### 2024, Issue 2

MEMORIAL SLOAN KETTERING CANCER CENTER

### **The MSK Campaign** Leading Science. Changing Lives.

Dana Vergara holds her baby, Hudson, born thanks to MSK innovation.



**MSK's Hospital of Tomorrow** A CAR T Breakthrough for Solid Tumors **Clues to the Rise of Cancer** in Younger Adults



### Dear MSK Community,

Our knowledge of cancer — what it is and how it progresses — has developed at a staggering pace over the past 20 years. Today, thanks to remarkable advances in the understanding of how cancer cells behave and evolve, many led by MSK, researchers have devised previously unimaginable strategies to detect and treat the disease. We are at a moment of unprecedented hope and opportunity, and we would not be here without the generous philanthropic support of MSK Giving, our donor community.

MSK has achieved many "firsts" in its 140-year history, and philanthropy has been essential to every one. From establishing the first fellowship program to playing important roles in developing the first chemotherapy, the first cancer immunotherapies, and the first laboratory-developed test authorized by the Food and Drug Administration to screen for cancer-causing mutations in tumors, all of these innovative and creative ideas relied on philanthropy to get their jump-start.

This is because donor support is the best way to fund a good idea, and every breakthrough begins with an idea. Traditional funding sources, like the National Institutes of Health, usually kick in only after there is ample evidence indicating the idea will work. Philanthropy allows MSK doctors and scientists to apply courage and creativity to answer cancer's biggest questions.

The Empire State Building, lit blue to celebrate MSK's 140th birthday

Today, despite all of our progress, cancer rates are rising, due largely to an aging population that has a higher risk of cancer and an unexpected increase in the disease among people under 50. We have many innovative tools and quantities of data available to us, but we need to invest in new technologies to unleash their full potential. Cancer research has reached a critical turning point, and, once again, we need donor support to ensure that our approach to cancer can successfully adapt to meet the demands of the future.

To respond to this urgency, MSK has launched "The MSK Campaign: Leading Science. Changing Lives." We are committed to raising \$6 billion by 2030, under the leadership of our co-chairs Stanley F. Druckenmiller, Member of the Board of Trustees; Marie-Josée Kravis, Vice Chair of the Board of Trustees; and Scott Stuart, Chair of the Board of Trustees.

Organized across six strategic initiatives, The MSK Campaign ensures that our doctors and scientists will have the resources needed to create new treatments and cures, turning a legacy of innovation into impact.

This special issue of MSK News tells the story of how far MSK has already come — and how much further we can go with the partnership of MSK Giving, our donor community.

Last year, more than 415,000 people donated to MSK, each one a valued member of the community. Ninety-seven percent of these donors contributed less than \$1,000. Whether you ride with Cycle for Survival<sup>®</sup>, run with Fred's Team<sup>®</sup>, laugh with Comedy vs Cancer, give now or through thoughtful future arrangements, you can join The MSK Campaign and our effort to advance MSK's mission of ending cancer for life.

The MSK Campaign is ambitious and bold, and so is the MSK Giving community. To learn how you can change lives with us, visit giving.mskcc.org/msk-campaign.

#### Sincerely.

Selwyn M. Vickers, MD, FACS **President and Chief Executive Officer** 

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Dr. Anaeze Offodile is helping MSK navigate into the future as Chief Strategy Officer.

### **The MSK Campaign**

## Our Six Strategic Initiatives



Change lives with us. Scan here to give.

### Innovate Clinical Strategy

We are expanding our clinical capacity and creating a state-of-the-art patient experience, bringing our world-class care to people everywhere, through MSK's trailblazing new Pavilion, our regional sites, and even our patients' own homes. Not only will we improve their health, but we also will support their needs. We treat people in the context of their lives.

Nurse Brittney Grannum helps a patient recover by connecting on a personal level. Understanding what matters most to patients is an essential part of cancer care at MSK.





Before scientists could develop immunotherapies, they needed to find out how the immune system interacts with cancer cells. Before researchers could create precision oncology drugs, they needed to understand that many cancers are caused by genetic mutations. Beneath every bold and lifesaving innovation, there are teams of scientists driven to understand the fundamentals of human biology and apply those discoveries to improve and save lives.

Graduate student Lucia Wang and molecular biologist Dr. Dirk Remus are researching how DNA is copied when cells divide, grow, and repair.



### Harness the Immune System



Cancer immunotherapy is one of the most transformational breakthroughs in modern medicine, and many of the greatest advances were led by MSK. Our researchers continue striving to understand the immune system in all of its complexity, to boost the body's innate power to fight cancer — especially solid tumors.

Medical oncologists Dr. Luis Diaz, Jr. (Grayer Family Chair) and Dr. Andrea Cercek with patients who joined a practice-changing clinical trial. Immunotherapy achieved 100% remission in patients with a certain type of rectal cancer.



### Transform Data Into Cures



Data science offers unprecedented insights into each patient's cancer and helps guide treatment decisions. Because MSK has gathered a vast amount of information from caring for hundreds of thousands of patients, we are uniquely able to analyze key details that will help us improve cancer diagnosis, predict responses to therapy, and continuously advance patient care. The lessons learned at MSK benefit patients across America and around the world.

Computational oncologist Dr. Sohrab Shah (Nicholls-Biondi Chair) leads a team of skilled data scientists who have chosen to use their specialized knowledge to advance cancer research.



### Expand Precision Oncology



MSK helped usher in the era of precision medicine, in which a patient's cancer treatment is tailored to the molecular characteristics of their disease. We developed MSK-IMPACT<sup>®</sup>, the first tumor-sequencing test of its kind to be authorized by the Food and Drug Administration. Although we've since identified more than 500 genetic mutations linked to various cancers, much work remains to find more drugs to target and stop them from driving cancer growth.

Cancer biologist Dr. Nikolaus Schultz, molecular geneticist Dr. Debyani Chakravarty, and physician scientist Dr. David Solit (Geoffrey Beene Chair) collaborate on powerful new precision therapies and diagnostic tools.



### Develop the New Generation of Leaders



There is an urgent demand for exceptionally skilled physicians, scientists, and other professionals to discover new treatments and to make the best cancer care available to the most patients. We are committed to recruiting, training, and retaining the pioneers of tomorrow.

Cell biologist Dr. Philipp Niethammer talks to MSK students. Teaching is deeply engrained in MSK's culture. Each year, MSK trains more than 2,300 residents, fellows, and PhD candidates.



# The Hospital of TOMORROW

### The prognosis is sobering.

"There is a coming surge of cancer cases, on top of the storm that is already upon us," says Jeffrey Drebin, MD, PhD, Chair of Surgery at Memorial Sloan Kettering Cancer Center (MSK).

According to the Centers for Disease Control and Prevention, the number of people with cancer will increase by 50% by 2050, with more than 60,000 new cases each year in New York City alone.

Why? America is aging; some call it the silver tsunami. At the same time, more people are being diagnosed at a younger age with colon, prostate, and breast cancers. And ironically, successful therapies create a new set of concerns for the future.

"Thanks to advances in cancer treatment, patients will be living longer and their needs will change as we continue to care for them," says Lisa DeAngelis, MD, Chief Physician Executive at MSK. "Not only will more people have the disease, but their care also will become more specialized as they grow older. And the increasing number of younger patients will need support for a lifetime."

MSK is getting ready for the future demand now with plans underway to construct a 900,000-square-foot facility connected via a patient bridge to the current hospital at 1275 York Avenue, which is more than 50 years old and already operating at capacity. The new MSK Pavilion will provide the additional space and advanced technology necessary to keep pace with the evolving needs of cancer patients, ensuring high-quality care for generations to come. Devoted entirely to acute patient care, the building will house state-of-the-art operating suites and more than 200 private patient rooms, including 40 beds in intensive care. It's scheduled to open in 2030.

"The MSK Pavilion is the hospital of tomorrow," says Marcia Levine, MSN, RN, Vice President of Perioperative and Inpatient Nursing Services, who has been deeply involved in the Pavilion planning. "The building is being designed in close consultation with MSK doctors and nurses to deliver the care they want their patients to have. That priority is driving every decision."

This trailblazing facility will improve the patient experience in ways both large and small. For example:

- New technology will improve surgery and imaging, as well as the care coordination essential for complex cases.
- **The latest clinical techniques** will minimize pain and nausea.

The hospital atmosphere will welcome patients and caregivers with calming landscaping as they enter, a thoughtful patient drop-off area and parking system, abundant natural lighting, and private rooms.

### Scaling Up Lessons Already Learned

The coming Pavilion is not the only way MSK is preparing for the future and innovating right now. MSK is also looking to its past.

There are many lessons learned from the Josie Robertson Surgery Center (JRSC), which opened in 2016. Doctors perform more than 10,000 operations a year at JRSC, which specializes in outpatient and short-stay surgical procedures. According to urologic surgeon Vincent Laudone, MD, Chief of Surgery at JRSC, MSK researchers have published findings of more than 50 studies performed at JRSC and always have a dozen or more ongoing projects.

"In addition to serving patients," says Dr. Laudone, "JRSC has enabled us to do a great deal of research into ways to improve care." He adds, "The large number of people we treat and our ability to collect detailed information on the outcomes of every patient allows us to get answers quickly and put them into practice."

"The building is being designed in close consultation with MSK doctors and nurses to deliver the care they want their patients to have."

-Marcia Levine, MSN, RN

### **MSK PAVILION**

Scheduled to open in 2030

200+ private patient rooms including 40 ICU beds



### **ARTIST RENDERING**

MSK Pavilion, scheduled to open in 2030, will provide the additional space and advanced hnology needed for the dramatic increase in cancer cases in the coming decades.



Epidemiologist Dr. Sigrid Carlsson is focused on ways to improve a patient's experience in the hospital and after they are discharged.

### Improving Comfort and Recovery

"Effective pain and nausea management are crucial for facilitating a smooth transition from hospital care to home recovery, as they can be a major barrier to discharge especially in a busy ambulatory center," says MSK anesthesiologist Anoushka Afonso, MD, Director of MSK's Enhanced Recovery Programs, Anesthesia & Critical Care Medicine.

In recent years, MSK has developed new approaches for painkillers to reduce dependence on opioids. Researchers are also studying the best way to give nerve blocks to breast cancer patients undergoing a double mastectomy and breast reconstruction.

"There are many ways to do nerve blocks — from the front or back, and above or below certain muscles — and our research can give us a definitive answer as to which works best," says Hanae K. Tokita, MD, Director of Anesthesia at JRSC, who is leading the trial with 1,500 participants — an unprecedented size for a single institution. "It provides the kind of top-level evidence that could change clinical practice."

### Hospitality in the Hospital

No one enjoys being in the hospital. The jarring sounds and harsh lighting can add to an already stressful experience.

"We're always focused on finding ways to minimize the anxiety people normally feel in a hospital," says **epidemi-**

### ologist Sigrid Carlsson, MD, PhD, MPH, JRSC's Director of Clinical Research.

Seeking creative solutions for the future, MSK has tapped into health technology companies. One study is looking into masking disruptive hospital noises with "reactive soundscaping" to create a calm oasis for patients. Certain rooms at JRSC are now outfitted with standard white noise, while others receive gentle nature sounds such as wind, rain, or waves — that react and adjust to the sounds of the room in real time.

"We know noise is a big issue in hospitals, causing stress, interrupted sleep, and confusion for patients," says **Christopher Brause, the Clinical Experience Design Lead on MSK's Informatics team**. "We hope to improve how people feel. We also will look to see if there are more measurable benefits — better vital signs, improved sleep, faster discharge, or less need for pain medication."

Nurse leader Blanca Vasquez-Clarfield, PhD, hospitalist Barbara C. Egan, MD, and other medical staff have driven another approach to promote better rest at Memorial Hospital. For patients who are medically stable and

### Dr. DeAngelis holds the Scott M. and Lisa G. Stuart Chair.

Dr. Drebin holds the Murray F. Brennan Chair in Surgery.

alert, no vital signs are taken between 10 p.m. and 6 a.m., and early-morning blood draws are postponed until later.

### **Bringing the Hospital Home**

But no matter how hospitable a hospital environment may be, patients want to go home as soon as possible.

And when patients are discharged, they will take the hospital home with them, using new tools to keep close watch over their well-being.

The MSK Pavilion will implement practices developed at JRSC to bring the hospital home. At JRSC, patients wear devices so their activity can be closely watched to make sure they are recovering on schedule. And when they go home, MSK care teams continue to monitor them with Recovery Tracker, an electronic survey system that allows them to report symptoms such as pain, nausea, or fatigue for the first 10 days after discharge.

"This system reassures patients that even though they've walked out of the doors of the hospital, they haven't left MSK," Dr. Carlsson says. "It goes a long way toward easing anxiety."

It also reduces the odds that patients will need urgent care by 42%, according to a study led by Dr. Laudone and reported in JAMA Surgery.

"Because we take extreme care when patients are in the hospital and when they go home, we continue to have very low rates of readmission," Dr. Laudone says.

### Transforming the Cancer Journey

Dr. DeAngelis notes these are just a few examples of how MSK is building a bold new infrastructure that is centered on the patient and expands MSK's reach into communities to improve access to world-class cancer care.

"No matter the coming surge in cases, we will be ready," Dr. DeAngelis says. "We will continue to achieve the best possible outcomes for our patients, with compassion and our collective determination to support their very best quality of life."•





### ON THE CASE Why Are So Many Younger Adults Getting Cancer?

It's a disturbing mystery that has drawn the attention of investigators from across Memorial Sloan Kettering Cancer Center (MSK).

> Why are a growing number of young people under 50 being diagnosed with over a dozen forms of cancer around the world?

Men and women in the prime of their lives are increasingly being diagnosed with serious cancers, including colorectal, breast, prostate, uterine, stomach (gastric), pancreatic, and more. One forecast predicts cancer for this age group will increase by 30% globally from 2019 to 2030.

"This is serious and worrisome," says Shari Goldfarb, MD, breast oncologist and Director of MSK's Young Women With Breast Cancer program.

"This is not a blip," explains Andrea Cercek, MD, gastrointestinal oncologist and Co-Director of The Center for Young Onset Colorectal and Gastrointestinal Cancer. "The more data we gather, the clearer this becomes."

Charisma McDuffie, diagnosed with breast cancer at age 28, was treated by MSK's Dr. Shari Goldfarb in a program specifically tailored for young women with breast cancer.

### **Meet Some of MSK's Young Patients**



- Diagnosed at age 40, in 2023
- Stage 4 colon cancer
- Bronx



- Diagnosed at age 27, in 2019 Breast cancer
- Long Island

MSK is a pioneer in caring for the specific needs of people facing what are often called early-onset cancers, who confront very different challenges than older adults. The coming surge in cases is a key reason MSK is building a new state-ofthe-art hospital, called the MSK Pavilion (learn more on page 6).

Just as importantly, MSK experts are leading the investigation into why this is happening.

### Is Obesity the Culprit?

An obvious focus is the vicious circle of obesity, highly processed foods, and sedentary lifestyles, which are an epidemic in America and growing in many countries.

"We know obesity causes inflammation, which can lead to cancer," explains



- Diagnosed at age 27, in 2023
- Stage 2B gastric cancer

Manhattan

- **Christopher Williams** 
  - Diagnosed at age 48, in 2021 Stage 3 colorectal cancer
- Brooklyn

Dr. Goldfarb. "We believe that plays a role and needs to be addressed. But it doesn't fully explain the growing rates of young women with breast cancer."

Nor does it explain the increase in cases seen by MSK's Center for Young **Onset Colorectal and Gastrointestinal** Cancer, which is co-directed by gastroenterologist Robin Mendelsohn, MD. The center has tracked more than 4,000 younger adults. "They are actually less likely to be obese than the general population," says Dr. Mendelsohn. "They are also less likely to use tobacco or have other known risk factors."

### **Promising Leads**

MSK experts agree there is not a single smoking gun. "If there was, researchers would have found it," says Dr. Mendelsohn. "Instead, there are likely several causes."

Dr. Cercek explains, "The working hypothesis is that there is an environmental exposure - or multiple exposures that people born starting in the 1950s came in contact with." It's possible, she says, that the "exposures began in the 1960s or '70s and have been continuously present since then."

While MSK researchers don't yet know what that exposure might be, they have discovered promising leads.

### **Gut Instinct: The Microbiome**

In May, Dr. Mendelsohn presented preliminary data at a medical conference about the microbiome of people with earlyonset colorectal cancer. The microbiome, also known as the invisible organ, is the enormous community of bacteria and other microbes that live in our gut, which help regulate our digestive system.

"We found that younger people with colorectal cancer had less diversity in their microbiome than older patients," says Dr. Mendelsohn. "And the makeup of the two groups' microbiome is different too." That's important because more diversity generally means better health.

By scouring the vast amount of lifestyle data younger patients at MSK have provided, she says, MSK is "investigating factors we know affect the microbiome, including dietary changes, medications such as antibiotics, and even factors from childhood, such as breastfeeding and C-section patterns, age of parents at birth, and more."

The goal, says Dr. Mendelsohn, is to "look for a possible trigger that would explain why the microbiomes of these patients are different."

Stomach cancer research by gastroenterologist Monika Laszkowska, MD, MS, focuses on another angle: how to identify younger people at high risk so they can be screened.

"We know that certain groups, such as people of East Asian ancestry, are at higher risk of stomach cancer, which is often triggered by a microbe called Helicobacter pylori," she explains. "Our research involving patients at MSK also found other groups, such as younger Hispanic women, are more likely to develop early-onset stomach cancer." That insight could lead to more awareness among Hispanic and Latina women and their doctors.

Dr. Laszkowska's research also raises new questions. "Stomach cancer is slow moving. So why is it developing more quickly in younger people?" she asks. "Could the malignancy be growing through a different pathway? Or could it be spurred by another condition such as an autoimmune disease?"

### **Is Early-Onset Cancer Biologically Different?**

These questions led to another: Is early-onset cancer biologically different and more aggressive than cancer in older people?

A study led by Dr. Cercek discovered an intriguing dynamic involving colorectal cancer. Her research found that colorectal patients treated at MSK responded the same way to chemotherapy "whether they were 17 or 70," she says. "Those in the younger group were more likely to have rectal cancer. But the biology of the disease looked the same as in older patients."



However, cancer is not a single disease. Dr. Goldfarb points out, "Breast cancer

Instead, it is over 400 different diseases. subtypes called triple-negative and HER2positive are more common among young women — and have a worse prognosis."

She explains that "some of the risk factors for breast cancer are increasingly found in younger women." She adds, "For example, they are exposed to more years of unopposed reproductive hormones because they are experiencing menstruation earlier and having children later."

However, she stresses that this along with the rise of obesity — does not fully explain why more women under 50 are developing particularly aggressive forms of breast cancer.

MSK's investigation into why includes every tool at researchers' disposal, from surveys that reveal all aspects of lifestyle and personal history to next-generation genomic testing to determine what's happening on the genetic level.



Breast oncologist Dr. Shari Goldfarb is Director of MSK's Young Women With Breast Cancer program.

### **Breast Cancer Subtypes**

Dr. Goldfarb points to research by breast oncologist Pedram Razavi, MD, PhD, to uncover minimal residual disease in patients. She also uses blood tests that look for mutations in tumors to help guide treatment decisions by predicting which treatments will be most effective.

### **Meeting the Needs** of Younger People

As the investigations continue, MSK specialists support the unique needs of younger adults. "Our program helps with the specific concerns of this stage of life, including fertility preservation, talking with children, parents and colleagues about a cancer diagnosis, discussing impact on work, dating, sexual health, and much more," says Dr. Goldfarb.

"When a person is diagnosed with cancer, it turns their world upside down. We're there to help not just with their physical health, but their entire social and emotional well-being." •



Dana Vergara was the first person in the U.S. to deliver a baby after a groundbreaking surgery at MSK protected her from the side effects of radiation treatment for rectal cancer

When Dana Vergara cradles her sweet baby, Hudson, she can hardly believe it.

Dana was 33 years old and the mother of a 5-month-old daughter, Jolene, when she learned that she had stage 3 rectal cancer. She knew it was bad. She wasted no time reaching out to specialists at Memorial Sloan Kettering Cancer Center (MSK).

But Dana's dreams for her future collapsed as the doctors outlined a treatment plan. The cancer, fortunately, was treatable with radiation, chemotherapy, and surgery — the standard of care — but the therapy that would save her life would most likely have a devastating impact on her fertility.

MSK radiation oncologist Carla Hajj, MD, explained radiation to the pelvis can damage the uterus. "I told her that it would be high risk to carry a pregnancy after pelvic radiation therapy and likely that she would end up with premature menopause," Dr. Hajj recalls.



Big sister Jolene is "head over heels in love with Hudson."

For Dana and her husband, Thomas, the threat of infertility as a side effect of her cancer treatment was heartbreaking. "I always wanted to have more kids," Dana says.

But then, Dana's MSK doctors suggested yet another option: an innovative surgical procedure that might protect her uterus from the effects of radiation and enable her to give birth. If she agreed, she'd be only the third patient in the United States to undergo the experimental surgery.

### **Uterine Transposition: An Innovative Procedure**

MSK gynecologic surgeon Mario Leitao, MD, had learned of a pioneering technique called a uterine transposition, which involves temporarily moving the ovaries and uterus up the abdominal wall and out of the pelvis, away from the direct radiation field. After radiation therapy is completed, a second procedure is performed to move the organs back. In December 2020, Dr. Leitao along with his MSK partner, gynecologic surgeon Jennifer Mueller, MD, performed the first uterine transposition in the United States.

The profile of colorectal patients eligible for uterine transposition continues to evolve with each case, but one thing never changes: The primary focus is treating the cancer. "We always discuss with the patient's entire colorectal team if fertility preservation is best for the patient," Dr. Leitao says.

Dana was informed of the risks potential loss of the uterus and hysterectomy. So far, none of the U.S. patients had delivered a baby. She weighed the odds, thinking, "If I don't have this procedure, what are the chances I could carry after radiation?" she recalls. "It was basically no chance at all." After talking with her doctors and with her family onboard, Dana told Thomas, "Let's just go."

### A Team Approach and a Multistep Plan

In December of 2021, Dana had the groundbreaking surgery. It was a two-hour procedure, and she went home the same day.

A month later, Dana began six weeks of radiation treatments with Dr. Hajj, who recommended proton radiation therapy due to its extreme precision and ability to keep the radiation dose to the transposed uterus and ovaries close to zero.

A few weeks after the radiation concluded, Dana started four cycles of chemotherapy. In August 2022, Dr. Leitao put her uterus back into place. Then she had surgery that November to remove the low-lying tumor.

The following summer, Dana and Thomas were given the all-clear to try to get pregnant. "In the summer, we started trying naturally. We were like, 'Let's just give it a shot and see what happens,'" Dana says. "Basically, the first month that we tried, we got pregnant."

### **Hope Restored: A Baby**

Baby Hudson was born in the spring of 2024 via Caesarean section at 32 weeks and weighed 5 pounds. After spending time in the NICU to gain some weight, Hudson went home to his mom, dad, and big sister, who is "head over heels in love with Hudson," Dana says. About Hudson, Dana notes: "He's been a little champ. A totally healthy baby. The doctor is so impressed and has no concerns."

Meanwhile, Drs. Leitao and Mueller have now performed eight uterine trans-



Dr. Mario Leitao performed the first uterine transposition in the U.S., which helps women with rectal cancer preserve their fertility.

position procedures and have presented at national oncology conferences and created training videos for the American College of Surgeons. The MSK team hopes that by sharing their knowledge, their colleagues can offer it to more patients around the world.

When Dana was pregnant with Hudson, she shared another special surprise with her MSK doctors. Inspired by their care, Dana has begun training in MSK's School of Radiation Therapy. Dr. Hajj is thrilled for Dana's new chapter: "You don't have cancer. You have a baby. And now you're going to school. Amazing!"

Dr. Leitao is delighted to be a part of Dana's family story and says, "I almost feel like a grandparent."

### **Dana Is Forever Grateful**

"There's a special place in my heart for the doctors who saved me and who are responsible for me being able to carry another baby," she says. "I'd do that surgery again in a heartbeat. And I'd recommend it to any woman in a similar situation." •

### **Teaching Immune Cells To Attack Solid Tumors**

When Marylou Barton heard her biopsy results, she held her daughter Kristin's hand while they both sobbed in the doctor's office. The mesothelioma — a rare and aggressive cancer that arose in the lining of Marylou's lungs — appeared to have spread. She likely had about a year to live.

Marylou, then 71, had spent decades helping others in Pennsylvania — first as a child abuse prosecutor and then as an environmental lawyer. But it looked like nobody could save her.

"The physicians at my hospital said, 'Just go home, get your will and all your papers in order," Marylou recalls. "It seemed like there was no hope." It was February 2019.

Her three daughters — all present when the biopsy was taken two days earlier — had other ideas. Kristin, Rosemary, and Sara searched the web for options and unanimously decided that Memorial Sloan Kettering Cancer Center (MSK) was the place to go for a second opinion. Soon, Marylou had an appointment with MSK's multidisciplinary mesothelioma team, including surgeon Prasad Adusumilli, MD.

What they said to Marylou immediately gave her hope: Her cancer had actually not metastasized and could be held at bay with chemotherapy for the time being. Moreover, Dr. Adusumilli was gathering funds to start an innovative clinical trial testing a new form of immunotherapy called chimeric antigen receptor (CAR) T cell therapy.

Dr. Prasad Adusumilli has developed new techniques to increase the effectiveness of CAR T cell therapy against solid tumors. He is leading a clinical trial to treat patients with pleural cancers, which affect the area outside the lungs in the chest cavity.





"I'm a positive thinker, and Dr. Adusumilli saw that in me - he said his grandmother had always told him that was half the battle," Marylou says. "He said, 'When we get the money for this are vou interested?' And I said. 'Definitely.' "

CAR T cell therapy involves removing immune T cells from a patient and outfitting them in the lab with receptors that recognize specific targets - known as antigens - on the surface of a cancer cell. It has shown great promise for the treatment of blood cancers such as leukemia and lymphoma. But it had been much less effective against diseases such as mesothelioma and other solid tumors. which account for most cancers.

Dr. Adusumilli was determined to tackle this challenge. Thanks to funding from the Baker Street Foundation, he launched the clinical trial later that year. Marylou finished her chemotherapy and received her first CAR T cell treatment in the fall.

After receiving the CAR T cells, she was able to complete the last phase of her treatment back home at a hospital in Lancaster, Pennsylvania, where she received an immunotherapy drug called pembrolizumab (Keytruda®). Today, nearly five years after her treatment, Marylou is still going strong. "I would not she says.

### Why Solid Tumors **Are Hard To Treat**

This resistance has frustrated clinicians, who see that the CAR T cells detect the tumor but then appear to weaken and fail to finish the job.

"In order for CAR T cell therapy to work against these tumors, we need the T cells to be effective at infiltrating the tumors, killing enough cancer cells, and staying active long enough to stop the cancer from coming back," Dr. Adusumilli says.

Over the past decade, Dr. Adusumilli has made several important advances to overcome these hurdles. One solution, when possible, is to deliver the CAR T cells directly to the tumor site rather than infusing them into the bloodstream.

be alive today if I did not come to MSK,"

Marylou's treatment was one of the first in an exciting new wave of CAR T therapies for solid tumors. These cancers have been largely impervious to CAR T cell therapy because they are often difficult for T cells to penetrate. They also have a surrounding ecosystem - called the tumor microenvironment — that blocks CAR T cells from attacking until they just run out of steam, a state known as T cell exhaustion.

Marylou Barton was diagnosed with mesothelioma five years ago and told by another hospital that it could not be treated. But after receiving CAR T cell therapy in a research trial led by Dr. Adusumilli, she is enjoying life with her daughters and grandchildren.

Dr. Adusumilli's intervention radiology colleagues developed several new techniques to inject tumors without any complications.

For mesothelioma, that means injecting the cells directly into the pleural cavity - the area outside the lungs and along the pleural lining, which is a membrane that covers the inside of the chest cavity and surrounds the lungs. That's how Marylou received her cells.

"They rolled me on my side and injected it into my back, to an exact spot where the cancer was next to my lung," she says. "It was just one procedure, and I didn't feel a thing."

### **Innovations in the Lab**

Dr. Adusumilli's laboratory has explored additional ways to make the T cells themselves more effective. One approach uses low-dose radiation on the tumors to help the CAR T cells penetrate them. Another trick: genetically engineering the CAR T cells to contain a "decoy receptor" that stops cancer cells from blocking the immune cells before they become exhausted.

Perhaps the most audacious strategy involves bolstering the strength of the CAR T cells by stealing one of cancer's own



Marylou spent a career helping others in need. She is grateful for the generosity of donors who helped fund the trial that saved her life. "It's kind of like 'what goes around comes around,' in a positive way," she says. "And here I am, on the receiving end of it."

weapons: a genetic mutation in a gene

called c-KIT that is critical to the ability of

cancer cells to grow, multiply, and survive.

In lab studies, adding mutated c-KIT to

the CAR T cells enabled them to gain

strength and fight the tumor longer. The

researchers could regulate the c-KIT effect

with a drug, like turning a volume knob up

or down. This should allow the therapy's

irony of turning cancer's weapons against

it. A research brief written by Dr. Adusumilli

and MSK colleague (and study co-author)

Meriem Taleb, PhD, in Nature Cancer con-

cludes with a guote from the Dalai Lama:

These latest innovations tested in the lab

are now getting support for testing in

patients. In March 2024, the National

Cancer Institute recognized Dr. Adusumilli's

pioneering work by awarding him a pres-

tigious grant to pursue these new

"Your enemy is your greatest teacher."

**A Prestigious Grant** 

Dr. Adusumilli's team appreciates the

power to be harnessed more safely.

"Philanthropy is critical for this work because it supports high-risk, high-reward strategies that might not otherwise be funded by the government."

-Prasad Adusumilli, MD

approaches in a clinical trial. The substantial five-year award will support his efforts to incorporate all three lab innovations into a multicenter study treating patients with pleural cancers — those that affect the area outside the lungs in the chest cavity. If successful, the trial could represent a major milestone for treating many malignancies, in addition to mesothelioma.

In receiving the grant, Dr. Adusumilli credits his collaboration with MSK colleagues, including physician-scientist Michel Sadelain, MD, PhD, a pioneer in CAR T research, as well as medical oncologist Michael Offin, MD, and radiation oncologist Daniel Gomez, MD.

"Although we are starting with pleural cancers, we could potentially expand this to most people with advanced solid tumors," Dr. Adusumilli says, "especially those resistant to other treatments such as chemotherapy and immunotherapy."

As for Marylou, she's now retired and continues to make the most of her second chance, spending time with her daughters. five grandchildren, and many friends. She also loves to travel.

"I went to Sicily last fall for three weeks, Jamaica in February for five days, and I'm about to go to Florence soon," she savs.

Both she and Dr. Adusumilli are very grateful for the philanthropic support that brought the research this far and will continue to fund further research - especially from the Baker Street Foundation.

"Philanthropy is critical for this work because it supports high-risk, high-reward strategies that might not otherwise be funded by the traditional funding sources," Dr. Adusumilli savs.

Marylou says she is forever grateful to be a beneficiary of someone else's generosity and altruism after a life of serving others.

"It's kind of like 'what goes around comes around,' in a positive way. And here I am, on the receiving end of it, enjoying every moment of my life." •

Dr. Sadelain holds the Stephen and Barbara Friedman Chair.

Dr. Adusumilli holds the Min H. & Yu-Fan C. Kao Chair in Thoracic Cancer.

# Different Ancestries, Different Cancers

Attorney Gail Goode was diagnosed with multiple myeloma. Thanks to an MSK clinical trial, the cancer is under control.

As a trial attorney in New York City and a self-described warrior, Gail Goode is used to confronting adversaries. But without a doubt, multiple myeloma has been her most challenging opponent. After receiving a stem cell transplant, the cancer returned less than a year later. "I couldn't believe I had to go through more treatment," Gail says.

Multiple myeloma is a blood cancer that unfortunately takes a disproportionate toll on people who are Black. In fact, Black people are more than twice as likely to develop the disease as non-Hispanic white people.

Experts are not sure why. To learn more, medical oncologist Saad Usmani, MD, is focused on making sure research studies of new multiple myeloma treatments include patients from a variety of ancestries. "One in five people diagnosed with multiple myeloma in the

United States are Black, but only about 1 in 20 people enrolled in myeloma clinical trials are Black," says Dr. Usmani, who is Chief of the Multiple Myeloma Service at Memorial Sloan Kettering Cancer Center (MSK).

this disease?"

### **An Urgent Need: More Diverse Patients in Clinical Trials**

with certain ancestries:

### **Drive Scientific Discovery**





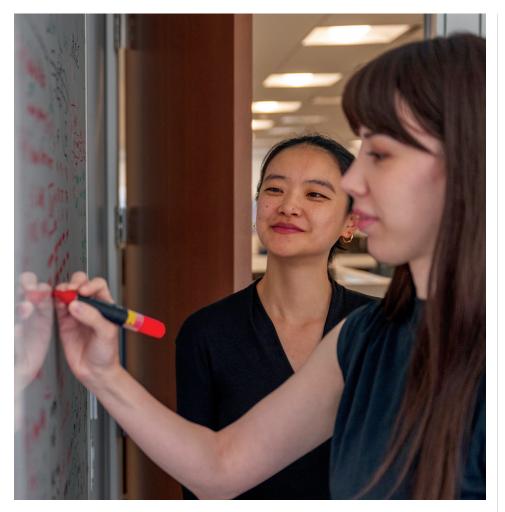
"If we're not enrolling these patients in clinical trials and we're not studying their specimens," he asks, "how can we truly understand what's happening in

- Researchers are learning that certain types of cancer occur more frequently in people
- African people of African ancestry are more likely to develop prostate cancer, triple-negative breast cancer, and uterine (endometrial) cancer, in addition to multiple myeloma.

- East Asian people of East Asian ancestry have higher rates of stomach (gastric) cancer and certain head and neck cancers.
- Hispanic people of Hispanic ancestry have faster-rising rates of early-onset colorectal cancer.

"With certain types of cancer, we know there is an overrepresentation in certain populations," says gynecologic oncologist Paul Sabbatini, MD, Senior Vice President for Clinical Research at MSK. "But it doesn't match up with the participation we see in clinical trials."

Nearly every cancer drug that's given to patients today exists thanks to clinical trials. "It's so important for the population of trial participants to have the same representation as the patients who will receive the treatment later," Dr. Sabbatini explains. "Treatments may not work the same way in every group, or they may



Dr. Jian Carrot-Zhang (left), shown with graduate student Leah Morales, studies how genes found in different ancestry groups affect cancer.

have different side effects. We won't know that if we don't include these patients in trials."

### Genes Matter: A Researcher's 'Aha!' Moment

Environmental factors and socioeconomic status certainly play a part, but a key reason why some cancers hit certain populations harder is genetics. In an era of personalized medicine, a patient's treatment is often based on the genetic mutations driving their cancer. But these mutations have not been studied as much in people with diverse ancestries.

MSK computational geneticist Jian Carrot-Zhang, PhD, had an "aha!" moment in graduate school that shaped her future research. She was studying a Canadian Inuit family with a widespread history of cancer that couldn't be explained by any known hereditary cancer genes.

"I realized the databases used to study cancer genes contain mostly data from people of European ancestry," she says. "By not including other groups, we are missing a lot."

Now Dr. Carrot-Zhang leads a lab that studies how specific genes found across ancestry groups influence the aggressiveness of cancer and its response to treatment. Recent research she published in *Cancer Cell* found that people of African ancestry have distinct mutations in a range of well-known cancer genes, including *KRAS*, *EGFR*, and *ROS1*. And these mutations potentially could impact the effectiveness of drugs that target these genes.

Other MSK investigators are on the same quest, led by **Carol Brown, MD**, **Senior Vice President and Chief Health Equity Officer**. To understand why endometrial cancer is deadlier in Black women than white, a recent MSK study found that Black women not only have more aggressive tumor types but also certain genetic factors that make their cancers more difficult to treat.

### **The Myeloma Mystery**

For multiple myeloma, any specific genes that might lead to differences across ancestry groups are still unknown. "We don't know why multiple myeloma is more common in people of African ancestry because we just don't have enough data," Dr. Usmani says. "That's why it's so important that more diverse patients be included in multiple myeloma trials."

Gail jumped at the opportunity to join Dr. Usmani's trial, saying now, "Participating in this trial was the best thing to happen to me."

The early-phase trial is testing a combination of two drugs: an immunotherapy known as a checkpoint inhibitor, along with teclistamab (Tecvayli®), which is a bispecific antibody. The drug is engineered to deliver immune cells directly to cancer cells to destroy them.

Gail started the treatment in the fall of 2022. Today, she has no signs of cancer — and she's still practicing law, recently taking a job at a private firm after decades of working for city agencies.

Because Gail's disease was very aggressive, Dr. Usmani says it's truly remarkable that the treatment has been so effective for so long. "This kind of response may suggest something positive for other Black patients in the future," says Dr. Usmani, who is sharing his data with the International Myeloma Working Group. He is also partnering with the International Myeloma Foundation to reduce inequities in treatment in the Black community.

Gail remains on the trial, receiving treatments every two weeks. In the beginning, she was susceptible to respiratory infections and had a persistent cough. But now she's back to enjoying life with her husband and feeding her passion for stylish clothing from her favorite vintage stores. She says she feels great.

"I have a good team, and I feel like they really listen to me," she says. "If this research can help other folks, that's wonderful." •

Dr. Brown holds the Nicholls-Biondi Chair for Health Equity.

### Soad Z. Usmani, MD, MBA C.

### How MSK Recruits Diverse Patients for Clinical Trials

### MSK's Office of Health Equity oversees several outreach efforts to help patients enroll in trials, including:

- Partnering with NYC Health + Hospitals to help their patients get access to clinical trials.
- Offering the MSK-IMPACT<sup>®</sup> test to determine if patients from these hospitals could benefit from an MSK clinical trial.
- Expanding clinical trials at MSK regional sites, especially at MSK Nassau on Long Island.
- Creating programs that make participation easier, such as travel expense reimbursement.





Dr. Harini Veeraraghavan, a computer scientist at MSK, is harnessing the power of artificial intelligence to make radiation therapy safer and more effective.

# Teaching Computers **To See Cancer**

She has helped robots learn to get around indoors and pick up balls from the ground. And she has developed computer programs to monitor traffic at intersections.

But these days, Harini Veeraraghavan, PhD, applies her expertise to fighting cancer. Her lab at Memorial Sloan Kettering Cancer Center (MSK) leads the development of new artificial intelligence (AI) models to improve the targeting of radiation therapy — teaching computers to better isolate tumors and spare more of the surrounding healthy tissue.

In radiation therapy, where highenergy beams are fired at cancer cells, precision is imperative. Every millimeter matters. Yet much of the human body is squishy inside. Organs, especially in the abdomen, naturally move around and change shape from day to day and treatment to treatment.

"It's actually a very challenging and interesting problem," says Dr. Veeraraghavan, an associate attending computer scientist in MSK's Department of Medical Physics. "These organs move quite a bit. Breathing, the contractions that move food through the digestive system, and even water flowing through can alter their shape."

Overcoming this, she says, requires developing computer models with a built-in understanding of how organs can change shape and position.

"Currently, we're developing a virtual digital twin that would model how a patient's abdominal organs move so we can better plan their treatment and ensure that the right doses of radiation are being delivered to precisely the right places," she says.

### **'Like Having Your Best Resident** on the Case'

And the abdomen isn't the only area where Dr. Veeraraghavan's innovations are being used. Her research is already being applied by MSK radiation oncologists across more than 40 tissue types including in head and neck, lung, pancreatic, liver, and prostate cancers, says Joseph Deasy, PhD, Chair of the **Department of Medical Physics.** 

Dr. Veeraraghavan leads a multidisciplinary effort, which includes radiation oncologists and other physicists, to safely implement novel AI technology in the clinic. The technology is used to guide hundreds of radiotherapy treatments given at MSK each day, making it a great example of the positive impact AI is already starting to have in medicine, Dr. Deasy adds.

Nancy Lee, MD, MSK's Chief of Head and Neck Radiation Oncology, says the algorithms have been a great help in treating patients with head and neck cancer.

In the past, doctors had to identify a patient's organs in imaging scans by hand a task often given to residents. Starting with the blank canvas of a CT or MRI scan, they would trace the outlines of a patient's eyes, nose, teeth, salivary glands, and so forth. This "contouring" process takes hours.

Today, a physician like Dr. Lee can start with computer-generated contours and apply her expertise to tweaking and refining some of the lines and boundaries -

### **Artificial Intelligence 101**

Algorithm: A set of instructions that a computer uses to solve a problem or accomplish a task.

Generative AI: Can create images, words, and other content resembling human-created works. Includes popular AI programs like ChatGPT, Midjourney, and DALL-E.

targeted and healthy tissues avoided.

Deep learning models developed at MSK have been shown to overcome the type of day-to-day variability that can cause not enough or too much radiation to reach a given spot. MSK researchers are also developing AI methods to better track precisely how much radiation a tumor or organ has received to date.

### **The MSK Difference**

While AI assistance is quickly becoming the industry standard in radiology, MSK stands apart both for the sophistication and innovation of its AI models as well as for the human expertise it's paired with, Dr. Veeraraghavan notes.

> Dr. Lee's research receives essential philanthropic support from the MSK Giving community, including James and Diane Rowen and Nancy and Howard Marks.

Artificial Intelligence (AI): Allows programs to apply complex reasoning to make predictions from data.

**Deep Learning:** A type of AI trained on neural networks, which are based on models of the human brain. Able to find and learn patterns they weren't specifically asked to look for.

Machine Learning: Algorithms and models that allow computers to learn patterns and insights from data. Sometimes used interchangeably with "Al."

making sure tumors are precisely

"It's like having your best resident on the case," Dr. Lee says. "If you asked 10 human radiation oncologists to contour the same image, there are going to be slight variations among them, even though we're all experts. The algorithm can help us be even more precise, consistent, systematic, and efficient."

She was recently awarded two RO1 research grants - the gold standard for federally funded research - totaling more than \$4 million. The first grant, from the National Cancer Institute, aims to develop new AI tools against lung cancer, offering less toxicity for patients while better targeting tumors in difficult-to-treat locations. The second, from the National Institute of Biomedical Imaging and Bioengineering and co-led by MSK associate attending physicist Neelam Tyagi, PhD, is to develop the virtual twin approach to modeling abdominal organs.

And more work is underway to provide radiation oncologists with "rough drafts" of regions to target in addition to outlining normal tissue, as well as to estimate how much mass tumors lose following radiation therapy.

"Together these tools will offer unprecedented insights into each person's cancer to help guide treatment decisions," Dr. Veeraraghavan says.

Dr. Deasy holds the Enid A. Haupt Chair in Medical Physics.

### **Training Cancer's Future Leaders**

The students and postdoctoral researchers who work and train in MSK's laboratories drive discovery forward every day. Today they are vital partners. Tomorrow they will lead further progress at hospitals, research centers, and biomedical companies around the world.







Above left: Graduate student Monica Acosta enters the Zuckerman Research Center to start her day in the lab.

Above right: Research scholar Mihir Pendse, PhD, left, in the lab with immunologist Gretchen Diehl, PhD. The Diehl Lab studies how gut microbes train the immune system.

Left: Graduate student Justin Hachey, left, prepares to work with frozen samples, alongside research fellow Michele De Franco, PhD. The work is part of the Jason Lewis Lab's efforts to develop new approaches for the targeted diagnosis and treatment of cancer.





Above left: Postdoctoral fellow Frank Arnold, PhD, prepares a slide as part of the Mara Sherman Lab's research into pancreatic cancer. Above right: Members of the Jason Lewis Lab discuss research to improve the detection and treatment of cancer cells. Left to right: research scholar Shaniqua Hayes, PhD; research scholar Candace Parker, PhD; graduate student Justin Hachey; and graduate student Olufolake Majekodunmi.







Above left: Developmental biologist Eric Lai, PhD (left), discusses a research project with graduate student Mir-Mammad Javad-Zada. The Lai Lab studies how cells orchestrate behaviors so they happen at the right times and in the right places.

Above right: Lounge spaces allow trainees to foster collaboration and camaraderie outside the lab, too. From left: graduate student Dasom Kim, research scholar Mihir Pendse, PhD; research scholar Sofia Tortora Morel, PhD; and research technician Lisette Peres-Tintin.

Left: Research scholar Yanan Ma, PhD, prepares to review a sample under the microscope. The work is part of the Philipp Niethammer Lab's study of wound healing, inflammation, and regeneration.

### Meet MSK's Chief Strategist

### "We are in a moment of historic change in cancer care," says Anaeze Offodile, MD, MPH.

Dr. Offodile joined Memorial Sloan Kettering Cancer Center (MSK) in 2023 as Chief Strategy Officer, after serving as the Executive Director for Clinical Transformation at MD Anderson. Among his many responsibilities is helping MSK steer a course into the future.

"There are multiple macro trends such as artificial intelligence, a focus on health equity, and adapting to climate change that are all converging in healthcare now," says Dr. Offodile. "And the COVID-19 pandemic pulled these trends forward by a decade."

Specifically, the pandemic exposed dramatic gaps in equitable access to healthcare. It also accelerated digital transformations, changing everything from how patients use telemedicine to engage their physicians, to the breadth of acute care they can receive at home.

"It's an incredible privilege to help MSK figure out how to respond and



Memorial Sloan Kettering Cancer Center thrive," Dr. Offodile says, "particularly because MSK occupies a unique position in the oncology ecosystem as the reference organization for many of our peers."

Dr. Offodile's path to becoming a doctor started in Nigeria, where his family moved from London. "Growing up, the primary doctor for my family was a man named Dr. Egejuru. I remember fondly his patience and deep fund of knowledge while caring for my entire family."

As a medical student at New York's Columbia University, Dr. Offodile found himself drawn to surgery. "I really enjoyed the technical, problem-solving aspect of surgery, particularly for cancer patients," he recalls.

He also found that plastic surgery "fosters a deep bond with patients because it's inherently restorative, whether it's physically or emotionally or function-wise."

Known as Anii (pronounced AH-nee), he believes that "making meaningful connections is an important value, whether it's engaging with our world-class clinicians or MSK's excellent environmental services staff." He brings a similar mindset to thinking about MSK's future. "I approach strategy planning with humility and respect," he says. "A favorite quote of mine is from Dr. Peter Pronovost, a healthcare safety expert: 'Change only happens at the speed of trust.' "

Oncology care has radically transformed in the past 25 years, says Dr. Offodile, also noting that many of those changes originated at MSK, from pioneering research in immunotherapy to shifting care to the ambulatory setting and building out a regional network across New Jersey and New York.

For Dr. Offodile, the advances to come will be just as profound. "Because of MSK's unique status in cancer care, it's our responsibility to not just meet this important moment, but to lead it to help cancer patients around the world." •



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