CONQUEST

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

TAKING STEPS

TO PRESERVE FERTILITY WHEN CANCER STRIKES

MISSION

The mission of The University of Texas MD Anderson Cancer Center is to eliminate cancer in Texas, the nation and the world through outstanding programs that integrate patient care, research and prevention, and through education for undergraduate and graduate students, trainees, professionals, employees and the public.

VISION

We shall be the premier cancer center in the world, based on the excellence of our people, our research-driven patient care and our science.
We are Making Cancer History®.

CORE VALUES

Caring

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

Integrity

We work together to merit the trust of our colleagues and those we serve.

Discovery

We embrace creativity and seek new knowledge.

On the cover: "Being diagnosed with cancer and told that it may rule out parenthood can be devastating for people who haven't yet started or completed their families," says Terri Woodard, M.D., assistant professor of Gynecologic Oncology and Reproductive Medicine. Woodard directs MD Anderson's Oncofertility Clinic, where oncology and reproductive medicine intersect.

David Trood/Creative RF/Getty Images

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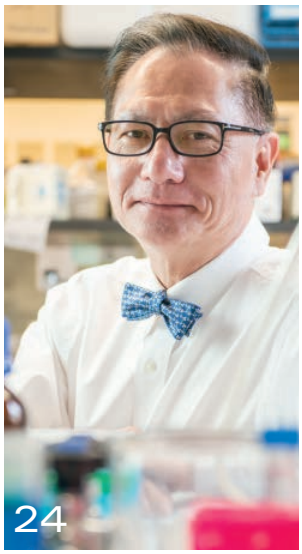


FEATURES

MD ANDERSON JOINS WITH PARKER FOUNDATION'S IMMUNOTHERAPY ALLIANCE

Cancer immunotherapy leaders at MD Anderson will work with experts at five other cancer centers in a new alliance funded by the largest single contribution ever made to the field.

The Parker Institute for Cancer Immunotherapy, created with a $250 million grant from the Parker Foundation, will focus on accelerating progress in the breakthrough field that helps the immune system attack cancers.

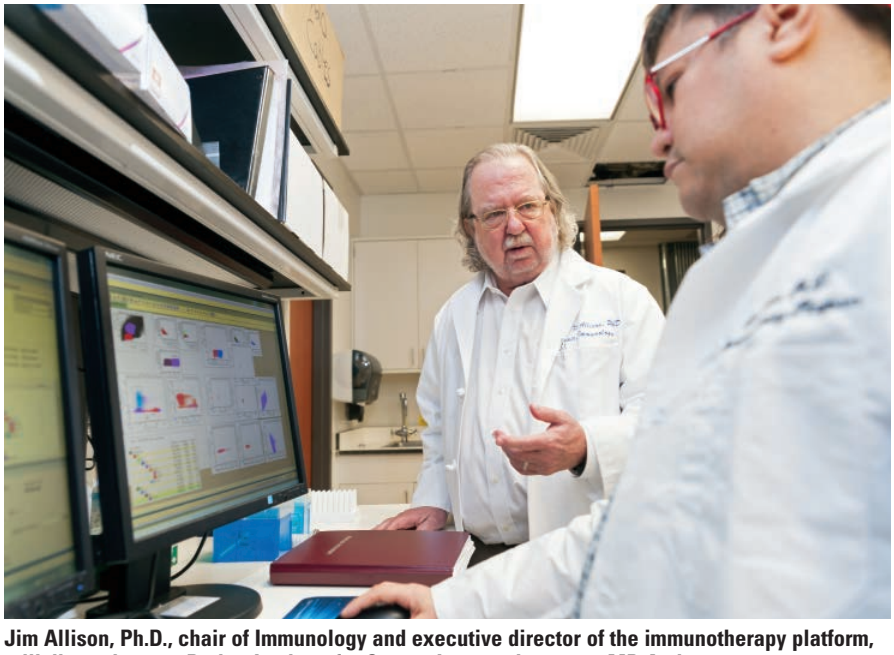
"By bringing institutions with different strengths and expertise together, providing stable funding and access to truly cutting-edge technologies, the Parker Institute empowers us to make big strides in cancer immunotherapy," said Jim Allison, Ph.D., chair of Immunology and executive director of the immunotherapy platform — an essential component of MD Anderson's Moon Shots Program to more rapidly convert scientific discoveries into life-saving advances.

Each of the six centers received initial funding of $10-15 million in the first year to establish the Parker Institute on site. This investment will continue to grow annually via additional project grants, shared resources and central funding.

Parker Institute at MD Anderson Co-Director Padmanee Sharma, Md.d, Ph.D.

Allison will serve as director of the Parker Institute for Cancer Immunotherapy at MD Anderson. The other cancer centers involved are Memorial Sloan Kettering Cancer Center, Stanford Medicine, the University of California, San Francisco, the University of California, Los Angeles, and the University of Pennsylvania.

"We are at an inflection point in cancer research and now is the time to maximize immunotherapy's unique potential to transform all cancers into manageable diseases, saving millions of lives," says Sean Parker, president of the Parker Foundation. "We believe that the creation of a new funding and research model can overcome many of the obstacles that currently prevent research breakthroughs. Working closely with our scientists and more than 30 industry partners, the Parker Institute is positioned to broadly disseminate discoveries and, most importantly, more rapidly deliver treatments to patients."



Jim Allison, Ph.D., chair of Immunology and executive director of the immunotherapy platform, will direct the new Parker Institute for Cancer Immunotherapy at MD Anderson. Adolfo Chavez III

The Parker Institute has chosen three areas of concentration to address issues in immunotherapy:

- Develop novel approaches to modify T cells to enhance their function and then develop a new generation of more effective T cell therapies.
- Compare patients who respond to checkpoint inhibitors, those who don't respond and those who relapse, to improve rates of durable responses and broaden the use of these drugs alone or in combination.
- Conduct DNA sequencing, immune monitoring and antigen discovery to identify new targets for therapeutic vaccines and T cell therapies.

Five MD Anderson researchers will fully participate in the Parker Institute at MD Anderson. Allison said others can be added and researchers also can participate on a project-by-project basis. In addition to Allison, the team includes:

Parker Institute at MD Anderson Co-Director **Padmanee Sharma, M.D., Ph.D**., professor of Genitourinary Medical Oncology and scientific director of the immunotherapy platform. Sharma is a clinician-scientist and immunologist whose research includes identifying and characterizing immune-stimulating molecules and checkpoints as well as understanding response and resistance to treatment.

Cassian Yee, M.D., professor of Melanoma Medical Oncology and co-leader of the adoptive cell therapy platform. Yee has developed a method for gathering white blood cells from patients through apheresis, identifying among them the T cells that attack their cancers, expanding those T cells in the lab, and giving them back to patients.

Elizabeth Mittendorf, M.D., Ph.D., associate professor of Breast Surgical Oncology. Mittendorf is a surgeon and immunologist who developed therapeutic vaccines to prevent breast cancer recurrence that are being tested in Phase III clinical trials.

Jennifer Wargo, M.D., associate professor of Surgical Oncology and Genomic Medicine. Wargo is a surgeon, immunologist and a translational scientist who has an active research laboratory focused on better understanding patient responses to cancer therapy using longitudinal tissue and blood sampling. She also leads several clinical trials testing novel approaches to improve outcomes for patients with melanoma and other cancers.

— Scott Merville

CATEGORIZING COLORECTAL CANCER TUMORS TO BETTER GUIDE TREATMENT

Researchers with MD Anderson's Colorectal Cancer Moon Shot are sharpening the focus of a genetic tool designed to classify colorectal cancer into one of four categories — a vital step toward improving treatment.

They're addressing a challenge posed by the complexity of colon and rectal cancer, which leads to major differences in responses to treatment and patient survival.

"Some cancers have two or three very well-defined biomarkers that, if found in a patient's tumor, can be reliably used to guide treatment," says project co-leader Jeffrey Morris, Ph.D., professor of Biostatistics. "For many cancers, it's not that simple, and colorectal cancer is one of those."

Morris, co-leader Dipen Maru, M.D., professor of Pathology, and colleagues are working to impose some clarity on the problem of heterogeneity — a fancy word for the genetic and molecular diversity found among cancer cells in the same tumor, across tumors in the same patient, and in the results of various genetic tests that seek to characterize cancer.

The team is working with the Moon Shots Program's Cancer Genomics Laboratory platform to apply an integromic approach — an integrated analysis of genetic variations, expression of genes and regulation of genes by nongenetic factors — in 200 tumor samples.

Morris says the researchers have whittled down the 500-gene beginning set to a 100-gene test that accurately places tumors in one of the four categories 94% of the time. They're working to get the number of genes down much lower, which would make a final test much less expensive.

While hints about potential treatment are emerging from the characteristics of the four categories, Morris says much work remains to get to the point of treating patients based on tumor category.

"This information could help us do a better job choosing among standard therapies. We have some preliminary ideas there to pursue," he says. "And we'll try to identify and validate some targeted-therapy strategies."

Preclinical research, in conjunction with the Moon Shots Program Center for Co-Clinical Trials, has developed cell lines and mouse models from patient-derived tumor samples to better understand each category's mechanisms and to apply the gene test to these tumors.

The new categories were described by MD Anderson investigators and five other research groups, which make up the Colorectal Cancer Subtyping Consortium, in a paper that was published in Nature Medicine late in 2015. The investigators folded six independent classification systems into the four consensus subgroups.

Biostatistician Jeffrey Morris, Ph.D. Eric Kayne

The consensus molecular subtypes of colorectal cancer, which come from their analysis of 18 studies involving more than 4,000 patients, are:

CMS1 – Genetic/immune, hypermutation with a strong immune response, 14% of tumors

CMS2 – Canonical, classic tumor of epithelial tissue, the lining of the organ, with specific tumor-promoting pathways activated, 37% of tumors

CMS3 – Metabolic, epithelial tumors with metabolic defects, 13%

CMS4 – Mesenchymal, with prominent transforming growth factor-beta activation, invasion of supportive tissue and generation of new blood vessels, 23%

About 13% of tumors in the study had mixed features, which the authors note could represent a transition from one category to another or major molecular heterogeneity within the tumors

Colorectal cancer in general has resisted immunotherapies, but those in CMS1 may be vulnerable to this approach.

Interestingly, a drug that targets a vital metabolic pathway in some tumors that's under development at the Institute for Applied Cancer Science, the moon shot small-molecule drug development platform, has potential against CMS3.

And the researchers note that the prime characteristics of CMS2 and CMS4 lend themselves to possible targeted therapy.

"It won't be as simple as one target per group," Morris says, "These classifications provide a foundation for improved prognostics, and for identifying new targets in well-defined groups of patients that we can move into clinical trials quickly."

— Scott Merville

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

With enhanced recovery, surgery interrupts life less

By Laura Sussman

Survivor Linda Jenkins benefited from MD Anderson's Enhanced Surgical Recovery Program. Wyatt McSpadden

When Linda Jenkins was diagnosed with a slow-growing ovarian cancer in 2004 and needed a hysterectomy, she underwent traditional surgical preparation procedures.

"I wasn't allowed to eat for two days prior to surgery, I had to do a bowel preparation, and I was incredibly weak when I was wheeled into the operating room. After surgery, I was in bed for quite some time," Jenkins recalls. "When I finally could walk around, it was really painful. After going home, I distinctly remember my husband cooking — the smell of spices made me cough, and the coughing caused such incredible pain that I had to tell him to stop."

A decade later, when Jenkins' cancer returned and her MD Anderson doctors determined that surgery was again necessary, she jumped at the chance to participate in a protocol designed to relieve patients' symptom burden and improve functional recovery.

To her absolute surprise, Jenkins' experience with her second operation was dramatically different than her first.

"The night before, I enjoyed a family dinner, drank clear liquids until two hours prior to surgery, and didn't have to endure a bowel preparation that had caused so much discomfort," she says. "After surgery, I had almost no pain — I was up and walking and was soon eating a full meal. I even felt well enough to talk to my friends and put on my makeup in recovery."

The principles of MD Anderson's Enhanced Surgical Recovery Program (ESRP) involve making interventions before, during and after surgery that get patients through their surgery and recovery process much quicker and with better outcomes.

The movement is not new. Rather, it was pioneered almost two decades ago by a group of surgeons in Europe. It's only more recently that physicians and institutions in the United States, including MD Anderson, have started to look more closely at its components.

Actually, many surgical practices are based more on traditions and previous teachings than sound scientific evidence, explains Pedro Ramirez, M.D., professor of Gynecologic Oncology and Reproductive Medicine.

"The pioneers of the movement questioned many traditional standards of practice that had been ingrained in the care of patients before, during and after surgery, and by doing so, came up with strategies that could benefit the patient," says Ramirez, an ESRP co-lead. "With implementation, they found that patients were recovering much faster and getting back to their regular activities much sooner, resulting in an obvious improvement in quality of life."

A gynecology ESRP has already registered 597 patients since its initiation in November 2014. Since then, there's been a one-day drop in average length of hospital stay, an 80% reduction in opioid consumption and an improvement in patient-reported outcomes, without noting any differences in postoperative complication rates or readmissions. The program also has significantly lowered the cost of caring for patients.

All Gynecologic Oncology patients who undergo traditional, open surgery performed through an incision are enrolled in an enhanced recovery protocol, "from pre-operative patient education to post-operative return visit."

Pedro Ramirez, M.D., professor of Gynecologic Oncology and Reproductive Medicine
Wyatt McSpadden

Principles of ESRP include patient education, opioid-sparing strategies for pain management, minimizing drains and tubes whenever possible, and managing intravenous fluid therapy. Also fundamental to the movement's success are changes in anesthesiology practices, with an increasing focus on using short-acting intravenous anesthetics. This helps lessen patients' post-operative confusion and allows them to emerge from anesthesia with less nausea, less vomiting and better pain control, says Vijaya Gottumukkala, M.D., professor of Anesthesiology and Perioperative Medicine.

"Patient education and engagement is paramount to the success of the program. We educate them on what to expect from their surgical experience. Just before surgery, we give the patients opioid-sparing oral medications that reduce pain immediately after surgery," says Gottumukkala.

The plan also encourages patients to ambulate earlier and return to normal nutrition and physical activity as soon as possible.

All Gynecologic Oncology patients who undergo traditional, open surgery performed through an abdominal incision are enrolled in an enhanced recovery protocol, "from pre-operative patient education to post-operative return visit." Ramirez and colleagues also have published inaugural enhanced recovery treatment guidelines for their field, with hopes of sharing best practices beyond MD Anderson.

In Thomas Aloia's opinion, enhanced recovery is the most important surgery advancement in the past 30 years.

"It's a care philosophy that's exclusively focused on the patient, with the primary goal to return the patient to normal function," notes Aloia, M.D., a liver surgeon who, with Gottukmukkala, is credited with introducing the concept at MD Anderson.

Starting a RIOT

A major goal of the liver team's ESRP is patients' return to intended oncologic treatment, or RIOT. It's imperative, says Aloia, that patients are able to receive necessary chemotherapy or other cancer treatments after surgery.

Prior to initiating the program, Aloia, Gottumukala and colleagues found that, historically, 75% of liver surgery patients returned to systemic therapy, on average, in 45 days. In dramatic contrast, since ESRP was initiated, 95% of MD Anderson patients returned to therapy in an average of only 22 days.

"In liver surgery, we perform some surgeries that can be fairly intense, so we run the risk that surgery could derail the larger plan of care. ESRP helps us ensure that patients receive all their treatments," explains Aloia.

A team effort

Almost all MD Anderson surgical departments have implemented variations of ESRP, with the specific needs of patients in mind. In collaboration with MD Anderson's Institute for Cancer Care Innovation, the teams are mining patient information on a variety of clinical data points, including cost effectiveness.

Since its origin 20 years ago, every enhanced recovery study has shown patient benefit, says Ramirez, including the work published by MD Anderson. In their respective disciplines, Ramirez's and Aloia's research has shown reductions in functional impairment and symptom burden, including pain, length of hospital stay, opioid needs, and readmission and complication rates.

Thomas Aloia, M.D., associate professor of Surgical Oncology F. Carter Smith

Paramount to ESRP's success is the partnership across myriad specialties: surgery, anesthesiology, nursing, pharmacy, nutrition support and data coordination, to name a few.

"ESRP exemplifies one of our best successes of bringing together multiple disciplines," says Steven Swisher, M.D., head of Surgery. "MD Anderson is also unique in that we are incredibly disease-focused at all levels, and the teams can enact changes that are most specific to their patients' needs."

Swisher believes MD Anderson is paving the way for enhanced recovery in oncology, with more active research and patients enrolled on protocols.

For Jenkins, the experience was such a positive one that when a friend called to tell her she was also diagnosed with ovarian cancer and would be treated at MD Anderson, Jenkins strongly encouraged her to participate in the same protocol.

"I just wanted her to have the same positive experience that I had."

Moon shot sets sights on first targeted therapy for triple-negative breast cancer

By Ronda Wendler

Triple-negative breast cancer, an aggressive form of the disease with limited treatment options and a high rate of recurrence, is the target of a new MD Anderson study that launched this past November.

The project's goal? Find new drugs to combat the cancer, which doesn't rely on the hormones estrogen and progesterone or the protein HER2, which fuel the growth of most breast cancers.

"Given this, the drugs that treat most breast cancers by blocking their ability to use those three things to survive don't work on triple-negative breast cancer," says Stacy Moulder, M.D., associate professor of Breast Medical Oncology and the trial's principal investigator.

Instead, doctors are left to treat triple-negative patients with traditional chemotherapy drugs, surgery and radiation.

Typically, patients with a triple-negative breast tumor that's larger than one centimeter and hasn't spread to other parts of the body are given chemo before surgery. In nearly half of these patients, chemo works well. It kills all or nearly all of the cancer cells, and little to no cancer in the breast or lymph nodes is present at the time of surgery.

"This is associated with an extremely good prognosis," Moulder says.

But the other half of patients who do not respond well to chemo face a high probability their cancer will come back within three years after treatment. When the disease returns, prognosis is poor.

"This is why triple-negative breast cancer is part of MD Anderson's Moon Shots Program," says Debu Tripathy, M.D., chair of Breast Medical Oncology and a collaborator on the trial. "We need drugs that work, and we need them now."

It's complicated

Only a few years ago, researchers discovered that triple-negative breast cancer isn't a "one-size-fits-all" disease. Instead, six distinct subtypes have been identified so far, "and more will likely be discovered in the future," Moulder says. Within each subtype, tumors have different genetic defects. Therefore, "it stands to reason that each subtype should be treated differently," says Jennifer Litton, M.D., associate professor of Breast Medical Oncology and a trial collaborator.

Yet the current standard of care is to use the same chemotherapy for all subtypes of the disease.

"This is a very complex group of cancers and they don't all behave the same way," Litton says. "To treat these patients we have to gain more knowledge of the molecular events that drive each subtype. Then and only then can we match the right drugs to the right patients."

Drugs that specifically target a cancer's genetic abnormality are called targeted therapy or precision medicine. Triple negative is the only form of breast cancer for which there is no targeted therapy, Litton says.

MD Anderson's project is part of an effort to bring precision medicine to triple-negative breast cancer patients for the first time. Here's how it works:

Patients who've been advised to start chemo before surgery (those whose tumors haven't spread and are larger than one centimeter) first have their tumors biopsied. They then can immediately start the first of two sequential chemo regimens.

MUCH WORK REMAINS BEFORE PRECISION MEDICINE BECOMES THE STANDARD OF CARE FOR TRIPLE-NEGATIVE BREAST CANCER, ACCORDING TO ASSOCIATE PROFESSOR OF BREAST MEDICAL ONCOLOGY STACY MOULDER. BUT EXPERTS FROM MD ANDERSON AND BEYOND ARE WORKING DILIGENTLY TO MAKE IT HAPPEN.

Janine Blackwell is enrolled in a new triple-negative breast cancer study led by MD Anderson's Stacy Moulder, associate professor of Breast Medical Oncology. Professor of Pathology W. Fraser Symmans developed a chemo-sensitivity predictor test that determines if patients' tumors are responding to chemotherapy or not.

Wyatt McSpadden

While patients are undergoing their first round of chemo, a chemo-sensitivity predictor test, developed by MD Anderson professor of Pathology W. Fraser Symmans, M.D., is run on their biopsied tumor samples to determine if their tumors will respond to chemo. If a tumor tests "chemo-sensitive," the tumor is responding to the chemo. If a tumor tests "chemo insensitive," the chemo is ineffective.

"You may wonder why patients in this trial are placed on chemo when we don't yet know if their tumor is chemo sensitive," Moulder says. "We start chemo immediately so we don't waste time and allow the cancer to spread. If the chemo-sensitivity test determines that chemo won't work for a particular patient, we haven't done any damage and we can adjust their course of treatment."

During this testing, the tumor's molecular makeup is also revealed, and the patient's triple-negative breast cancer subtype is identified.

After completing the first round of chemo, those patients whose tumors are found to be chemo-sensitive are prescribed a second round of standard chemo treatments before undergoing surgery. They need chemo only, not the toxicity of more drugs. In the second round of treatment, patients with chemo-insensitive tumors are placed in clinical trials for targeted drugs that are predicted to work best on their individual tumor's molecular makeup and subtype, in combination with standard chemo.

Two-thirds of patients enrolled in the study receive the treatment described above. The other third do not receive the results of the molecular testing. All patients are allowed to enter a clinical trial for the second part of their treatment, but only the first group will have the molecular testing results to guide their choice of clinical trial.

"This helps us determine if our new approach of adding a targeted drug based upon the molecular testing results will benefit patients," Moulder says.

No placebos are used in these trials. Some of the drugs tested already are approved to treat other cancers. Others are new and haven't yet gained Food and Drug Administration approval. If they perform well and increase the number of patients with minimal or no cancer at the time of surgery, the drugs will enter the path to FDA approval.

AS PART OF THE TRIPLE-NEGATIVE BREAST AND HIGH-GRADE SEROUS OVARIAN CANCERS MOON SHOT, ALL SUCH PATIENTS 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.

"This is personalized medicine at its finest," Moulder says. "The practice of tailoring drugs and therapies to individuals based on their genes or their cancer's genes is the way of the future."

An added benefit, she says, is that genetic testing may identify some tumor abnormalities that until now have been unknown.

"I'm sure there are many more triple-negative subtypes that we don't yet know about," she says. "I'm guessing in the next decade we'll identify 20 or 30 more. The challenge will be to find drugs that work best for each one."

Win-Win

Developing a cancer-fighting drug can cost more than a billion dollars and the journey from research lab to patient can take more than a decade. Even then, only one of five drugs is ever approved for human use.

MD Anderson's trial streamlines the process by testing multiple drugs from different manufacturers simultaneously. This approach is called a "platform" design because it works much like multiple delivery trucks simultaneously depositing their goods for inspection on a warehouse loading dock. In the trial, multiple drugs are inspected simultaneously. Those that are ineffective are removed from the trial, and new drugs are added as the trial progresses.

In conventional breast cancer trials, sample sizes as large as 5,000-10,000 patients are required to ensure statistical accuracy. But because the platform trial is using molecular testing to match people with drugs, the number of patients needed is much less. As few as 14 and no more than 37 patients need to be treated on the targeted therapy clinical trial before a pharmaceutical company learns if a drug shows promise.

It's a win-win for everyone, Moulder says.

"Because there are multiple drugs within the study, patients have a good opportunity of getting an investigational drug that, by virtue of being in the study, appears promising," she says. "And ineffective drugs are eliminated sooner."

Much work remains before precision medicine becomes the standard of care for triple-negative breast cancer, Moulder says. But experts from MD Anderson and beyond are working diligently to make it happen.

This trial alone involves faculty members specializing in surgery, oncology, pathology, radiation, diagnostic imaging and basic science research. By harvesting cancer cells that remain after treatment, they're studying disease resistance using leading-edge laboratory science, an effort led by Helen Piwnica-Worms, Ph.D., vice provost of science and professor of Cancer Biology. Other translational research scientists, including Beth Mittendorf, M.D., Ph.D., associate professor of Surgical Oncology, and Naoto Ueno, M.D., Ph.D., professor of Breast Medical Oncology, will determine the effects of targeted therapy on the body's immune response and use preclinical models to find the best combination of drug treatments to move forward into clinical trials. Additional imaging projects are being led by Diagnostic Radiology faculty Wei Yang, M.B.B.S., Mia Rauch, M.D., Ph.D., Beatriz Adrada, M.D., and Rosalind Candelaria, M.D., to improve researchers' ability to evaluate tumors' response and sensitivity to chemotherapy. Their goal is to use what's learned to design more clinical trials, with each one getting closer to identifying the best drugs for each disease subtype.

"Right now, the idea of using a test to predict a patient's response to chemotherapy and to identify the molecular features of the patient's tumor, then matching drugs to those features, is all very new," Moulder says. "This study is designed to confirm that this approach works. And if it does, it'll be a game changer for women with triple-negative breast cancer."

TRIPLE-NEGATIVE BREAST CANCERS...

Account for 15% of all breast cancers

Occur more frequently in women under age 50

Tend to be more aggressive than other types of breast cancer

Are more likely to recur after treatment

Disproportionately strike women of African, Latina or Caribbean descent, and those with BRCA1 and BRCA2 mutations

Have poorer survival rates than most other breast cancers for the first five years after diagnosis

Have as good as, and sometimes better, survival rates than most other breast cancers after the five-year survival mark

Wyatt McSpadden

His full-time, lifelong, 100% commitment: Treating childhood cancer

By Katrina Burton

As a pediatric cancer clinician and laboratory researcher, Patrick Zweidler-McKay, M.D., Ph.D., has devoted his career to treating children with particularly difficult or relapsed forms of cancer. As section chief of Pediatric Leukemia and Lymphoma at MD Anderson Children's Cancer Hospital, he gives hope to families facing these diseases.

"Cancer can be devastating to families," says Zweidler-McKay. "Especially when it strikes children. Although childhood cancer treatments have advanced over the years, more targeted therapies that attack cancer cells without harming normal cells are still desperately needed."

To meet that need, Zweidler-McKay and his team are developing targeted therapies for children with cancers of the blood, including acute lymphoblastic leukemia, acute myeloid leukemia, T cell leukemia and lymphoma, and for neuroblastoma, a type of cancer that starts in the nervous system.

The research in Zweidler-McKay's lab is focused on understanding various forms of cell-to-cell communication that contribute to the growth and survival of these types of childhood cancers.

"Some normal cells make factors that stimulate the growth of cancer cells," he explains. "With new therapies, we can target some of these factors."

Zweidler-McKay visited Congress last September during Childhood Cancer Awareness Month to advocate for increased funding for pediatric cancer research and to voice support for "compassionate use" – the treatment of seriously ill children using new drugs not yet approved by the Food and Drug Administration when no other treatments are available.

"Treating childhood cancer patients is a lifelong commitment I made as a pediatric oncologist," he says. "Across the board, the cure rate for all forms of childhood cancer is now 80%, compared to 10% in the 1950s. But for some forms of childhood cancer, and for nearly all children who relapse, the outlook is much worse. We have so much more to do for those children."

PRESERVING FERTILITY
in the face of cancer

By Ronda Wendler

"What would you like for your birthday?" Mike Lingerfelt would ask his wife each year.

Pati Lingerfelt's response was always the same: "A baby."

This year, Pati will get her wish.

After 11 years of marriage, the Lingerfelts are expecting a baby girl in October.

"We're ecstatic," says Pati, 45, cradling her growing baby bump. "Motherhood is the greatest gift."

For years, the couple tried to conceive the "old-fashioned way," as Pati puts it, but with no results. Determined to not give up, they visited a fertility specialist in 2014. But the week they agreed to begin treatments, Pati learned she had breast cancer. Even more crushing was her doctor's prediction that she'd never have a child. The harsh chemotherapy and radiation designed to cure her cancer would also make her infertile, the doctor said.

"I left that appointment in tears, trying to grasp this challenge to my faith," says Pati, who served with her husband as an overseas missionary before returning home to Houston three years ago.

Bolstered by her beliefs, she summoned her strength and decided to knock the curve ball she'd been dealt out of the park.

"I was on a mission to conquer cancer and have a baby."

HARSH TREATMENTS

"Being diagnosed with cancer and told that it may rule out parenthood can be devastating for people who haven't yet started or completed their families," says Terri Woodard, M.D., assistant professor of Gynecologic Oncology and Reproductive Medicine.

"A cancer diagnosis alone is bad enough, but the treatments that go with it can reduce or erase future chances to have children."

Radiation and chemo can cause ovaries to fail and sperm production to stop. Effects can be temporary or permanent, depending on the type of treatment and its duration. Age also plays a role.

> "PARENTHOOD MAY NOT HAPPEN THE WAY IT WAS EXPECTED TO BEFORE CANCER, BUT IF YOU CAN BE FLEXIBLE, YOU'LL FIND THERE ARE OTHER OPTIONS."
>
> — Terri Woodard, M.D., *assistant professor of Gynecologic Oncology and Reproductive Medicine*

"Women are born with all the eggs they'll have in a lifetime," Woodard explains. "Younger women typically are starting out with more eggs, so they can usually take a bigger hit."

Sometimes reproductive organs must be surgically removed to eliminate cancer, "and patients may assume the door has shut," Woodard says.

SECURING THE FUTURE

Even then, the dream of having a child may still be possible if patients take steps to preserve their fertility before cancer treatment begins.

"Parenthood may not happen the way it was expected to before cancer," Woodard says. "But if you can be flexible, you'll find there are other options."

Woodard directs MD Anderson's Oncofertility Clinic, where oncology and reproductive medicine intersect.

Working collaboratively with Texas Children's Hospital's state-of-the-art in vitro fertilization lab nearby, clinic staff offer the latest fertility preservation procedures to patients with cancer.

"It's there that patients boost their chances to have biological children after their cancer is gone," says Woodard, who has a dual appointment at Texas Children's.

A FAMILY OF OPTIONS

Preserving fertility in men is as simple as freezing and storing sperm for future use. "It's usually a slam-dunk," Woodard says of this straightforward and simple solution.

Even if a young man with cancer is unsure whether he wants children, he should still consider banking sperm, she advises.

"By storing sperm, he can decide later. If the samples aren't used, they can be discarded or donated for research."

Top: Terri Woodard, M.D., is helping Sarah Benys maintain the option of having children in the future. Above: Houston realtor David Rainey and his wife are expecting a baby later this year. Wyatt McSpadden

David Rainey, 32, was diagnosed with Hodgkin's lymphoma at age 20. A doctor urged him to consider freezing his sperm before treatment.

"I was young and single and hadn't thought much about starting a family," says Rainey, who now is a successful Houston real estate agent. "Looking back, I'm glad I followed my doctor's advice."

After undergoing radiation, chemo and a stem cell transplant, he's cancer-free and expecting a baby with his wife, Amelia, later this year.

"If I hadn't been proactive a dozen years ago," he says, "this baby wouldn't be happening."

Wyatt McSpadden

"I'M HAPPILY SINGLE. I DON'T WANT KIDS UNTIL I'M IN MY 30s, BUT I DO WANT THE CHANCE TO HAVE CHILDREN WHEN I'M READY."

— Sarah Benys, a 20-year-old college student who was diagnosed with non-Hodgkin's lymphoma in January

IT'S COMPLICATED

For women, preserving fertility isn't as easy.

"If a man needs to start cancer treatment the next day, he can bank his sperm in an hour," Woodard says. "Women have several options, and unfortunately, all require a considerable amount of time and coordination."

Freezing eggs is the usual route for a single woman who doesn't yet have a partner or a sperm donor. Years later when she meets the man or identifies the donor she wants to have a child with, her eggs can be thawed and fertilized in a laboratory dish with his sperm. The resulting embryo will be implanted in the woman's uterus or in a surrogate, if she's unable to carry a child.

"Egg freezing is a choice that's available to someone who is unsure of whom she wants to share this journey with," Woodard says.

Freezing literally suspends the age of a woman's eggs. A 22-year-old woman who freezes her eggs will have 22-year-old eggs available, even if she waits until age 32 to become pregnant.

"The bottom line for extracting eggs is generally 'the younger, the better,'" Woodard says. "The younger the woman, the greater the number of healthy eggs she'll produce."

Sarah Benys, 20, froze her eggs after she was diagnosed with non-Hodgkin's lymphoma in January.

"I'm happily single," she says. "I don't want kids until I'm in my 30s, but I do want the chance to have children when I'm ready."

A geology major at the University of Texas in San Antonio, she's delaying her graduation by a semester to battle cancer at MD Anderson. Surrounded by family back home in a suburb of Corpus Christi, she maps out her future.

"First I'll beat cancer, then graduate and get a job, a husband and two children — in that order," says the ultra-organized Benys.

BOOSTING THE ODDS

Women with husbands, long-term partners or sperm donors can undergo in vitro fertilization, where their eggs are combined with their partner's sperm. The resulting embryos are frozen, then implanted after cancer treatment ends.

"Freezing embryos has a longer track record of success than freezing eggs," Woodard says. "Eggs are more delicate and we can't predict their ability to fertilize. But with embryos, fertilization has already taken place so we're one step ahead."

Two-year-old Margaret was conceived through in vitro fertilization and delivered by a surrogate after her mother, Caroline, completed breast cancer treatment at age 30.

"My doctor advised me not to become pregnant – now or possibly ever," recalls Brown. "He said pregnancy could create a surge in hormones that could cause my cancer to return and spread."

Brown and her husband were devastated.

"We really wanted children," she says. "In some ways, the news that I couldn't get pregnant was worse than the news I had breast cancer."

The couple visited Woodard who suggested they freeze embryos before Brown's treatment commenced.

"Dr. Woodard was very reassuring, and we followed her advice," Brown says.

After four months of chemo followed by a double mastectomy and breast reconstruction, "one of the embryos we froze was implanted in a surrogate, and we were pregnant!" she says.

Margaret was born April 1, 2014.

"She's our silver lining," Brown says. "I'd go through it all again for another like her."

And she did. Once again, Brown and her husband underwent successful in vitro fertilization. Margaret will welcome a baby brother or sister in October.

Margaret Brown's mother sought the help of the Oncofertility Clinic before she began treatment for breast cancer.
Wyatt McSpadden

"She's our silver lining," Caroline Brown says of her daughter. Wyatt McSpadden

NEW LIFE FOR FAILED OVARIES

Egg, embryo and sperm banking are tried-and-true, but other, less traditional ways to achieve parenthood after cancer treatment are also on the rise.

One such method involves snipping tissue samples from a woman's ovaries before she begins treatment, freezing those samples, then transplanting them back into the woman's body when she's completed cancer treatment and is ready to have a baby. Within a few months, the tissue grows follicles with maturing eggs, and fertility is restored. So far, almost 70 babies worldwide have been born this way.

Woodard says pediatric patients will benefit from this procedure even more than adults.

"They haven't gone through puberty yet, so we can't get eggs that are mature enough to extract and freeze. The only option for preserving their fertility is to freeze ovarian tissue."

A 9-year-old girl doesn't have a concept of what it means to reproduce and be a mother, she says. "But years later, she might care. Without this, she may never get a chance to become pregnant."

The technique can be performed on the youngest patients, even toddlers. An 18-month-old from Ohio is believed to be the youngest child so far to undergo the procedure.

The world's first baby conceived through childhood ovarian tissue freezing was born in 2014 to a 27-year-old Belgian woman who at age 13 had tissue frozen. The case was reported in the journal Human Reproduction.

"Four out of every five children survive their cancer and become long-term survivors," says Woodard, who's leading an initiative to offer the technique to MD Anderson's pediatric patients. "Protecting their future ability to become parents is a major concern."

BUT CAN YOU AFFORD IT?

Medical advances aside, cancer patients face other roadblocks to fertility, like insurance — or lack of it.

Few insurance plans cover cancer-related fertility preservation, even though they pay for procedures like hair-loss treatment after chemo and breast reconstruction after mastectomy.

"Fertility preservation should be treated no differently from any other post-cancer health issue," Woodard says.

The American Society for Reproductive Medicine estimates the average cost for a single cycle of in vitro fertilization is $12,400. Add to that medications, monitoring and storage, and patients can expect to pay out as much as $20,000, with additional cycles costing more.

Facebook and Apple announced in 2014 that they would begin paying $20,000 toward fertility preservation for their employees. Woodard says those companies are the exception.

"We still have a long way to go," she says. "Most companies cover only part of the expenses, or nothing at all."

Eric Kayne

The power of pre-implantation genetic screening

Pati and Mike Lingerfelt used in vitro fertilization to conceive their soon-to-arrive-daughter.

And they did something more.

Because Pati is 45 years old, her embryo, while still in a lab dish, was tested for chromosomal abnormalities before being transferred to her uterus.

The test known as pre-implantation genetic screening, detects missing or extra chromosomes or those with structural defects. Down syndrome, for example, is caused by an extra copy of chromosome 21. About 70% of miscarriages in early pregnancy and a large number of failed in vitro fertilization attempts are also caused by chromosomal defects.

"Older women have a greater risk than their younger counterparts for conceiving a child with a chromosomal defect," says Banu Arun, M.D., medical co-director of MD Anderson's Clinical Cancer Genetics Program.

National Institutes of Health statistics show that a 23-year-old woman has only a one in 500 chance of having a baby with a chromosomal abnormality, compared with a 45-year-old, whose odds escalate to one in 20.

Given those numbers, Pati and Mike were "hugely relieved" to learn that out of their four embryos tested, one was free of abnormalities.

That's the embryo they implanted — "our little girl," Mike says.

"Pre-implantation genetic screening can almost completely eliminate chromosomally abnormal embryos from the pool of embryos being considered for transfer," says Arun. "This significantly increases the chance for a healthy baby."

While Pati's test looked for chromosomal abnormalities, another test known as pre-implantation genetic diagnosis examines embryos for a specific genetic disease.

"Many diseases such as cystic fibrosis, sickle cell anemia, hemophilia and Tay-Sachs are caused by a specific gene mutation," Arun says. "This is where pre-implantation genetic diagnosis comes in to determine which embryos are carriers for such diseases and which are not."

The test looks for a specific gene that has been identified within a family. More than 100 different genetic conditions can be identified.

Testing is conducted on day five or six of the embryo's development, when it's grown to include about 100 cells. Five or so cells are snipped off and analyzed for mutations — a small enough number to avoid any damage.

Prospective parents can choose not to implant embryos that are found to have the mutation identified by the test, and can instead select an embryo that is free from the genetic abnormality.

"With pre-implantation genetic diagnosis, future parents can cross one worry off their list by knowing that they won't pass along a known hereditary risk for disease," Arun says.

Sharon Dent, Ph.D., director of of the Virginia Harris Cockrell Cancer Research Center, Science Park, in Smithville

COURAGE UNDER FIRE

By Ron Gilmore

Wyatt McSpadden

Thanks to teamwork and quick thinking, valuable cancer research was saved when wildfires threatened the Smithville campus last October

There was nothing "hidden" about the Hidden Pines wildfire that charred nearly 540 acres of MD Anderson's Smithville research campus in October 2015.

The fire, first reported mid-day on Oct. 13, quickly became an inferno that threatened the very existence of the Virginia Harris Cockrell Cancer Research Center, Science Park, home to MD Anderson's Epigenetics and Molecular Carcinogenesis department.

Were it not for the quick thinking and dedication of facility staff, thoughtful plans put into place after another wildfire in 2011, the rapid response of area fire departments and authorities, and long-standing ties to the Smithville and Bastrop County communities, it might have been a devastating event setting vital research back years.

Despite a fire that burned nearly 75% of the campus property, no facilities — including highly specialized laboratories, research animal areas and administrative and academic offices — were touched.

Sharon Dent, Ph.D., chair of Epigenetics & Molecular Carcinogenesis and director of Science Park, credits many people within the campus and in the community for this outcome. But it's the devotion people have for the campus that, perhaps, mattered most.

"It was nothing short of an amazing effort by everyone involved," says Dent. "Everyone stepped up and asked, 'What can I do?'"

The Hidden Pines fire wasn't Dent's first time facing a threat to the campus, perched atop a hill in verdant loblolly pine woodlands near Smithville, a town of 4,000 located in the Texas Hill Country. Dent experienced the devastating Bastrop County Complex fire that destroyed more than 34,000 acres and 1,645 homes in 2011, but spared the campus. This was a learning experience that, combined with the collective knowledge gained from other campus personnel during previous fire events, prompted Dent and her team to make sure they would be prepared in the future.

Those preparations paid off during the Hidden Pines fire that burned some 4,600 acres, 64 homes and other structures before being extinguished by firefighters in a concerted effort between the city, county and state.

As home to MD Anderson's largest basic science department, Science Park has been a center for investigative discovery since the Texas Legislature set aside 717 acres for a cancer research facility in the 1970s. Today the campus includes 14 structures and nearly 101,500 square feet of research space, in addition to a 27,600-square-foot animal facility and an administrative support building with a conference center. It employs about 250 people, and is recognized for its work in unlocking the mysteries of cancer's molecular biology and developing new approaches for cancer prevention and detection. Francesca Cole, Ph.D., assistant professor of Epigenetics & Molecular Carcinogenesis, is one scientist who was concerned about her life's work.

"We had a lot of timed mice experiments that were in jeopardy," says Cole, who studies how damaged DNA is repaired its implications for potential new therapeutic targets. "We had mice that were three years into the breeding process, and to lose them could have really set our research back."

The fire "made a bee line" for Lab 4, a large research facility that houses her laboratory. Although the fire did not damage the lab, it was shut down for two weeks due to smoke and cleanup from the firefighting effort. Cole credits Dent for the advance preparation that saved labs, protected animals and kept staff safe.

"There was a lot of 'smart' practice that occurred," she says. "We'd just had an all-campus fire drill three months before. Also, our animal facility had a 24/7 monitoring system installed that measures air quality and temperature, so that we were able to keep up with how our mice were doing."

The monitoring system was just one of several campus enhancements following the Wilderness Ridge and Bastrop County Complex fires. These included adding fire hydrants and improved water lines, clearing small trees and undergrowth near the campus to reduce wildfire "fuel," constructing a loop road around the campus for easier evacuation and firefighter access, IT systems to ensure safety of crucial research data, annual campus evacuation drills, and plans for setting up an Incident Command Center (ICC) in the event of a disaster.

Dent and designated staff established the ICC in the conference center within five minutes of smoke being reported near campus. Evacuation of non-essential personnel began one hour after the ICC was established. Shortly thereafter, all personnel evacuated and the ICC reconvened first at a nearby restaurant, then later at the Smithville Recreation Center.

The teamwork did not end with Science Park employees, however. Volunteer firefighters from Smithville and the surrounding area, Bastrop County authorities and members of The University of Texas Police Department, including Lt. Wayne Smith, who was key to bridging communications between Science Park and the county, worked tirelessly to not only stop the fire, but ensure safety.

Dent, who has long cultivated close community ties with Smithville and Bastrop County through quarterly dinners, public tours and other activities, knows the value of establishing working relationships with local volunteer fire departments and other officials.

"Our Houston and Bastrop MD Anderson colleagues and the UT System had our backs and supported us throughout this emergency," she says. "And, of course, Mike Fisher, emergency management coordinator and former City of Bastrop fire chief, along with volunteer fire departments in Smithville, Heart of the Pines and Winchester, will always have a special place in my heart for saving our campus."

Francesca Cole, Ph.D., right, assistant professor of Epigenetics & Molecular Carcinogenesis

'Pulling together accomplished amazing things'

Briana Dennehey, Ph.D., coordinator of departmental publications for Epigenetics and Molecular Carcinogenesis, carefully recorded early events related to the October 2015 fire, and reported these and subsequent events in a special edition of Science Park's newsletter, The Insider.

"The quick and orderly evacuation would not have been possible without the buildings' fire wardens," wrote Dennehey. "The evacuation was completed in under 20 minutes."

All who were involved agree on one thing: It was working together that was crucial to safety. John Chotkey, manager of information services, recognized his colleagues' efforts in The Insider.

"Everyone has to work as a team and make decisions with limited information that affect a lot of people, animals and systems," Chotkey is quoted as saying. "Sometimes these decisions are made in moments with very little warning. The effort of everyone pulling together accomplished amazing things in a very short amount of time."

Lisa Tannehill, director of operations and maintenance, was also quoted in the newsletter and echoed Chotkey's assessment.

"The operations and management emergency response team willingly and faithfully worked long, hard hours in extremely difficult circumstances and unpleasant conditions, going above and beyond daily, to help the team protect and care for our campus," said Tannehill, who also credited Dent for "always putting human lives and safety first."

The dream team vs. rare heart cancer

AN ONCOLOGIST AND A SURGEON FROM DIFFERENT HOSPITALS WORK TOGETHER TO TREAT PRIMARY CARDIAC SARCOMAS, AKA HEART TUMORS

By Ronda Wendler

Michael Reardon, M.D., left, and Vinod Ravi, M.D., work together to battle deadly heart tumors. Nick de la Torre

When Gene Duncan visited his family doctor for a respiratory infection, little did he realize he'd be diagnosed with bronchitis — and something much more serious.

"While I was there, my heart started to race, says Duncan. "I got dizzy and almost blacked out."

A cardiologist was consulted to perform a sonogram on the 40-year-old father of four. What he saw was startling. Lodged in the right side of Duncan's heart was a golf ball-sized tumor. It was crushing the atrioventricular node — a group of muscle fibers that control heart rate.

"I'd been feeling light-headed and weak for a while, but I thought it was due to the hot Kansas summer," says Duncan, a metal worker from Wichita who worked long hours outdoors making and installing airplane parts.

Months earlier, Duncan had consulted his family doctor about his dizzy spells, but received a clean bill of health.

"My treadmill test was normal and my heartbeat was fine," he says. "I thought I was OK."

Elusive and rare

Vinod Ravi, M.D., isn't surprised by the delay in detecting Duncan's tumor.

"Cardiac tumors are often missed altogether or misdiagnosed because they're so rare," says Ravi, an associate professor of Sarcoma Medical Oncology at MD Anderson.

THEIR APPROACH HAS DOUBLED SURVIVAL TIME AND IS ATTRACTING PATIENTS AND DOCTORS FROM AROUND THE WORLD.

"Most doctors see only one or two in their entire careers — if even that."

Ravi partners with Michael Reardon, M.D., a professor of Cardiothoracic Surgery at both Houston Methodist and MD Anderson, to treat patients like Duncan who have primary cardiac sarcomas — malignant tumors that originate in the heart. Only about a dozen cases are recorded each year, according to a National Cancer Institute database.

"By the time these patients come to us, they're in trouble," Reardon says. "Their tumors had time to grow and spread because they went undetected for so long."

Like Duncan, Chriss Schwiderski's heart tumor eluded medical professionals. Doctors in his hometown of Dallas said the chest pain he was feeling was caused by pericarditis, an inflammation of the sac surrounding the heart. The condition would resolve on its own, the doctors said. When Schwiderski returned to the emergency room in severe pain for the fourth time, the perplexed staff ordered an MRI, which revealed a lemon-sized tumor growing in the right chamber of his heart.

The 36-year-old IT consultant was referred to Ravi and Reardon in Houston, who identified his tumor as a cancerous cardiac sarcoma.

Chemo first, surgery second

In the medical arena, Ravi and Reardon are known as the cardiac sarcoma "dream team." Several years ago they developed a unique protocol that uses unconventionally high doses of chemotherapy to shrink the tumor before surgically removing it. Their approach has doubled survival time and is attracting patients and doctors from around the world.

When Reardon began operating on cardiac sarcomas in 1998, he learned removing them wasn't easy.

"These tumors are big and bulky," he says. "Often they're attached to delicate structures in the heart."

During a typical six-hour surgery, Reardon meticulously cuts out the tumor, carefully avoiding the heart's vital network of valves, veins and arteries. Unless he can cut clearly around the entire tumor — achieving what's known as negative margins — cancerous tissue will be left behind and the tumor likely will grow back.

Only two in five patients achieve negative margins because surgeons are afraid to cut out too much tissue and potentially damage the heart.

Reardon knew there had to be a way to get better results. He consulted Ravi, an expert in the use of chemotherapy, and together they devised their inventive protocol. Here's how it works:

First, the tumor is biopsied to determine the stage of the cancer and to identify the molecular components inside the tumor. Next, Ravi prescribes chemotherapy to shrink the tumor to a fraction of its original size, making it easier for Reardon to eventually remove. Because no two patients' tumors are alike, the chemo is tailor-made to target each one's unique molecular makeup.

Ravi and Reardon treated Gene Duncan, a metal worker from Wichita, Kansas, for a primary cardiac sarcoma. Only about a dozen cases of the cancer are recorded each year. Jeff Tuttle

Tough regimen

Patients get very high doses of chemo, for as long as they can tolerate. It's a tough regimen, Ravi says.

"We push the envelope to shrink that tumor way down," he says. "The smaller it is, the likelier Dr. Reardon will get it all out."

Schwiderski had 32 rounds of chemo over the course of a year. With each successive round, his tumor shrunk a little more.

"It was brutal," says the physical fitness enthusiast. "I lost 20 pounds of muscle mass. All my hair fell out."

When his tumor had shrunk to the size of a thumbtack, Reardon was able to remove it completely.

Like Schwiderski, Duncan endured intense chemo, though his lasted almost a year and a half. After surgery with negative margins, he still shows no signs of cancer. He's gone from a checkup with Ravi every six weeks to once a year.

Buying time

Even with surgery, most cardiac sarcoma patients can expect their cancer to return somewhere in their body.

"Because their cancer originates in the heart, the cancerous cells are pumped out through the bloodstream to the rest of the body," says Ravi. "The heart beats 70 times a minute, so it distributes these cells very efficiently."

In patients whose margins were negative, the cancer usually shows up in the lungs or the brain. Average survival time is two years.

In patients whose margins were not negative, the tumor regrows in the heart. Average survival time is 10 months.

Still, there are exceptions. Duncan's surgery was five years ago, while another patient Ravi and Reardon call their "greatest success" lived nine years and 10 months.

Surgery buys patients time, they say, but it's an incomplete solution. The cure, they believe, lies at the cellular level.

Sharing knowledge

The two doctors organized a cardiac tumor group of local physicians and scientists that meets monthly at MD Anderson to discuss advances and brainstorm treatments. Medical school and hospital staffs across the country join in through videoconferencing to share their most challenging cases.

"By sharing knowledge about this rare cancer, we'll achieve better outcomes faster," Reardon says.

The team plans to establish an international registry of cardiac sarcoma tissue samples that will be housed at MD Anderson and shared with researchers worldwide. The goal is to study the samples to learn more about the genetics behind these tumors.

"We have an excellent clinical program," Ravi says. "Our goal now is to become the premier science center for cardiac tumor research."

A career built on a fascination with T cells

From the AIDS epidemic to fighting T cell lymphomas and skin cancer, much of Madeleine Duvic's work has dealt with these special white blood cells

By Ron Gilmore

Madeleine Duvic, M.D., is a clinical investigator with many interests.

Her eclectic portfolio of biomedical pursuits and successes has incorporated study of and treatment for AIDS-related dermatological conditions, hair loss due to alopecia areata, and significant research and treatment contributions to T cell lymphomas and skin cancer.

At the center of all she does is close communication with her patients.

"A clinician-scientist keeps his or her eyes open and they sometimes make remarkable discoveries based simply on talking to patients," Duvic says. "I have learned to listen to my patients a lot."

Perhaps it's such inspiration that has resulted in her life-enhancing advances in cutaneous T cell lymphoma (CTCL), leading to therapies being made available to patients with an "orphan" disease often overlooked by the pharmaceutical industry.

Duvic, professor and deputy chair of Dermatology, first took interest in the confounding world of T cells in the late 1970s while enrolled in a National Institutes of Health course on the subject. It spurred her interest enough to specialize in immunology at Duke Medical School, and she found herself at the forefront of the emerging AIDS epidemic. When she joined MD Anderson in the early 1980s, the dramatic loss of T cells in AIDS patients resulted in her running one of the first AIDS clinics in the country and ultimately led to her life's work in developing therapies for CTCL.

As a medical student and intern, Duvic saw patients who had an aggressive leukemic form of CTCL known as Sézary Syndrome, which caught her interest early on. CTCL occurs when T cells known as Sézary cells become cancerous, generally affecting the skin, causing skin lesions.

Sézary cells are found in the skin, lymph nodes and blood, and cause red, severely itchy skin that covers large areas of the body. Other signs and symptoms include thickened skin on the palms and soles of the feet, hair loss, abnormalities of fingernails and toenails, and difficulty regulating body temperature.

Sézary Syndrome, which generally strikes people over age 60, is rare, accounting for only 2 to 3% of the estimated 16,000 to 20,000 CTCL cases seen each year.

Duvic has treated more than 3,000 CTCL patients and sees about 200 each year, many who travel from far outside of Houston. A laboratory scientist as well as a doctor, she's been instrumental in helping develop the five drugs currently on the market to treat the disease.

Last November, she and colleagues published an article in the journal Nature Genetics that identified genetic mutations in patients with Sézary, which she hopes will lead to additional therapies.

The common thread throughout her career has always been about improving her patients' lives.

"When you relieve suffering and help patients participate in life again, that's what it's all about," says Duvic.

Eric Kayne

Other Interests

In 1987, Duvic created Texas' first photopheresis center at MD Anderson. During photopheresis, blood is taken from a patient's vein and separated into its different components. White blood cells are treated with a medication, exposed to ultraviolet light, and then returned to the patient, along with other blood cells. These treated cells stimulate the immune system, which helps the patient's body fight CTCL.

"Our lab has been studying the mechanisms behind photopheresis," says Duvic. "In particular, how does it work in both CTCL and graft versus host disease, since they are polar opposites?"

Duvic operates the world's largest clinical program for patients with another form of CTCL known as mycosis fungoides. In its most advanced stage, the disease causes skin tumors that may develop ulcers and become infected. Duvic and her team identified three areas within Houston where incidences of mycosis fungoides were unusually high. Those findings were published in Cancer.

She also developed an interest in alopecia areata, which occurs when the immune system mistakenly attacks hair follicles, resulting in significant hair loss. She created and oversees the Alopecia Areata Registry, the world's largest database of genetic samples from alopecia areata patients.

Researchers consider the connections between cancer and other diseases

By Ron Gilmore

Wyatt McSpadden

At its most basic level, cancer is the result of runaway cells and an immune system under attack. While MD Anderson's clinicians and scientists are passionate about treating and curing cancer with a laser-like focus, it's easy for them to appreciate its connectivity with other illnesses.

MD Anderson physicians recognize that their patients are often not just cancer patients, but may bring with them a host of other health issues such as heart conditions, diabetes, Alzheimer's disease, HIV/AIDS, alopecia areata (See related article on Page 23) and multiple sclerosis. They also understand the cellular functions commonly shared by cancer and other diseases.

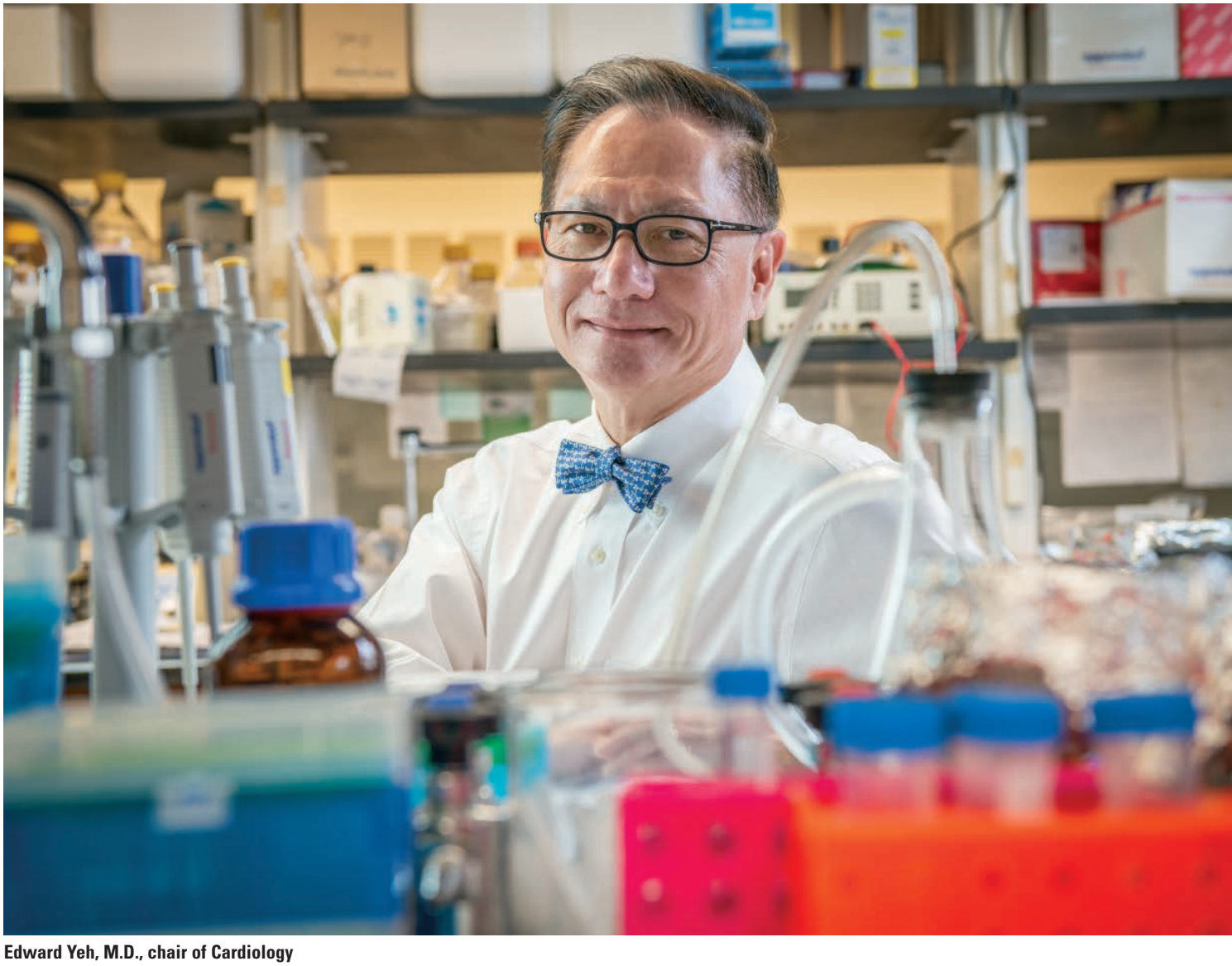
Epilepsy and heart attacks

Take epilepsy for example. While studying potassium channels — the body's electrical breaker boxes that regulate cells, cancerous or otherwise — MD Anderson's Edward Yeh, M.D., chair of Cardiology, revealed important new findings about a gene called Sentrin/SUMO-specific protease 2 (SENP2), which is crucial to brain and heart development. It appears that SENP2 deficiency can result in spontaneous seizures and sudden, unexplained death. His study results, published in Neuron, may very well explain the most common cause of early mortality in epilepsy patients.

"Understanding the genetic basis for sudden, unexplained death is crucial, given that the rate of sudden death in epilepsy patients is 20-fold that of the general population, accounting for the most common epilepsy-related cause of death," says Yeh.

Yeh's group also revealed new findings about a form of stem cell therapy used for cardiac repair. Just as stem cell therapy has become a viable option for many cancer patients, the use of mesenchymal stem cell therapy has been studied for people who've had heart attacks or who live with congestive heart disease. The team saw improvement in cardiac function following stem cell transplantation. Clinical trials are underway in collaboration with the Texas Heart Institute to determine whether mesenchymal stem cells can improve heart function in cancer patients who have chemotherapy-induced heart failure.

Yeh also led an atherosclerosis study with results reported in the Journal of Clinical Investigation. Like cancer, atherosclerosis is associated with cell death and inflammation. His team's study, which focused on inhibiting a protein called SENP2, could open up new possibilities for drug targets for this common disease in which plaque builds up inside the arteries, increasing the risk of heart attack and stroke.



Edward Yeh, M.D., chair of Cardiology

Targeting diseases of the elderly and chemotherapy-related nerve pain

Scientists have long known there are molecular themes common to neurodegeneration, cancer and other age-associated diseases. The Neurodegenerative Consortium, a collaboration between MD Anderson's Institute for Applied Cancer Science, Baylor College of Medicine and the Massachusetts Institute of Technology, was launched in 2011 with a $25 million matching gift from the Belfer Family Foundation. The foundation followed up with another $5 million gift in 2015.

The consortium was initiated to share promising discoveries across the three institutions with the goal of developing the next generation of targeted drugs and diagnostics for illnesses associated with advanced age such as Alzheimer's disease, ALS, and Huntington's and Parkinson's diseases. It's hoped discoveries will also address chemotherapy-induced neuropathy, a painful condition for many cancer patients.

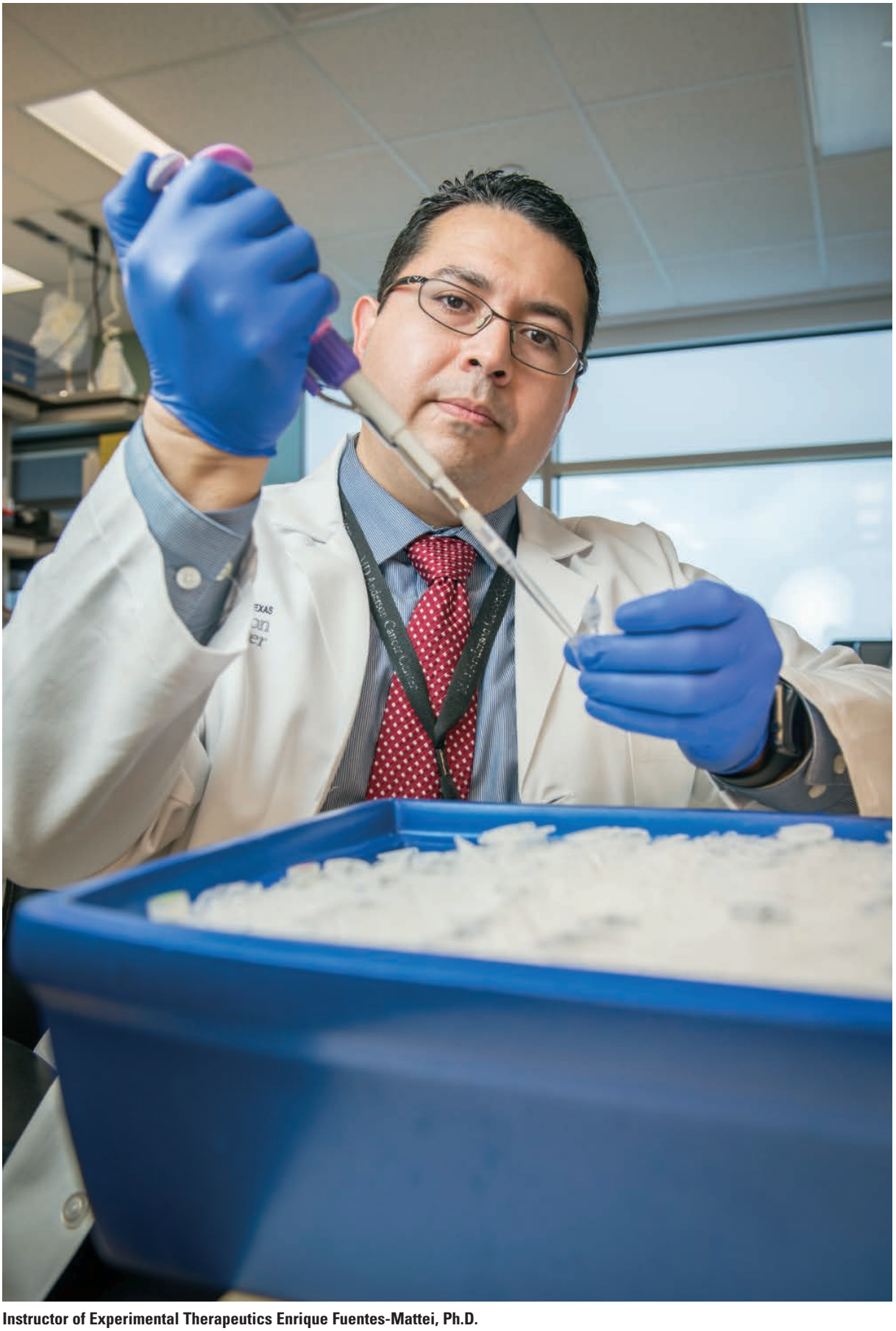
"The large numbers of MD Anderson patients who suffer from this side effect provide an opportunity for collaboration between their physicians and researchers to better understand the underlying biology associated with neuropathy," says Ronald DePinho, M.D., president of MD Anderson. "Such a discovery could lead to the development of prevention and treatment strategies."

Finding a protein linked to multiple sclerosis and inflammatory diseases

Multiple sclerosis patients could benefit from a study that identified potential therapeutic targets for a devastating disease striking some 2.3 million people worldwide.

The study was led by Shao-Cong Sun, Ph.D., professor of Immunology at MD Anderson. Sun's findings, published in Nature Immunology, identified a protein regulator known as Trabid as an important piece of the puzzle that leads to autoimmune inflammation of the central nervous system in multiple sclerosis patients.

Inflammation is an important part of the body's response against infections and tissue damage, but unresolved inflammation promotes cancer development and can be a contributing factor in a variety of diseases.



Instructor of Experimental Therapeutics Enrique Fuentes-Mattei, Ph.D.

A diabetes drug for cancer?

Since the mid-1990s, metformin has been prescribed for Type 2 diabetes. The popular and inexpensive drug works by impacting cell signaling pathways directly or indirectly at several locations in the body. The commonality between diabetes and cancer appears to be obesity.

Scientists at MD Anderson believe metformin may benefit women with breast cancer. A study by Experimental Therapeutics' Enrique Fuentes-Mattei, Ph.D., compared a newly developed obese-mice model with breast cancer and biological changes in breast cancer samples from patients. The results indicated a tie between obesity and a more rapid onset of disease and higher rate of death for women with estrogen-positive (ER+) breast cancer.

"Obesity increases the risk of cancer death among postmenopausal women with ER+ breast cancer, but the direct evidence for how this occurs is lacking," says Fuentes-Mattei, whose study results were published in the Journal of the National Cancer Institute. "Our study reported direct evidence about the breast cancer-promoting impact of obesity, which is like jet fuel for cancer."

Fuentes-Mattei's team found that fat cell proteins known as adipokines change the gene expression profile in breast cancer cells, promoting tumor growth and proliferation. The researchers also revealed that metformin, when combined with the targeted-therapy drug everolimus, suppressed fat cell-induced tumor growth in the obese mice and secretion of adipokines by fat cells.

"We believe that our mouse model will be a useful tool for future research on the development of therapeutic strategies that would block or reverse the effect of obesity on cancer," says Sai-Ching Jim Yeung, M.D., Ph.D., professor of Emergency Medicine and senior co-leader of the study with Mong-Hong Lee, Ph.D., professor of Molecular and Cellular Oncology.

An MD Anderson clinical trial based on the study is being led by Vicente Valero, M.D., professor of Breast Medical Oncology. Aung Naing, M.D., associate professor of Investigational Cancer Therapeutics, has also studied metformin and conducted a combination clinical trial that paired metformin with temsirolimus, a chemotherapy drug.

Additional MD Anderson studies are focusing on metformin and other diseases such as lung and endometrial cancer.

Seeking a sickle cell treatment alternative

Priti Tewari, M.D., assistant professor of Pediatrics, is an oncologist who specializes in stem cell transplantation for malignant and non-malignant pediatric diseases. She and her colleagues treat conditions such as anemia, clotting disorders, hemophilia, leukemia, lymphoma and sickle cell disease (SCD).

SCD is a group of inherited disorders in which red blood cells form into a crescent shape, like a sickle, and break apart easily, causing anemia. The damaged cells also clump together and stick to the walls of blood vessels, blocking blood flow. This can cause severe pain and permanent damage to the brain, heart, lungs and other organs. The disorder affects 90,000 to 100,000 people in the United States, primarily African-Americans and Hispanics.

Tewari's interest in sickle cell disease led to a clinical research trial that is studying the safety of giving NiCord® as an alternative therapy to the standard bone marrow transplantation prescribed for many patients with blood disorders. NiCord® is an umbilical cord stem cell-based treatment.

"MANY PATIENTS WHO COME TO MD ANDERSON SUSPECTED OF HAVING CANCER TURN OUT TO HAVE INFECTIONS INSTEAD, AND WE MAKE GAME-CHANGING DIAGNOSES NEARLY EVERY DAY."

— Xiang-Yang Han, M.D., Ph.D.

New findings about an ancient disease

The word "leprosy" often conjures up images of Biblical suffering or sanitorium settings. And yet the illness, properly known as Hansen's disease, continues to strike hundreds of thousands of people worldwide each year, primarily in developing countries.

An MD Anderson pathologist, Xiang-Yang Han, M.D., Ph.D., professor of Laboratory Medicine, has studied mycobacterium lepromatosis, a species of bacteria he first reported in 2008 as another cause of the disease. Up to that point, the only known cause of Hansen's disease was mycobacterium leprae.

In studying 20 genes of mycobacterium lepromatosis in comparison with mycobacterium leprae, Han found that the two bacteria came from a common ancestor some 10 million years ago. No one knew how long the disease had existed, but Han's work clearly showed it is, indeed, an ancient disorder, with its genetic beginnings as old as 20 million years.

This discovery offers new insights into disease pathogenesis beyond Hansen's disease, a finding that has implications for cancer microbiologists like Han.

"Many patients who come to MD Anderson suspected of having cancer turn out to have infections instead, and we make game-changing diagnoses nearly every day."

Matching the need for bone marrow transplants

Cord blood and half-match options provide patients with a whole lot of hope

By Katrina Burton

Seventeen-year-old Travis Arnold plays golf for Klein High School, just outside of Houston. Eric Kayne

Travis Arnold is in it to win it. The 17-year-old is a top-rated golfer on Klein High School's Bearkat Golf Team. Academically, he ranks in the top 2% of his class. And two years ago, he kicked cancer to the curb.

At age 12, Arnold was diagnosed with a bone marrow disorder that evolved into acute myeloid leukemia — a fast-growing cancer of the white blood cells.

Doctors hoped a bone marrow transplant rich with stem cells could save his life. Arnold underwent two transplants at another hospital, using marrow from donors who tested genetically as his perfect match. Both transplants failed.

That's when his parents sought help at MD Anderson Children's Cancer Hospital, where doctors decided to try something different. They performed a so-called half-match bone marrow transplant, known medically as a haploidentical transplant, with "haplo" meaning "half."

While half-match donors aren't a perfect match, they're close enough to allow patients to move ahead with a transplant.

To test whether a donor's bone marrow is a suitable match for a recipient, doctors examine genes in the human leukocyte antigen, or HLA System — the part of the immune system that recognizes self and not self.

In a full match, eight to 10 HLA genes need to match between donor and recipient. In a half match, only half of these HLA genes need to match up.

"Parents are always a half-match for their children, and vice versa," says Stefan Ciurea, M.D., associate professor of Stem Cell Transplantation. "Siblings have a 50 percent chance of being a half-match for each other."

In Travis Arnold's case, his father served as his half-match.

Because the matching between donor and recipient is only half, the donor's immune system may generate a stronger attack against the recipient's tissues — a condition known as graft-versus-host disease. Certain therapies given before and after the transplant have been very effective in controlling this reaction.

"With chemotherapy and immunosuppressive treatments, the rates of graft-versus-host disease are surprisingly less than or similar to the rates with matched donors," Ciurea says.

Life begins with second chances

Similar to haploidentical transplants, cord blood transplants are providing effective new treatment options for cancer patients.

At the time of a baby's birth, after the umbilical cord is cut, a needle is inserted into the vein of the cord, and the blood in the cord and placenta is collected and frozen until it is needed for a transplant.

This infant blood is rich in new stem cells that haven't yet been educated against foreign invaders, like bacteria and viruses. So its stem cells are less likely than bone marrow stem cells to attack a recipient's tissues. As a result, the donor and recipient don't need to be as closely matched as those in a bone marrow transplant.

"A match in four of six HLA markers in cord blood is usually considered acceptable," says Elizabeth Shpall, M.D., Ph.D., deputy chair of Stem Cell Transplantation and Cellular Therapy and chair of the Cord Blood Transplant Program at MD Anderson.

Since the first umbilical cord blood transplant performed in France almost 30 years ago, the banking of cord blood has played a significant role in saving lives.

Avoiding delays

With half-matched and cord blood transplants providing new sources of stem cells, patients no longer need to delay transplantation while waiting for a perfect or near-perfect donor match.

"People who need transplants are usually very ill, and rapid access to stem cells can save lives," Shpall says.

Today, practically all patients find a donor, says Dean Lee, M.D., Ph.D., associate professor of Pediatrics and Arnold's doctor. "With new sources of stem cells, we no longer have to turn away someone who needs a transplant for lack of a donor."

A study published in the New England Journal of Medicine in 2014 verified that lack of a donor is no longer a major limitation to transplants. More than 99% of white European-Americans and 95% of African-Americans who need a transplant will have a suitable match, according to the study.

Minority donors needed

This is especially relevant for minorities, who are underrepresented in the National Marrow Donor Program's Be the Match registry — the nation's largest bone marrow registry. More than 10 million people who are willing to donate their bone marrow to a stranger have signed up. If patients cannot find a match within their family, they must attempt to find an unrelated donor from the registry.

"Bone marrow donations must be matched to very specific genetic markers that are overwhelmingly more likely to appear in donors of the same ethnicity," Shpall explains. "Because minorities are under-registered, it's harder for them to find a non-family donor."

Minorities make up only 25% of donors in the Be the Match registry, according to Cheekswab, an organization dedicated to increasing minority participation. As a result, minorities have a 66 to 73% chance of finding a matching donor through the registry, compared with Caucasians' 93% likelihood of finding a match.

"Additionally, some ethnic groups have a more complicated gene pool that makes it difficult to find a match through traditional methods," Shpall says.

Using half-matched donors now compensates for the lack of donors in Be the Match and other registries, Ciurea adds.

"With half-matched transplants generating improved outcomes that are comparable to full-matched transplants, every patient has a chance," he says.


Special tips for
EVERYDAY CANCER PREVENTION
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BACON
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or
SUN EXPOSURE
DO NOT SMOKE OR CHEW
TOBACCO
LIMIT
SUGARS · WHITE BREAD
GRILLED OR PAN-FRIED FOODS
ALCOHOL & SUGARY DRINKS
MAINTAIN A HEALTHY WEIGHT
ENJOY REGULAR
EXERCISE
Eat more
FRESH FRUIT
VEGETABLES
WHOLE GRAINS
Remember:
ALL THINGS IN
MODERATION

Carcinogen is a word that inspires a certain amount of healthy respect and wariness. After all, it designates something that may cause cancer, which most people make every effort to avoid. Many well-known carcinogens, such as tobacco, radon, plutonium and asbestos, are obvious offenders, but many others are not so obvious.

Navigating the maze of possible carcinogens is no small task, especially as cancer prevention researchers continue to report new behavioral or environmental cancer risk factors.

Is there a menu item that should be avoided at all costs? A superfood for cancer prevention? An electronic device that increases your risk?

Research reveals that up to half of all cancers may be avoided by making lifestyle choices such as eliminating tobacco use, maintaining a healthy weight, improving diet and limiting sun exposure.

Crafting a healthy diet

When trying to avoid carcinogens in the diet, the multitude of reports linking foods to cancer risk can be overwhelming. Just recently, MD Anderson researchers have contributed several studies to this field.

Their findings (see "Is what we're eating giving us cancer?" on page 32) reveal increased cancer risks associated with eating more sugar, nutrient-poor carbohydrates and meat — especially when charred by cooking. And last year, the World Health Organization (WHO) determined that enough evidence exists to classify processed meats such as bacon, sausage and hot dogs as carcinogens.

Xifeng Wu, M.D., Ph.D., professor of Epidemiology, also discovered that diets with a high glycemic index, defined by nutrient-poor carbohydrates that rapidly increase blood sugar levels, are linked to higher lung cancer risk in certain populations.

Peiying Yang, Ph.D., assistant professor of Integrative Medicine Research, and Lorenzo Cohen, Ph.D., professor of Palliative, Rehabilitation & Integrative Medicine, determined that fructose increased the risk of breast cancer and metastasis in laboratory mice.

Despite these reports, avoiding meat, carbs and sugar altogether isn't the only answer, says Carrie Daniel-MacDougall, Ph.D., assistant professor of Epidemiology.

"Some foods thought of as vices may actually be good for you when consumed in moderation. For example, coffee, wine and chocolate have components rich in phytochemicals that seem to be cancer-reducing," Daniel-MacDougall points out.

"On the other side of the coin, there may be concerns about each," she cautions. "For example, excess alcohol may cause several types of cancer and other diseases."

Daniel-MacDougall explains it's not wise to make sweeping judgments about individual foods. Instead, people should practice moderation and understand how foods fit into overall dietary habits.

"It's a delicate balance of a lot of different things," she says. "It's just like a financial portfolio, you don't want to put all of your eggs in one basket — you want to diversify."

To minimize cancer risk, MD Anderson and the American Institute for Cancer Research (AICR) recommend eating more fruits, vegetables and whole grains; limiting red meat, alcohol and salty foods; and avoiding sugary drinks. The AICR also suggests maintaining a healthy weight and getting regular exercise.

Minimizing harmful exposure

People are constantly exposed to environmental health hazards such as pollution, radiation and chemicals. Some of these are harmful; others are harmless. Knowing the difference and how to avoid the former can help prevent several types of cancer, says Therese Bevers, M.D., medical director of MD Anderson's Cancer Prevention Center.

It's important to separate fact from fiction, she says.

Some chemicals found in everyday items are incorrectly labeled as carcinogens. Bisphenol-A (BPA) is found in hard plastics and food containers and may be linked to early childhood development problems. But there isn't conclusive evidence to suggest that it causes cancers, Bevers says.

Anecdotal evidence suggests chemicals found in deodorants or even sunscreens may be carcinogens. Once again, Bevers says there is no data to back this up. In fact, not using sunscreen is far more harmful, she explains.

Excessive exposure to ultraviolet (UV) radiation is a major risk factor for all types of skin cancer, Bevers says.

"People should practice sun safety outdoors and avoid ultraviolet tanning beds," she advises. "Especially when young."

Other forms of radiation are emitted by cell phones and microwaves, and some people worry they cause cancer. Their concern is unnecessary, says Bevers.

"Both the National Cancer Institute and WHO advise there isn't enough evidence to label cell phones as a carcinogen," she says. "As for microwaves, unless you're crawling inside, you're well shielded from any radiation."

An additional source of radiation comes from mammograms and low-dose lung CT scans. Could it be that cancer screening itself could increase your cancer risk?

Bevers is asked about mammogram radiation daily. She explains that both imaging tests produce relatively low doses of radiation. Most people undergoing lung screenings have been heavy smokers all their lives and are already at an increased risk for lung cancer.

"More women will die of breast cancer by not getting a mammogram than from the exceedingly rare and unlikely development of a cancer due to the radiation exposure from a mammogram," says Bevers.

For the best approach to lowering cancer risk, Bevers recommends maintaining a healthy lifestyle that focuses on avoiding major risk factors such as tobacco use, an unhealthy diet and a sedentary way of life.

MD Anderson researchers have recently published studies that point to a connection between cancer and our diets and eating habits.

Researchers led by Xifeng Wu, M.D., Ph.D., professor of Epidemiology, discovered that diets with increased meat consumption were associated with increased kidney cancer risk. The increased risk is primarily the result of ingesting carcinogenic compounds created by certain high-temperature cooking techniques such as grilling or pan-frying. The study was published in the journal CANCER.

Peiying Yang, Ph.D., assistant professor, and Lorenzo Cohen, Ph.D., professor of Palliative, Rehabilitation & Integrative Medicine, published findings in the online issue of Cancer Research that revealed a connection between dietary sugar intake and breast cancer development. In laboratory mice, increased sucrose intake fueled breast cancer development and metastasis to the lungs.

Xifeng Wu's team also published a study in Cancer Epidemiology, Biomarkers & Prevention describing an association between dietary glycemic index and lung cancer risk in certain populations, including nonsmokers. The study found that lung cancer patients were more likely than healthy individuals to consume diets with a high glycemic index, a value assigned to carbohydrates to indicate how rapidly they increase blood sugar levels.

LOCATIONS

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

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