother was having yearly mammograms but is now going every six months. She's also having her ovaries removed this year," Arriola explains. "My daughter is only 20, but she'll start screening early and



Karen Lu. M.D., left, and Banu Arun, M.D., are co-medical directors of MD Anderson's Clinical Cancer Genetics program. Wyatt McSpadden

is considering future options. She wants to have kids one day, and now knows she may need to start earlier than planned."

Arriola also is undergoing regular ovarian cancer screenings.

Clinical Cancer Genetics program faculty members are conducting research to increase existing knowledge. They're building an evergrowing genetic database that's influencing screening guidelines and prevention strategies.

Current guidelines recommend that women with BRCA1 or BRCA2 mutations have their ovaries and fallopian tubes removed by ages 35 to 40, explains Lu, although doing so will cause early menopause.

However, research conducted in the last five years suggests ovarian cancer may begin in the fallopian tubes. An ongoing clinical trial conducted through MD Anderson's High Risk Ovarian Cancer Screening Clinic will determine if a two-stage surgery — removing the fallopian tubes first and ovaries later — can delay menopause while still preventing cancer.

Studies like this are made possible through information obtained through genetic testing.

"We know that patient care and research goes hand in hand," Arun says. "We need to ask and answer meaningful clinical questions while we're seeing patients."

Heredity's role in cancer

Below is the National Cancer Institute's list of the most common inherited cancer syndromes, the gene or genes that are mutated in each, and the types of cancer most often associated with them.

Hereditary breast cancer and ovarian cancer syndrome

Genes: BRCA1, BRCA2

Related cancer types: Female breast, ovarian, and other cancers, including prostate, pancreatic and male breast cancer

Li-Fraumeni syndrome

Gene: TP53

Related cancer types: Breast cancer, soft tissue sarcoma, osteosarcoma (bone cancer), leukemia, brain tumors, adrenocortical carcinoma (cancer of the adrenal glands) and other cancers

Cowden syndrome (PTEN hamartoma tumor syndrome)

Gene: PTEN

Related cancer types: Breast, thyroid, endometrial (uterine lining) and other cancers

Lynch syndrome (hereditary nonpolyposis colorectal cancer)

Genes: MSH2, MLH1, MSH6, PMS2, EPCAM

Related cancer types: Colorectal, endometrial, ovarian, renal pelvis, pancreatic, small intestine, liver and biliary tract, stomach, brain and breast cancers

Familial adenomatous polyposis

Related cancer types: Colorectal cancer, multiple non-malignant colon polyps, and both non-cancerous (benign) and cancerous tumors in the small intestine, brain, stomach, bone, skin and other tissues

Retinoblastoma

Gene: RB1

Related cancer types: Eye cancer (cancer of the retina), pinealoma (cancer of the pineal gland), osteosarcoma, melanoma and soft tissue sarcoma

Multiple endocrine neoplasia type 1 (Wermer syndrome)

Gene: MEN1

Related cancer types: Pancreatic endocrine tumors and (usually benign) parathyroid and pituitary gland tumors

Multiple endocrine neoplasia type 2

Gene: RET

Related cancer types: Medullary thyroid cancer and pheochromocytoma (benign adrenal gland tumor)

Von Hippel-Lindau syndrome

Gene: VHL

Related cancer types: Kidney cancer and multiple noncancerous tumors, including pheochromocytoma



ROBERT SATCHER HAS ALWAYS REACHED FOR THE STARS.

By Ronda Wendler

s a child, Robert Satcher dreamed of becoming an astronaut, an engineer and a doctor. He couldn't decide on one, so he became all three.

"I was always pushing the boundaries," he says, "looking for the next big adventure."

Today, he's an orthopedic oncology surgeon who treats bone cancer patients at MD Anderson. But his high-flying résumé also includes stints as a chemical engineer and a NASA astronaut.

Taste for adventure

Satcher grew up in the coastal town of Hampton, Virginia, where his father was a chemistry professor at Hampton University, a historically black institution, and his mother was an English teacher.

An avid encyclopedia reader who devoured articles about early explorers, young Satcher would stroll along the Virginia coastline and imagine ships from long ago on the horizon, making their way to shore. On board were the British colonials, Spanish conquistadors, French Huguenots and others who would colonize the Americas.



Robert Satcher, M.D., Ph.D., assistant professor of Orthopaedic Oncology, participated in two spacewalks during his 11-day mission on the International Space Center in 2009. Wyatt McSpadden

"I wondered what it was like to put your entire life on the line and sail to the other side of the world," he says, "not knowing what you would find. How exhilarating and terrifying that must have been. I wanted to be part of that."

Satcher enjoyed science and math and "tinkering with things to make them work." At age 16 he enrolled in MIT where he majored in chemical engineering and graduated at the top of his class. But halfway through college, his interests began shifting toward medicine.

"A lot of my engineering classwork focused on solving medical problems," he explains.

After graduating, he enrolled at Harvard University and earned his M.D. while simultaneously completing a Ph.D. in chemical engineering at MIT. "I appreciated how engineering interfaced with medicine."

Along the way, he met several physicians and scientists who were also astronauts, including Ronald McNair, who later would die during the launch of the Space Shuttle Challenger in 1986, Leland Melvin, an aeronautics engineer and fellow Virginian, and Scott Parazynski, a veteran of five Space Shuttle flights and seven spacewalks. They shared their tales of adventure with Satcher, and he was hooked.



Satcher and his fellow astronauts trained at the bottom of a 40-foot pool, where conditions mimic the weightlessness of space. 🛛 NASA

"I've always been interested in space travel," says Satcher, who grew up watching "Star Trek," "Star Wars" and "2001: A Space Odyssey." "But as I got older, I dismissed it as a childhood fantasy."

But meeting fellow physicians who were astronauts convinced him that, "if they could do it, so could I."

While working as an orthopedic oncologist at Northwestern University in Chicago, he succumbed to space's pull and sent an application to NASA.

"My family and friends thought I was crazy," he says, "but I had to try."

It turns out he wasn't crazy. He was accepted into NASA's astronaut training program.

"I packed up," Satcher says, "and headed to Houston."

Practice makes perfect

Like surgical education, astronaut training was rigorous.

Practicing for spacewalks takes place mostly underwater, where conditions are similar to the weightlessness of space. Astronauts dive to the bottom of a 40-foot-deep NASA swimming pool that is two-thirds the length of a football field.

Full-scale working models of the Space Shuttle and the International Space Station's experiment areas are submerged in the pool. This allows astronauts to practice every experiment or project they'll perform while on board the shuttle or space station, before they head into orbit.

"Any task to be done in space is first rehearsed over and over again in the pool," Satcher says. "Practice makes perfect, and when the environment is as foreign as the solar system, it's a good idea to log as many practice hours as possible."



NASA

To mimic the absence of light in deep space, pool training sometimes takes place in virtual darkness, with only a helmet-mounted headlamp providing a narrow beam of illumination.

"You don't have cues to tell you which way is up and which way is down," Satcher says. "It's disorienting, but you adjust and you keep working."

Mission accomplished

In 2009, Satcher's training paid off when he and five other crew members boarded the Space Shuttle Atlantis and skyrocketed 220 miles to the International Space Station (ISS).

During the 11-day mission, dubbed STS-129, the doctor-turned-astronaut participated in two spacewalks. Hovering high above the Earth while tethered to a safety harness, Satcher used the same surgical skills required for complex joint replacements to help repair two robotic arms on the space station's exterior. He also installed an antenna

to improve satellite communication. Crew members nicknamed him "the cable guy."

The ISS, which travels at a speed of 17,150 miles per hour, covered approximately 4.5 million miles during the mission.

"I wish I'd earned frequent flyer miles," Satcher quips. "I'd be set for life."

And floating outside the spacecraft in a spacesuit afforded Satcher "spectacular" views.

"The colors on Earth are fantastic, like nothing you've ever seen. There's no crayon in the crayon box or Hollywood production to match what I saw."

Drifting silently above Earth while looking back at the planet that looks "just like a globe," is awe-inspiring and humbling, Satcher says.

"Earth is just a dot in the universe — a tiny, miniscule dot."

Fat faces and more

But Satcher couldn't be a tourist for long.

"Spacewalks average six to seven hours each, and you're working the entire time," he says. "The tasks are very involved and detailed. I had to pace myself and keep focused, just like in an operating room. My surgical training helped."

Aboard the shuttle, he conducted experiments to determine how weightlessness affects the immune system, and how astronauts' height changes when they go into outer space.

"They get taller," he says. "Low-gravity conditions elongate the spine."

Satcher grew two inches taller in space. Already 6'4" before the launch, he worried about fitting into the spacesuit he'd wear when re-entering Earth's atmosphere.

"Fortunately, I squeezed in and made it fit," he says.

Satcher also was the mission's medical doctor and helped crew members deal with some unique medical problems.

"One of the first things astronauts complain about," he says, "is nausea and vomiting."

Apart from the unpleasantness of vomit globules floating around the capsule, space sickness can impede an astronaut's piloting skills, he says.

"Weightlessness affects your inner ear, which throws off your balance, coordination and spatial orientation. Try navigating a shuttle under those conditions."

Sleep deprivation is another frequent problem. At the speed it travels, the International Space Station orbits the Earth every 92 minutes, affording astronauts a view of 16 sunrises each day.

"Who could sleep through all that?" Satcher asks. "You spend a lot of time wide awake in outer space."

Nasal stuffiness and congestion is another common complaint.

"Being in space is like standing on your head," Satcher says. "Without gravity, blood tends to float up to your face, which causes you to feel stuffy."

"Fat face syndrome" is how he describes it.

"You look funny and you feel funny."

Satcher retired from NASA and joined MD Anderson in 2011, but his taste for adventure persists. Someday, he says, he may go back.

"There's nothing like those last 15 seconds or so of the countdown, when you realize you're on your way. It's a thrilling ride."

ONTOP OF THE WORLD

Ellen Baker: MD Anderson doctor and NASA astronaut

When Ellen Baker, M.D., was completing medical school in the late 1970s, she read a newspaper article that announced NASA was accepting astronaut applications. Women, in particular, were urged to apply.

"I never imagined I could be an astronaut," Baker says. "When I was growing up, only boys became astronauts."

But the newspaper article got Baker thinking about the possibility of a career in space exploration. After completing an internal medicine residency, she joined NASA as a medical officer in 1981, and was selected as an astronaut in 1984.



Ellen Baker, M.D.

NASA

Over the next 11 years, she flew in space on three missions:

1989, mission STS-34

The crew of Space Shuttle Atlantis deployed the Galileo probe to explore Jupiter, mapped atmospheric ozone on Earth and conducted medical and scientific experiments.

1992, mission STS-50

Space Shuttle Columbia was the first flight of the United States Microgravity Laboratory and the first Extended Duration Orbiter flight. For more than two weeks, the crew conducted scientific experiments involving crystal growth, fluid physics, fluid dynamics, biological science and combustion science.

1995, mission STS-71

This was the first space shuttle mission, flown aboard Atlantis, to dock with the Russian Space Station Mir, and involved an exchange of the station crew. The crew also performed various life sciences experiments and data collections.

After returning from space, Baker held a variety of NASA positions that supported the Space Shuttle, Space Station and Exploration Programs. She also was appointed chief of the medical branch and education branch for NASA's Astronaut Office.

In 2011, she retired from NASA. She joined MD Anderson in 2014, where she heads Project ECHO (Extension for Community Healthcare Outcomes). The ECHO program connects cancer specialists at MD Anderson with providers in rural and urban areas, domestically and internationally, who work with underserved populations.

Spaceflight gave Baker a deep appreciation for the "oneness" of Earth.

"From space you can't see where one country starts and where another ends," she says. "It makes you feel that we're all one people."



Space Suit Art Project lifts off

By Katrina Burton

unique collaboration that spotlights the similar challenges faced by children battling cancer and NASA astronauts exploring space has launched at

MD Anderson Children's Cancer Hospital.

It's called the Space Suit Art Project, and through it, pediatric patients and their families, as well as NASA astronauts and the hospital's staff, are hand-painting decorative fabric swatches that are then stitched together to create two replica spacesuits.

So far, the project has produced a spacesuit named "HOPE" from more than 600 swatches painted by patients, families, astronauts and MD Anderson staff. A second suit, "UNITY," will be assembled from hand-painted swatches provided by the space centers that partnered to build the International Space Station and by children's hospitals around the world, symbolizing the global issues surrounding childhood cancer.

A third suit, "COURAGE," is not a patchwork suit, but a NASA-issue flight suit hand-painted by patients, their families and hospital staff. On July 18, COURAGE flew aboard a cargo vessel to the International Space Station where it will be worn by astronaut Kate Rubins, who is conducting research aboard the space station.

The Space Suit Art Project was developed through the hospital's Arts in Medicine Program, which helps pediatric patients cope with cancer treatment through art.

"Art is a creative way for patients to forget about their treatment. I've seen patients' spirits lifted when they come to my art classes," says Ian Cion, program director of the Arts in Medicine Program. "When I told them that their artwork would be used on spacesuits, they were really excited."

Retired NASA astronaut Nicole Stott collaborated on the project. Stott is the first astronaut to paint what she saw while looking out the window of the International Space Station.

"The Space Suit Art Project is the most meaningful project I've ever been apart of," says Stott. "The power and inspiration of the artwork that each of these kids are producing is overwhelmingly impressive. I'm in awe of the very positive impact I see on everyone participating."

Jacob Ballard, a 17-year-old Ewing's sarcoma survivor, provided artwork for the first two suits.

"I'm excited to tell people that my art went to space," he says. "One day, I hope to work with the space exploration vehicles at NASA."









Top photo, from left: Ellen Ochoa, Ph.D., retired astronaut and director of Johnson Space Center, Lorenza Fabre, Ian Cion, retired astronaut Nicole Stott, Clara Fabre and MD Anderson President Ronald DePinho attended the unveiling of the Space Suit Art Project. Pediatric patients from MD Anderson Children's Cancer Hospital and their families, along with NASA astronauts and MD Anderson staff, hand-painted decorative fabric swatches that were stitched together to create the suits.

A Healing Light

How lasers are used to attack 'inoperable' brain and spinal tumors

By Ronda Wendler

hen Allison Easley awoke one morning with soreness under her right armpit, she thought she'd pulled a muscle. But the pain soon became worse, and her lymph nodes started to swell.

"I wondered if I'd caught an infection from one of the kids," says Easley, 29, a special events photographer who days earlier had taken class portraits at an elementary school.

Antibiotics prescribed by her family doctor didn't help, and when her pain became unbearable, Easley, who lives just north of San Antonio, visited her local emergency room. Doctors there did a lymph node biopsy and found melanoma, the deadliest form of skin cancer. It wasn't Easley's first encounter with the disease.

Ten years earlier, at age 19, she'd been diagnosed with melanoma when a suspicious-looking mole alerted doctors to the disease. They surgically removed it, allowing Easley to live cancer-free for almost a decade.

But now, the melanoma was back with a vengeance. Imaging scans revealed thirty tumors scattered throughout her body. Within months, six would spread to her brain.

"The possibility I'd relapse was always at the back of my mind," Easley says. "When you've had cancer, you're always waiting for the other shoe to drop."

Her cancer had been spreading swiftly and silently, and was now stage 4 — the most advanced form of the disease.

This time, Easley sought care at MD Anderson, where doctors prescribed chemotherapy, radiation and powerful new immunotherapy drugs that rallied her immune system and helped her body fight hard. The drugs eliminated all Easley's tumors — except those in her brain.

"A protective network of blood vessels known as the blood-brain barrier prevents foreign substances from crossing into the brain, but it also can prevent life-saving drugs from entering," says Ganesh Rao, M.D., associate professor of Neurosurgery at MD Anderson's Brain and Spine Center.

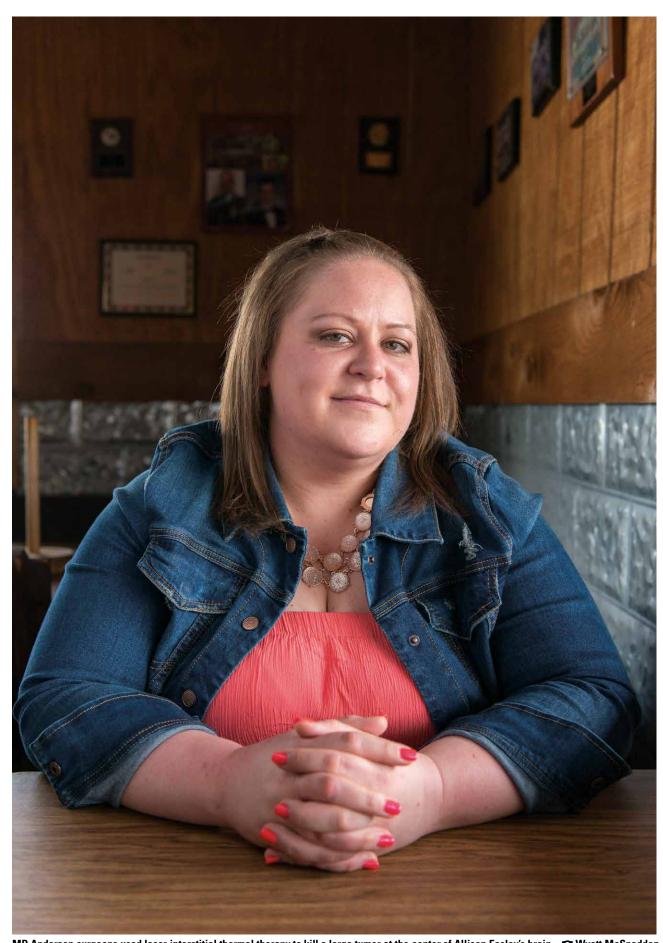
Brain surgery to remove Easley's tumors seemed like her only remaining option, but there was a problem. A particularly large tumor had embedded itself deep in the center of her brain, between the right and left hemispheres. Any attempt to reach it surgically would most certainly damage areas that control motor skills affecting coordination and movement.

"This is the juncture where many doctors tell patients their condition is inoperable," says Rao. "But at MD Anderson, we have another way to reach unreachable tumors."

Turning up the heat

The cancer center is one of a select few in the nation using a probe that's specially designed to heat and destroy brain and spinal cord tumors — regardless of their size or location. The treatment is known as laser interstitial thermal therapy, or LITT. Put simply, the name means that laser heat penetrates interstitially — inside tissue — to destroy tumor cells.

"Many types of tumors previously thought to be inoperable can be treated with this technology, including aggressive tumors that originate in the brain or spinal cord, or tumors that have spread to the brain or spine from other areas of the body," says Sujit Prabhu, M.D., a professor of Neurosurgery who works side by side with Rao in the Brain and Spine Center. "We're visited by a lot of patients from around the world who've been told nothing can be done. We offer them LITT."



MD Anderson surgeons used laser interstitial thermal therapy to kill a large tumor at the center of Allison Easley's brain. 💿 Wyatt McSpadden

How it works

To perform the procedure, surgeons first study MRI scans of the patient's brain to create a map of coordinates they'll follow as they navigate the probe through the brain and into the tumor. The patient is then put to sleep with general anesthesia and placed inside an MRI machine that's open on both ends.

Next, a dime-sized hole is drilled in the patient's skull, and the probe is inserted into the brain. Guided by the previously mapped coordinates, the surgeon carefully advances the probe through the brain and into the middle of the tumor. Because the probe is no wider than a pencil lead, it creates the tiniest of tunnels.

"Tissue damage is nil or close to nil — nothing like that caused by surgical instruments," says Prabhu.

With the probe in place, the doctor fires a laser beam from its tip. Intense heat emanates from the laser and destroys the tumor's cells.

"Each burst lasts anywhere from 30 seconds to a few minutes and generates heat ranging from 158 to 176 degrees Fahrenheit," Rao explains. "It 'cooks' the tumor from the inside out."

Because the patient is continuously imaged inside the MRI, the surgeon can watch the tumor destruction on a monitor as it's happening. With each firing of the laser, the tumor turns green, yellow, orange, then red as it becomes increasingly hotter. Temperatures are displayed on-screen, confirming that the targeted tissue is thoroughly "cooked" and dead.

Multiple passes with the probe can be made for larger tumors.

"The system knows to burn precisely to the edges of the tumor without crossing over into healthy tissue," Rao says. "A built-in, emergency off switch engages automatically if the laser heat starts going where it shouldn't."

The key to success, Rao says, is achieving the right temperature in the right spot.

"With this technology, we have that assurance," he says. "We watch the cancer cells on-screen as they're dying."

After Rao used the procedure on Easley eight months ago, five of her six brain tumors vanished, and the sixth — the troubling one buried deep in her brain — has shrunk to a fraction of its original size.

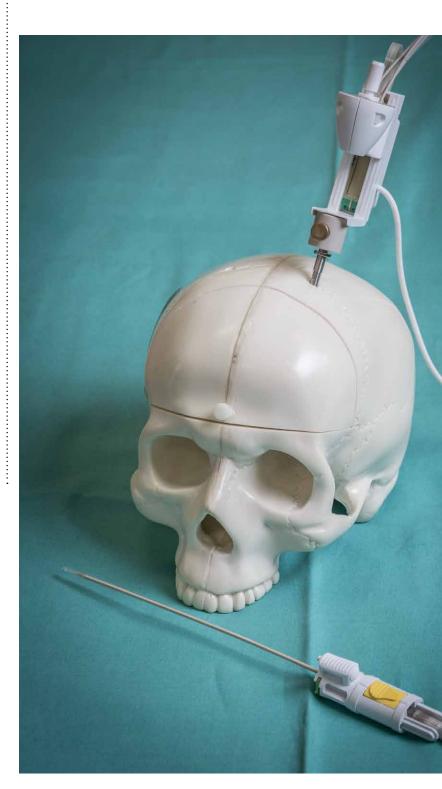
From left: Claudio Tatsui, M.D., Ganesh Rao, M.D., and Sujit Prabhu, M.D., are neurosurgeons in the Brain and Spine Center who use LITT to remover cancer in delicate parts of the body.

Nick de la Torre

"I return to MD Anderson every three weeks for scans, and each time the tumor has shrunk a little more," she says. "Pretty soon, it won't be there at all."

Easley looks forward to hearing she's "NED," a medical acronym meaning "no evidence of disease."

"The three most beautiful letters in the alphabet," she says with a grin.



Pamela's story

Like Easley, Pamela Lynn had cancer that at first glance seemed inoperable.

Lynn, a high-tech firm retiree, visited her family doctor two years ago complaining of abdominal discomfort. A CT scan revealed a 3-pound, football-shaped tumor on her kidney. The tumor had spread to multiple spots on her lungs and to two locations on her spine.

"I was flabbergasted," says the 62-year-old resident of Round Rock, Texas, just north of Austin. "I don't smoke, I don't drink, and no one in my immediate family has had cancer."

Doctors at Lynn's local hospital spent nine hours removing her left kidney with its attached tumor. In the same surgery, they removed only a small piece of one spinal tumor, and didn't try to remove the second one.

The tumors, they said, were inoperable.

"They were wrapped around the spinal cord, touching vital nerves and arteries, and the doctors just couldn't risk removing them," says Lynn, who spent four days recovering in the hospital with hooks and screws implanted in her spine to keep it from collapsing.

Not ready to give up, Lynn headed to MD Anderson, where she arrived in a wheelchair and back brace. She enrolled in a clinical trial for an experimental medication that significantly reduced her lung tumors but did nothing for those on her spine.

"The blood-brain barrier," Rao explains, "shields the spine as well as the brain."



Claudio Tatsui, who was the first person in the world to use LITT on spinal tumors, performed Pamela Lynn's surgery. **™** Wyatt McSpadden

Having exhausted the usual options, Lynn's oncologist referred her to Claudio Tatsui, M.D., assistant professor of Neurosurgery and a spine surgery specialist in the Brain and Spine Center. Tatsui is the first in the world to pioneer laser interstitial thermal therapy for the treatment of spinal tumors.

"We'd successfully used LITT to eliminate brain tumors," he says, "so I thought, 'Why not spinal tumors?"

He used the technique on Lynn a year ago.

The effect was dramatic. Images taken the next day showed no obvious signs of cancer in her spine. And her recovery took days instead of weeks.

"I went home the day after surgery with just two round bandages covering two small incisions in my back," she marvels. "I walked out of the hospital on my own, with no pain and no back brace."

Today, she travels the world with her husband, creates stained glass art, researches her family's Swedish ancestry and enjoys being "mom" to her three cherished Cocker Spaniels.

"If I hadn't come to MD Anderson," she says, "I wouldn't be doing any of those things."

Combined technologies

Laser and MRI technologies have been in existence for a couple of decades, Tatsui says. However, what is new is the combination of the two to allow imaging in real time.

"This technology is unique in that it allows a surgeon to precisely control where the treatment is delivered, and to see the actual effect on the tumor tissue as it's happening," he explains. "This lets us adjust the treatment continuously as it's delivered, and increases our precision in eliminating tumor tissue and sparing surrounding healthy tissue."

If the treatment fails to achieve the desired results, patients can still undergo traditional surgery afterward, he adds.

"But standard surgery has a higher risk of blood clots and infection," Tatsui says. "And it requires patients to discontinue their chemo and radiation for several weeks. There's no such schedule interruption with LITT."

Patients are alert, responsive and walking within hours, he says, and ready to go home the next day. With traditional surgery, recovery can take weeks, sometimes months.

Virtually anyone can undergo the procedure, except heart patients with implantable pacemakers or defibrillators that can be damaged by MRI imaging. Even then, newer-model heart devices can be programmed to be safe during an MRI.

LITT is a game changer for virtually anyone with a brain or spinal tumor, Tatsui says.

"This technology is lighting the way to improved treatment, and allowing us to go where we've never gone before."

They made Jonathan Cope's new jaw with a 3-D printer

By Ronda Wendler

onathan Cope lay sedated on an operating table as Matthew Hanasono, M.D., removed his cancerous lower jawbone. Meanwhile, another doctor extracted the fibula bone from Cope's lower leg.



Jonathan Cope and his wife, Michelle

Using surgical tools resembling those of a sculptor, Hanasono painstakingly whittled away at the fibula, fashioning it into a new jawbone for his patient.

When he was done, he placed the new jaw where Cope's cancer-riddled jaw had been, adjusting it till it "fit like a puzzle piece." The arduous surgery lasted eight hours and challenged Hanasono's skills not only as a doctor, but also an artist.

"Contouring straight leg bone into curved jaw bone is extremely challenging," says Hanasono, a professor of Plastic Surgery. "If the fit isn't precise,

patients can become disfigured and have trouble chewing, swallowing or talking."

He and other experts have long realized the need for a way to increase surgical precision and efficiency. Luckily, three-dimensional printing has emerged as a solution.

Eliminating the guesswork

MD Anderson is one of a growing number of cancer centers embracing 3-D printer technology to create exact replicas of body parts damaged by cancer. These replicas, or models, serve as templates to guide doctors like Hanasono as they carve and shape customized, implantable body parts out of patients' own bones or tissues. The fibula is used to form jawbones for patients such as Cope because it's a non-weight-bearing bone and, therefore, not essential to walking.



A 3-D printer was used to make this jawbone replica. Wyatt McSpadden

"Designing and making replacement body parts out of bone or cartilage once involved a lot of trial and error," Hanasono says. "Getting accurate measurements and a good fit wasn't easy, but 3-D printing eliminates the guesswork. Models are printed in three dimensions — length, width and height — and are precise replicas of the patient's original jaw or other body part that needs replacing."

Hanasono uses these models not only to create replacement body parts, but also to plan exactly how a surgery will go.

"I can take precise measurements of the model from different angles before surgery. That helps me strategize my every move," he explains.

This surgical planning cuts down on time spent in the operating room and leads to better outcomes for patients.

A layered approach and faster recovery

Hanasono implanted Cope's first replacement jaw five years ago after melanoma migrated from his lip to his jaw.

The surgery was performed "the old-fashioned way," without the aid of a 3-D printed model. But radiation treatment afterward to wipe out any remaining cancer weakened Cope's new jaw and caused it to fracture in two places.

"The docs told me my jaw was so brittle, it would continue to break," recalls Cope, 48, a South Carolina home appliance sales manager. "I needed another one."

Last year, Hanasono and Cope once again headed back to the operating room, but this time they had a plastic model of Cope's jaw created with threedimensional printing.

"The technology had arrived," Hanasono says, "and we took advantage of it."

From left: Patrick Garvey, M.D., associate professor of Plastic Surgery, and Matthew Hanasono, M.D., professor of Plastic Surgery Wyatt McSpadden

To create Cope's new jaw, Hanasono and bioengineers studied a CT scan of his original jaw. Like a map, the scan guided them as they used computer-assisted design (CAD) software to produce a digital blueprint with instructions for making an exact replica.

The blueprint instructions were sent to a 3-D printer, which "printed" the jaw using plastic polymer — the "ink" used in 3-D printing. The plastic heats until it melts inside the printer, then squirts out of a nozzle resembling a miniature glue gun. After it's expelled from the printer, the plastic solidifies and hardens into a thin layer, then more plastic is pushed out on top of it. The jaw is built one layer at a time, from the bottom up, until it's complete.

"This process is called 'additive' manufacturing," Hanasono explains, "because individual layers of material no thicker than a dollar bill are added to each other in succession, one on top of the other."

Sometimes, prostheses are made not from plastic, but from titanium, a corrosion-resistant metal commonly used in surgery. Titanium powder is fed into the printer, then fused together with heat one layer at a time. The finished product is coated with ceramic and implanted directly in the patient.

But more commonly, the printed 3-D model, or mold, is made from plastic and is used to help the surgical team get as close to the shape and size of the original body part as possible as they carve the replacement from the patient's bone.

Cope recovered faster from his second surgery than his first. After the first operation, he was hospitalized 12 days; after the second, just eight. But a faster recovery is only one of the advantages of 3-D printer-assisted surgery.

"My new jaw fits better, it's stronger and more durable, and my facial symmetry has improved," Cope says. "Overall, it's just better. I'm working full time, golfing and enjoying life."

And he's looking forward to "a big steak, medium rare," next month when doctors implant teeth in his new jawbone.

3-D PRINTING AND THE FUTURE OF CANCER CARE

The use of 3-D printing in cancer research and treatment is still in its infancy, but its implications are enormous, says Patrick Garvey, M.D., an associate professor of Plastic Surgery who uses 3-D printed models to plan his patients' surgeries before stepping into the operating room.

"With the introduction of 3-D printing come a myriad of new applications that will someday revolutionize health care," says Garvey, who shares a few examples:

- Surgeons are studying 3-D printed models of patients' tumors to rehearse how
 they'll remove them during surgery without harming blood vessels and nearby
 structures. This technology also helps medical students rehearse in a safe and
 forgiving simulated environment, years before they'll operate on human patients.
- Prosthetic limbs are now being produced faster and more accurately with the technology. A CAD file that includes a person's measurements is sent to a 3-D printer, which prints out a custom-fit limb.
- 3-D bio-printers are using living cells as "bio-ink" to print human tissue. The safety
 of potential new drugs can be tested on these tissues, which is less risky than testing
 drugs in human patients. Bio-printing also has the potential to create human organs
 for transplant, printed from the recipient's own genetic matter. This will allow the
 new organ to precisely match the patient's own body, and decrease the risk of rejection. Bio-printers are still experimental, but are expected to transform medicine.
- Cancer patients often have to take multiple pills each day. With 3-D printing, all
 a patient's drugs could be combined in one tablet, using a printer equipped with
 multiple nozzles. Each nozzle would contain a different drug, and would squirt
 tiny amounts of each into one pill, formulated specifically for that patient.
- Patients may someday print their own drugs at home. Instead of purchasing drugs, they'll visit an online drugstore with their digital prescription, buy the blueprint and chemical "ink" needed to make that drug, then print the drug at home on a 3-D printer that's capable of assembling chemical compounds. The first 3-D printed pill was approved by the Food and Drug Administration last year for the treatment of epilepsy.



or most teenagers, prom is one of their best high school memories. Unfortunately, teens being treated for cancer often are forced to miss out on such memorable events.

But on a glitzy and glamorous night in April, MD Anderson Children's Cancer Hospital became a place where not only lives are saved, but lasting memories are made when it hosted a Great Gatsby themed "Prom Party Palooza" for teen cancer patients and their families.

For 18-year old David Olazaba, a two-time Hodgkin lymphoma survivor, the event was the chance to have the prom he's always envisioned, with plenty of friends, fun, food and dancing. Olazaba, who was first diagnosed at age 9, missed a lot of school when he was going through treatment and eventually had to press pause on high school during his junior year.

Though he finished school, receiving his GED last December, Olazaba hadn't experienced a real prom.

"I was disappointed that I was not able to attend prom with my high school friends, but the prom at MD Anderson made up for that," he says.

Teens were able to choose from more than 300 dresses donated by the local community and businesses. Al's Formal Wear donated the tuxedos and provided alterations and fittings for the dresses and tuxedos. On prom day, patients and their families made jewelry at Kendra Scott's Color Bar to wear, and Pageboy provided hair styling and manicures for the special occasion.

The main event took place on the 24th-floor observation deck atop the Albert B. and Margaret M. Alkek Hospital, which offers views of downtown Houston's skyline to the north. DJs Johnny "JKB" Nguyen and John "Johnny Mac" McLaughlin provided the soundtrack.

The whole thing was the brainchild of Thomas Nguyen, co-owner of Houston-based restaurant Peli Peli.

"We've always wanted to do something special for young cancer patients," says Nguyen. "I am grateful for the local businesses, restaurants and community that worked with me and MD Anderson to make this happen for the kids."

News anchor Lily Jang from CBS affiliate KHOU kicked off the celebration with a \$10,000 check presentation from event co-sponsor Marine Foods Express, a family-owned seafood distributor.

"It was a breathtaking experience," says Olazaba. "The prom gave us some time to escape the real world and just have fun."









MD Anderson is helping an at-risk group beat nicotine addiction People with psychiatric disorders

By Clayton Boldt, Ph.D.

ore than 50 years after the U.S. Surgeon General first warned about the dangers of cigarettes, smoking rates have plummeted.

Yet despite irrefutable evidence that smoking causes cancer and other diseases, 15% of the population still smokes. A number of these smokers are people with what is commonly referred to as a mental health condition, such as schizophrenia or bipolar disorder. Many experts now refer to these conditions as behavioral health disorders — a term that collectively describes mental illness and substance use disorder. People who suffer from these types of conditions make up almost 50% of the U.S. tobacco market.

"The smoking rate for people with behavioral health disorders is about two times higher than for those without such conditions," says Janice Blalock, Ph.D., associate professor of Behavioral Science.

According to the Centers for Disease Control and Prevention, one in five U.S. adults has some form of behavioral health disorder, and 35 to 69% smoke cigarettes. In comparison, 15% of adults without such conditions are cigarette smokers.

"Smokers with behavioral health needs die 25 years younger than the general population, primarily of tobacco-related illnesses," Blalock says. "They smoke more heavily and more intensely, meaning they're getting a lot more of the negative stuff from tobacco."

Helping those diagnosed with such disorders quit smoking hasn't been a priority, until now.

"Because some health care providers and facilities are more focused on treating their patients' psychiatric diseases," Blalock says, "they may not consider treating tobacco addiction."

Some providers have feared that taking tobacco away might worsen patients' conditions, and some facilities have even offered cigarettes as rewards for good behavior, she says.

Blalock and Cho Lam, a senior faculty fellow in Psychology at Rice University, co-lead a program called Project TEACH (Tobacco Education and Cessation in the Health System), which trains community providers to deliver tobacco cessation services to behavioral health patients. Launched in 2015, Project TEACH is conducted in partnership with Rice University, the University of Houston and Austin Travis County Integral Care — Travis County's provider of behavioral health services.

"I've been working in the mental health field 31 years and we operated under the misconception that because a person had a mental illness, they couldn't stop smoking," says Deborah Shedrick, program manager at Spindletop Center, a community behavioral health clinic based in Beaumont, Texas. "We found out they really did want to stop smoking, but nobody had ever asked them."

The Spindletop Center is one of seven community behavioral health centers across the state participating in Project TEACH. They're working with Texas' Local Mental Health Authorities, organizations that are under contract with the Texas Department of State Health Services to deliver treatment in specific geographic areas of the state.

are more likely to be smokers. A new program is training community health providers to deliver tobacco cessation services.



From left: Alex Hurst of the cancer prevention and control platform, Janice Blalock, Ph.D., associate professor of Behavioral Science, and Jennifer Cofer, director of MD Anderson's EndTobacco program Wyatt McSpadden

To connect MD Anderson's experts with clinics statewide, Project TEACH uses a videoconferencing program called ECHO, or Extension for Community Healthcare Outcomes.

"The ECHO platform is readily available and used at the convenience of clinicians. This allows us to disseminate information effectively without having to visit and train in person," says Jennifer Cofer, director of EndTobacco, an initiative of the cancer prevention and control platform of MD Anderson's Moon Shots Program. The platform, along with the Lung Cancer Moon Shot, provides support for Project TEACH.

Using ECHO, counselors and physicians from MD Anderson's Tobacco Treatment Program meet one hour each week with community providers. Sessions teach them how to help people with behavioral health needs stop smoking, and offer a forum for providers to discuss their most difficult and challenging cases.

Everyone involved learns something, including MD Anderson experts.

"The experts listen to our feedback, and we share," says Shedrick. "We're all on the same team."

Shedrick describes a complete cultural shift at Spindletop Center. She's seen a number of clients successfully quit or reduce their tobacco use. Their lives, from health to finances, are transformed.

Project TEACH will soon expand to more clinics and provide more in-depth assistance.

"People with these conditions want to quit smoking and can quit, when given the proper assistance," Blalock says. "The process may take longer and require more intensive interventions, but it can be done."

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