

WINTER 2020

# MSKNews

MEMORIAL SLOAN KETTERING CANCER CENTER

## Taking Aim at Lung Cancer

Alexander Drilon is leading the development of new targeted drugs that can control tumors better than ever before.



Memorial Sloan Kettering  
Cancer Center



## THE SHOW MUST GO ON: MSK WATCH PARTY CELEBRATES AFRICAN AMERICAN DAY PARADE



Top row (from left): Julia Ramirez, Jocelyn Triplett, Lorna J. Lewis, and Glenni Santos. Middle row (from left): Esraa Soliman, Vanessa Rodriguez, Shakima Grant (with daughter Sariah), and Phoebe Kmeck. Bottom row (from left): Noel Collo, Carol Brown, Nicola Buchanan, and Akua Sarkodee.

**Julia Ramirez was looking at her computer screen with tears in her eyes, and her 6-year-old son, Teo, wanted to know why.** She tried to explain the deep emotions welling up as she viewed this year’s African American Day Parade at a Zoom watch party with her Memorial Sloan Kettering colleagues.

“I was part of the parade the past two years, and I remember the feeling of being on the MSK float and people in the crowd being so happy to see us and saying, ‘Thank you so much, you saved my life,’” says Ms. Ramirez, Director of Patient Relations at MSK.

MSK had floats in the previous two African American Day Parades, usually held in Harlem. This year’s parade, on September 20, was converted into an online event because of COVID-19 concerns and included a series of performances and testimonials honoring Black culture.

MSK takes part in the annual parade to bring awareness to cancer screening and treatment services, including at the MSK Ralph Lauren Center in Harlem. Gynecologic surgeon Carol Brown, who joined the watch party, emphasized the importance of MSK’s active presence in the parade and engagement with

the African American community in New York City.

“African Americans suffer a disparity in terms of their cancer outcomes,” says Dr. Brown, who was recently named MSK’s new Chief Health Equity Officer. “I’m very happy about MSK’s ongoing participation because we are a leader in cancer care, and we are striving to be a leader in cancer health equity.”

About 15 staff members attended the one-hour watch party, which was sponsored by MSK’s Black, Latino, Asian, and Multiracial (BLAM) Employee Resource Network and the Office of Diversity Programs in Clinical Care, Research, and Training. •

## LONG DISTANCE DEDICATION: TRANSPLANT ‘THRIVERS’ UNITE AND CELEBRATE ONLINE

**When Daniel Roeper first came to Memorial Sloan Kettering, he was struggling with a type of lymphoma that attacks white blood cells in the brain or spinal cord.** The tumor was even distorting his vision.

At Daniel’s first appointment, he was clearly overcome with anxiety. Hematologic oncologist Oscar Lahoud looked him in the eyes and said, “It’s going to be okay. We can do this.” Dr. Lahoud said Daniel’s best treatment option would be to undergo a bone marrow transplant (BMT) — a lifesaving but often grueling procedure.

Daniel — now healthy and thriving — was reunited with Dr. Lahoud by video on October 5 as part of MSK’s 25th annual celebration for BMT survivors, the first to be held online. The program enabled more than 200 patients scattered far and wide to celebrate their return to health along with family, friends, caregivers, and MSK medical staff.

BMT expert Sergio Giralto acknowledged the “incredible times” everyone has been living in — particularly the social distancing. Still, he said, there was no doubt that the BMT “Thrivers” event would be held this year in some format. “It was unanimous that having this event was important — that life goes on, that we will overcome this, as you’ve already overcome a lot,” he told the celebrants. •



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# The Power of the Patient Voice: PFACQ Celebrates Five-Year Anniversary

Eliza Weber (left) and Kate Niehaus say that patients have always taken the lead on the Council's efforts to improve care.

**In 2014, Kate Niehaus, a former patient active in volunteer work for Memorial Sloan Kettering, was approached by Kent Sepkowitz, an infectious disease specialist and Deputy Physician-in-Chief for Quality and Safety, with a proposal to make MSK's outstanding cancer care even better.**

"The idea was to bring patients and families into the center of everything that goes on at the hospital," she says. "Kent was a physician on the front lines during the AIDS crisis and had seen the power that patients can have in driving change." Over the next year, Ms. Niehaus worked with two MSK staff members to form the Patient and Family Advisory Council for Quality (PFACQ).

Now celebrating its five-year anniversary, PFACQ has become a partnership of current and former patients, family members, caregivers, and MSK staff that ensures the patient and family perspective is included in everything MSK does. The guiding principle of their work is that patients and caregivers who have gone through the cancer journey are able to provide insights that nobody else can.

"With PFACQ, we say 'our experience is our expertise,'" says Eliza Weber, PFACQ's current co-chair. "If you were a cancer patient or caregiver, you know better than anyone what it feels like to pass through the different stages of treatment and how the experience might be improved."

In its first year, PFACQ identified three pivotal points of care that patients found especially difficult — diagnosis, transitioning from active care to survivorship, and end of life — and then began implementing countless changes to address these concerns. For example, PFACQ helped set up clear, organized information on MSK's online patient portal to explain what documents and medical information are needed for a first appointment — easing the burden for often-overwhelmed, newly diagnosed patients. Moreover, they encouraged hundreds of MSK doctors, nurses, staff, and patients to come together around the dinner table (now virtual tables) to talk with each other about end-of-life preparedness in a monthly event called "Death Over Dinner."

More recently, PFACQ members spoke to hospital leadership about the anxiety of awaiting results from imaging scans, the variability of the waiting period, and its impact on the patient's emotional well-being. In response, MSK

began ensuring all imaging results were available on the portal within two business days after being read by a radiologist. In addition, PFACQ was an instrumental partner in the development of a "patient values tab," a new process by which nurses ask patients at the beginning of their care to talk about their needs and goals. That information is added to the patient's emergency medical record and can help guide treatment decisions.

PFACQ's 32 volunteer members continue the important work of finding ways to improve how care and support is given at MSK, serving on more than 25 committees relating to hospital quality and patient care. "Having a seat at the table makes a huge difference," Ms. Weber says. "We encourage anyone who has received care at MSK, whether as a patient or caregiver, to apply to join our group and see how rewarding it is to make the experience better for the next person." •

## INTERESTED IN JOINING PFACQ?

Would you like to become a patient or family advisor? PFACQ is seeking new members to share their voices and experiences to help improve the quality of care at MSK.

For more information or questions, please contact us at [pfacq@mskcc.org](mailto:pfacq@mskcc.org).

# Taking Aim at Lung Cancer

Middle school chorus and orchestra teacher Melissa Crouse had lived in the Pittsburgh area her whole life. But on a trip to visit her brother in southwest Florida, she decided on a whim to apply for teaching jobs there. The single mom, then 51, quickly received an offer.

“Three big things happened to me at the same time,” Melissa says. “I moved, I started a new job, and, after getting a physical for my new job, I was diagnosed with stage II lung cancer.”

Melissa, who hadn't had any symptoms, was grateful that her cancer had been detected early. She had surgery at a Florida hospital, followed by chemotherapy. For four years, scans of her lungs were clear, but in 2009, her radiologist saw something concerning in the corner of the image. Follow-up tests revealed that although her lungs were clear, her liver was full of tumors.

Around that time, she heard that Massachusetts General Hospital in Boston was looking for relatively young women who had never smoked for a trial of a new lung cancer drug. She was accepted into that trial, but the treatment didn't work for her for very long.

“After that, I got proton therapy, and I bounced from trial to trial,” she says. “Some of the treatments were tolerable, but most were not. None of them worked well, but together they kept me alive. Then I learned about a new drug that targeted a genetic change called a *RET* fusion, which had been found in my tumor.”

*RET* fusions occur when part of the gene *RET* gets rearranged and attaches itself to another gene. That creates what is called an oncogene, a kind of zombie gene that takes over normal behavior and drives cells to grow out of control — leading to cancer.

Researchers aren't sure what causes this to happen or why it's most often found in lung cancer. *RET* fusions have also been found in certain kinds of thyroid cancer and, less frequently, in other cancers.

Melissa's oncologist in Boston was slated to be an investigator on the new drug trial, but not right away. “He told me, ‘You need to be on this drug now,’” she remembers. “I couldn't wait.”

In April 2017, Melissa had her first appointment with Memorial Sloan Kettering medical oncologist Alexander Drilon. Dr. Drilon was leading the international trial of what was then called LOXO-292. Three months later, she received her first dose of the drug, which is taken as a pill.

A scan in September of that year showed that her tumors were shrinking, and since April 2020 she has had no evidence of disease. The only side effect she's experienced is fatigue, although at times it has been severe.

## Research Leads to Increasingly Specialized Drugs

Dr. Drilon leads MSK's Early Drug Development (EDD) Service, which conducts phase I trials of promising new targeted therapies for solid tumors in both adult and pediatric patients.

“Melissa's experience was remarkable,” says Lauren Kaplanis, a clinical trials nurse who works with Dr. Drilon. “And it was repeated in many of the nearly 100 people we've treated with this drug so far.”

In May 2020, LOXO-292, now known as seliperatinib or Retevmo™, received approval from the US Food and Drug Administration for the treatment of lung cancer and thyroid cancer with *RET* fusions or mutations. In September 2020, a study was published in the *New England Journal of Medicine* that looked further at the outcomes of people treated with the drug.


The research, led by Dr. Drilon, found that among people with lung cancer who had previously received other treatments, 64 percent had their tumors shrink substantially. After a year of taking the drug, nearly two-thirds of those patients were still responding well. For those who had never received any treatment, the response rate was even higher at 85 percent. Seliperatinib isn't the only *RET* drug that's shown success. Also in September, a drug called pralsetinib (Gavreto™) received FDA approval.

## Lung Cancer Treatment Gets More Personal

“We've known about the link between *RET* fusions and lung cancer since 2011, but prior to the start of the seliperatinib trial in 2017, there were no drugs that were designed to optimally target only the *RET* protein,” Dr. Drilon says.

“Seliperatinib works so well because it's very specific,” says MSK medical oncologist Ezra Rosen, a member of the EDD Service who was also involved in the trials. “That means that it doesn't have many side effects.”

Dazhi Liu is a clinical pharmacist who is a crucial part of the EDD team. Clinical pharmacists, along with nurses, are on the front lines of recognizing and

A close-up portrait of an older woman with grey hair, wearing dark-rimmed glasses and a blue top. She is smiling slightly and looking towards the camera. The background is dark and out of focus.

“I learned about a new drug that targeted a genetic change called a *RET* fusion, which had been found in my tumor.”

—*Melissa Crouse*

controlling side effects from cancer drugs, especially new drugs that have effects that are not yet completely understood. “The EDD Service was involved in this clinical trial from the beginning,” Dr. Liu says. “It was a great opportunity for us to see so many of our patients enrolled and helped by this drug.”

As Chief of MSK’s EDD Service, Dr. Drilon is involved in many trials studying newer, more-precise drugs to treat specific mutations in lung cancer. “Lots of people have heard about using immunotherapy drugs to treat lung cancer,” Dr. Drilon says, adding that his patients often ask him if immunotherapy is an option for them. “But for people whose cancer is caused by one of the mutations that drive tumor growth, targeted therapies tend to work much better.”

*RET* fusion is only one of the many cancer-driving gene changes found in lung cancer that now have drugs designed to target them. These sound like an alphabet soup — *EGFR*, *ALK*, *ROS1*, *BRAF*, *MET*, *NTRK* — but in an era of molecular testing and personalized medicine, they are becoming increasingly familiar among doctors and patients alike.

Each of these mutations or fusions make up only a small percentage of lung cancer cases, but because lung cancer is diagnosed in more than 228,000 people in the United States annually, together the combined influence of these targeted treatments can benefit tens of thousands of people with lung cancer every year.

Unfortunately, many tumors eventually outsmart targeted drugs like selpercatinib and learn to start growing again. Dr. Drilon and Dr. Rosen are doing research in this area, too. They have identified drugs that can be added to treatment with selpercatinib so that patients can continue to do well.

### From Teacher to Advocate

Melissa, who is now 67, had worked throughout all of her previous treatments, but when she was accepted into the selpercatinib trial, she decided to retire from teaching. “I didn’t think I could keep working and go through another trial because of the side effects on the other ones,” she says. “If I had known then what I know now, I wouldn’t have retired.” She continues to take selpercatinib daily, and so far her tests have shown no signs of her cancer returning.

A self-described Type A personality, Melissa has not been taking it easy in her retirement. She’s become an activist and patient advocate, even starring in an Emmy Award-winning documentary about lung cancer called *Melissa’s Story*. She lobbies Congress and the pharmaceutical industry for more research funding. She believes that lung cancer has been shortchanged due to the stigma of its connection to smoking. “Anyone can get lung cancer, whether they smoke or not,” she says. “That’s an important message to get out there.”

Another issue that she feels strongly about is that companies should do more to help people who want to participate in

### Providing Much-Needed Support to Move the Needle

Philanthropy has been essential to the growth of the Early Drug Development Service. Entrepreneur and philanthropist Michael Repole has provided crucial support to Alexander Drilon’s work through his private foundation, Nonna’s Garden, since 2018.

trials. “The drug company covered travel and lodging for my monthly trips to MSK, which had not been the case with previous trials I was in,” she notes. “I wouldn’t have been able to participate in the trial if they hadn’t offered that financial support.”

When the COVID-19 pandemic began in March 2020, Melissa started having her scans and bloodwork done at a hospital near her home in Florida and having telemedicine visits with Dr. Drilon. Although she misses seeing her MSK team in person, it was an easy transition.

As quarantine restrictions eased up over the summer and fall, she was able to spend time with her three adult children and their families, all of whom now live close to her. She doesn’t take any of it for granted.

“Selpercatinib was my sixth clinical trial,” she says. “I don’t think I’d still be here today without it.” •

The Early Drug Development Service, which is led by Alexander Drilon, sometimes gives drugs to patients for the first time anywhere.





## 8 Questions with Ken Manotti

Ken Manotti is Senior Vice President and Chief Development Officer at Memorial Sloan Kettering. He leads philanthropic fundraising efforts at MSK and has been in the role since 2018.

### **Why did you choose philanthropy as a career?**

I had no plans to be in this profession. But many years ago, a mentor asked me to help with fundraising at the University of Pennsylvania. She was very patient and taught me how to raise money for good causes.

### **Is it hard asking people to donate?**

At first, I thought: "There is no way I can ask people for money." But it feels great to offer opportunities to people who really want to make an impact. In some ways it's like being a matchmaker: I put together the right donor with the right project, like research or a clinical trial. When that happens, I know it feels meaningful for donors, which makes me feel good.

### **Why is philanthropy so important to MSK?**

The financial support is crucial for our research, patient care, and education efforts, of course. But it goes beyond that. Our scientists and doctors develop a real partnership with donors and their families. Regardless of the size of the gift, our donors are members of the MSK community, which is important. The relationship motivates both sides to work harder to see results, whether it's research or fellowships or programs like health equity. That's powerful.

### **These are unsettled times, financially. What do you tell people about supporting MSK?**

It goes back to the relationships we have with our donors. We recognize that personally and financially, it's been a difficult year. If a person is able to donate, we really appreciate it. If they can't, we understand that too. We know cancer isn't going to take a break, so we can't relax in supporting innovations that save lives. We'll keep having these conversations.

### **Are there ways to support MSK besides donating money?**

We have three programs that raise money for cancer research at MSK: Cycle for Survival, Fred's Team, and Kids Walk for MSK Kids. While they have been impacted by the pandemic, we still have exciting events that people can be part of. And there's a group in our department devoted to helping people find ways to get involved and make a difference. You can go to [giving.mskcc.org](https://giving.mskcc.org) to learn more.

### **Do you have a pet project that makes you think "this is why I do this job"?**

In May, we give awards to extraordinary nurses at MSK. I was talking about it with Cliff Robbins, who is a member of the MSK Board of Governing Trustees and Trustees and Chair of its Finance Committee. He told

me how much it meant to him that MSK nurses took such wonderful care of his father. Within five minutes of talking, he decided to make a generous gift to our nurses.

### **What have you learned about generosity outside MSK?**

I spent ten years raising money for the American University in Cairo, which taught me that pretty much everyone has the same core values and wants to make a difference.

### **What's something that surprises people about you?**

On 9/11, I was on a plane inbound to JFK from overseas, and it was one of those diverted to Gander, Canada. I spent ten days sleeping on a gym floor. The hospitality and generosity of the local people was amazing, and I'll always remember it. •

## **DRIVE RESEARCH FORWARD AT MSK**

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# MISSION POSSIBLE?

## Revisiting the ‘War on Cancer’ 50 Years Later

**In 2016, when Vice President Joseph Biden announced the “Cancer Moonshot” initiative, many in the scientific world felt a twinge of déjà vu. This wasn’t the first time that officials in the US government had set their sights on an ambitious plan to conquer cancer.**

In fact, a “War on Cancer” was launched in 1971, when President Richard Nixon signed the National Cancer Act into law. The aim of this legislation, which greatly increased funding for cancer research, was nothing short of the eradication of cancer. As Mr. Nixon said in his State of the Union speech that year, “The time has come in America when the same kind of concentrated effort that split the atom and took man to the moon should be turned toward conquering this dread disease.”

Yet from the beginning, the War on Cancer was controversial. Many leading scientists opposed it, fearing it would steal attention from other research.

Among the public, it led to unrealistic expectations that a cancer cure was just around the corner. It wasn’t.

But the National Cancer Act — which turns 50 years old in 2021 — did eventually pay off in ways that few could have expected at the time. It fueled breakthroughs in fundamental biological science that are finally turning the tide against many forms of cancer. And individuals close to Memorial Sloan Kettering played a big part in getting it passed.

### **Cancer Crusaders**

If there is one person who most deserves credit for the National Cancer Act, it’s

Mary Lasker, the philanthropist, activist, and widow of Chicago advertising executive Albert Lasker who died of cancer in 1952. A longtime supporter of public health causes, including national health insurance, Mrs. Lasker used her considerable power and influence to rally support for cancer research among legislators. The result was a panel convened by the US Senate to survey the landscape of cancer research and make recommendations for how to speed progress.

The Senate chose investment banker and MSK board member Benno Schmidt to chair the 26-person panel. A native of Texas, Mr. Schmidt was known for his straight-shooting style and strong leadership skills.

Also serving on the panel were Joseph Burchenal, Vice President of the Sloan Kettering Institute; Laurance Rockefeller, Chairman of the MSK Board; and Mathilde Krim, a virologist in SKI. Together, these individuals developed the framework of the National Cancer Act, which was signed into law on December 23, 1971.





Left: Mary Lasker circa 1950. Photo: Pictorial Parade/Archive Photos/Getty Images. Above: Richard Nixon with Benno Schmidt (right) and Mr. Schmidt's wife, Nancy (center), at the signing of the National Cancer Act in 1971. Directly above: One of the pens used to sign the legislation, currently on display in the Rockefeller Research Laboratory building at MSK.

## Mixed Messages

Though the Act's stated aim was the "conquest" of cancer, Mr. Schmidt and his fellow panelists knew that effective treatments were unlikely to come without sustained investment in fundamental biological research.

"Whether it was cancer or Alzheimer's or another condition that the NIH [National Institutes of Health] was studying, the thing that was depressing about it to me was we didn't know what any of those things were," Mr. Schmidt recalled in 1995. "We clearly needed fundamental basic research to understand those diseases before we could hope to cure them."

Yet the rhetoric surrounding the initiative sent a different message and led many scientists to line up against it.

"In the eyes of those who did not know us, we were twofold wrong," Mr. Schmidt said. "We were one, taking money from other things for cancer, and two, we were going to misuse it because we were trying to do applied research [focused on solving practical problems] when we didn't have the

fundamental knowledge to make our research productive."

Neither was true. But this history helps explain why talk of a new "Cancer Moonshot" in 2016 created some hesitance among scientists, even if they were grateful for the financial support.

Whether in 1971 or 2016, "basic scientists are going to resist the idea of a 'cancer moonshot,'" says Craig B. Thompson, President and CEO of MSK. "Putting a man on the moon was primarily a spectacular engineering effort. NASA had all the necessary physics knowledge in hand when they planned the Apollo missions. With cancer, we don't understand all of the basic science to be able to engineer a solution."

## Finding a Better Metaphor

A better way to think about the National Cancer Act, Dr. Thompson says, is as an investment that has paid substantial dividends over time.

"No one would have expected that within ten years of Nixon signing the National Cancer Act, Harold Varmus and

Mike Bishop would discover the first cancer-causing genes lurking in our own cells," he says.

And while a few cancer researchers in 1971 held out hope that one day the immune system might be harnessed to fight cancer, certainly no one dreamed that today one-third of all people with cancer would be receiving some form of immunotherapy, which does exactly that.

To make these advances, Dr. Thompson says, "We needed the tools of cell and molecular biology that were developed over the last 50 years through funding provided by the National Cancer Act."

Thanks to those advances, one of the deadliest cancers — metastatic melanoma — is now curable in more than half of all cases. It joins testicular cancer, leukemia, and lymphoma as types of cancer that can be cured even when they have spread.

And there have been enormous strides in understanding and treating other cancers, including breast, prostate, lung, and thyroid cancers. The investment made nearly 50 years ago is still paying off. •



# PLAYING WITH FIRE

## Fish, Ferroptosis, and the Combustible Chemistry of Wound Detection

“Wouldn’t it be cool if we could get a death wave to occur in a fish?”

—Mike Overholtzer

**Cell biologist Philipp Niethammer left the camera running while he went to get a cup of coffee.** Aimed at tiny zebrafish bathing in a translucent dish, the camera was recording the movements of immune cells as they migrated through the fish’s tail fins toward the tip of a pipette. This slender tube emits chemicals that the cells follow like breadcrumbs.

Dr. Niethammer is a kind of molecular fisherman. He is hoping to hook the signals that cells use to communicate with their neighbors and warn each other of danger. These signals are key to how animals, including us humans, detect wounds.

Dr. Niethammer usually films his zebrafish for just a few minutes at a time. But in this case, the camera kept rolling for nearly an hour. When he returned with his coffee, he saw that he had captured something extraordinary: a sudden, dramatic wave of tissue swelling and buckling. The reaction spread from the tip of the pipette down the length of the fin.

He’d never before seen something like this in a fish, but it wasn’t entirely unexpected, either. Dr. Niethammer had been trying to capture this type of event ever since a colleague told him about a surprising overlap between the process of wound detection and a particular form of cell death called ferroptosis. But the first hundred times or so he cast his net, it came up empty.

His mind swirling with ideas, Dr. Niethammer raced to share the news with the one person he knew would most appreciate it.

### Death Becomes You

Just down the hall, Dr. Niethammer’s colleague, cell biologist Mike Overholtzer, was watching his own experiments with cell death, a process that is crucial to life. For example, your hand would look more like a mitten if not for properly timed cell death during embryonic development to create the spaces between your fingers; and our immune system kills infected cells to stop a virus from spreading.

Though Dr. Overholtzer is fascinated by many kinds of cell death, his current focus is ferroptosis. Ferroptosis means “death by iron,” and it depends on a corrosive kind of chemistry — the sort that causes iron to rust. Not much is known about ferroptosis because it was only discovered in 2012, which makes it all the more compelling to him.

Understanding ferroptosis raises intriguing possibilities in medicine. It could explain why injuries such as a heart attack are so damaging: Cell death spreads out from the site of injury and takes out healthy cells too. It also suggests the possibility of using ferroptosis as a cancer treatment — by igniting a controlled burn inside a tumor to destroy cancer cells.

In 2016, Dr. Overholtzer and a colleague from Memorial Hospital, physician-scientist Michelle Bradbury, found that it was possible to trigger ferroptosis in cancer cells by zapping them with a type of pinhead-sized particle called a C prime dot. This caused a deadly chain reaction that spread like a wave through the tumor, killing it completely. They knew C prime



“To sense a wound in a tissue, you’re pretty much playing with fire.”

— Philipp Niethammer

### Ferroptosis and Cancer: A New Frontier

**What scientists are learning about ferroptosis could translate into new therapies for cancer.** That’s because many cancers seem especially vulnerable to this type of cell death. A recent *Nature* study led by postdoctoral fellow Jiao Wu and graduate student Alex Minikes in Xuejun Jiang’s lab at SKI explains why.

It comes down to connections. Normal cells make snug connections with their neighbors and actively share information through a signaling pathway called NF2-Hippo. They are resilient in the face of chemicals that trigger ferroptosis. Many cancer cells, on the other hand, have lost these connections, so they succumb.

That has excited cancer researchers and drug developers alike. “The idea is that if you can induce ferroptosis in a controlled manner, it might be a great way to treat cancer,” Dr. Jiang says.

The findings have particular relevance to mesothelioma, an aggressive cancer affecting the lining of internal organs that tends to spread quickly. Mesothelioma cells often contain NF2 mutations that aid their spread and make them resistant to many types of chemotherapy. But there is an upside: “The same NF2 mutations that make cancer cells more malignant and harder to treat also make cancer cells more susceptible to ferroptosis,” Dr. Jiang says. “This could be their Achilles’ heel.”

More recently, in November 2020, postdoctoral fellow Junmei Yi from Dr. Jiang’s lab and postdoctoral fellow Jiajun Zhu from Craig B. Thompson’s lab published in the journal *Proceedings of the National Academy of Sciences (PNAS)* another striking connection between ferroptosis and cancer. One of the most commonly mutated signaling pathways in cancer is called PI3K-AKT-mTOR, which plays a role in metabolism. Cancer cells with mutations in this pathway have adaptations that make them more resistant to ferroptosis. The researchers found that by combining drugs that block this mutated pathway with ones that promote ferroptosis, they could dramatically shrink both breast and prostate cancer tumors bearing these mutations in mouse models. ●

dots could cause ferroptosis, but they didn’t quite understand how ferroptosis worked — or how it spread between cells.

That fascinated Dr. Overholtzer. Was there some kind of active signal that conveyed a “death wish” from cell to cell? Or did the spread occur more passively as collateral damage? Fortunately, a world expert in how signals move through tissues was working next door.

### A “Crazy” Idea

The collaboration between Dr. Niethammer and Dr. Overholtzer began as do many at the Sloan Kettering Institute: a conversation over coffee.

“Wouldn’t it be cool if we could get a death wave to occur in a fish?” Dr. Overholtzer said to his colleague one day back in 2018. It sounded far-fetched — and a bit macabre — but there were good reasons to explore the idea.

“The chemistry behind ferroptosis and the chemistry of wound detection are similar and overlapping,” Dr. Niethammer says. “Both rely on iron and reactive chemicals called free radicals, and both spread quickly like a wave.”



Gerstner Sloan Kettering Dean Mike Overholtzer (left) with GSK graduate student Michelle Riegman in 2018.

If ferroptosis could be elicited in a healthy fish, it would mean that this form of cell death is more than just a destructive consequence of disease — it could be built into the way the body has evolved to protect itself.

The two scientists hashed out their ideas over the next several weeks and then got to work.

While Dr. Niethammer perfected a mechanism for delivering precise amounts of inflammation-promoting chemicals to the tail fin of a zebrafish, Dr. Overholtzer and his lab took an in-depth look at what happens inside a cell that is undergoing ferroptosis. A graduate student in the lab, Michelle Riegman, found that before a cell dies, it begins to swell. This swelling, it turns out, is actually what relays the death wish to neighboring cells, rather than the death itself.

“This was really surprising to us,” Dr. Overholtzer says. “We had imagined that the spreadability might be a hallmark of ferroptosis.”

### Think Tank

Finding the chemistry of ferroptosis at the heart of wound detection raised still more questions for the scientists: Why would an animal’s immune system rely on a risky method to heal scrapes and cuts? You might think it would have evolved to develop a safer and more foolproof method.

“The way that I think about this volatile chemistry,” Dr. Niethammer says, “is as a kind of trade-off: Yes, it carries a risk, but that risk is outweighed by the benefit of being able to rapidly alert the immune system to danger.”

The scientists reported their results in back-to-back articles in August in the journal

*Nature Cell Biology*. In an accompanying editorial published in the same issue of *Nature Cell Biology*, colleagues compared the wound-detection situation to a smoke signal that gets out of control and sets the forest ablaze.

“To sense a wound in a tissue, you’re pretty much playing with fire,” Dr. Niethammer says.

The discovery has important consequences for how scientists think about the relationship between normal body chemistry and disease: One can very easily slide into the other.

The jointly published papers reflect a strength of the SKI model: “There’s a natural synergy that you get when scientists working in different areas are encouraged to freely share ideas,” Dr. Overholtzer says. “It’s part of what makes SKI such a special place to do research.” ●



MEMORIAL SLOAN KETTERING | EQUINOX

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No matter where you live, you can be part of the movement to beat rare cancers. There are many ways you, your friends, and family can get involved, including our first-ever virtual event experience. One hundred percent of every dollar raised goes to rare cancer research led by MSK.

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## YOUR IMPACT: MEETING URGENT NEEDS

**Thank you to Memorial Sloan Kettering's extraordinary donor community.** Your commitment to supporting MSK's mission — this year and always — is essential to advancing our goals. Thank you for standing with us through every challenge.

This year, with the help of our donors, MSK's 20,000-plus doctors, scientists, nurses, and staff have achieved new levels of innovation, remained steadfast in our mission, and inspired hope for people with cancer around the world.

At the beginning of the COVID-19 pandemic, we adapted swiftly to increase patients' access to care, wherever they live. We developed strategies to treat people with cancer in their homes and pursued life-changing scientific advances to improve their lives.

**Here are some of MSK's achievements that donor support helped make possible:**

### Telemedicine

To continue cancer treatment for many people during the COVID-19 shutdown, MSK rapidly increased telemedicine visits

from less than 100 per day to more than 1,400. Conducting virtual appointments has allowed MSK care teams to keep people safely sheltered at home while providing necessary care.

### Virtual Clinical Trials

In a pioneering endeavor, MSK developed tools to conduct virtual clinical trials so our physician-scientists could sustain the momentum of creating novel cancer drugs and treatments to benefit patients.

### Social Work Fund

Nearly 50 percent of all people being treated for cancer in the United States deplete their savings during the first two years. At MSK, we have increased financial assistance to ensure that patients and their families can focus on what matters most — recovery.

### Food to Overcome Outcome Disparities (FOOD)

The FOOD program was initiated in 2011 to supply healthy food to people experiencing economic hardship during their cancer treatment. Since the beginning of the COVID-19 pandemic, MSK pantries and other participating pantries have gone from serving roughly 200 people to 350 people per week across all food pantry locations. FOOD staff have also begun delivering groceries and gift cards to people with cancer who should remain at home. ●



## LOOKING AHEAD TO THE SOCIETY'S 2020-2021 CAMPAIGN

Since its inception, The Society of Memorial Sloan Kettering has been a philanthropic mainstay that supports leading research and patient care programs to improve outcomes for people with cancer worldwide. In the past ten years, this essential funding has catalyzed breakthroughs in metastasis and targeted immunotherapy research and sustained the pursuit of innovative strategies to address health equity challenges.

The 2020-2021 Society Campaign will focus on pediatric precision medicine initiatives and novel research projects spearheaded by junior and senior investigators at the Sloan Kettering Institute. With donor support, The Society of MSK is helping shape a future in which every type of cancer can be understood and treated.

To learn more, please visit [society.mskcc.org](http://society.mskcc.org). ●

Rihanna, age 3, was treated on a clinical trial of a precision medicine called larotrectinib. The groundbreaking targeted therapy was the first to be developed and approved based solely on its effect on a specific genetic change in a tumor, regardless of where in the body the tumor originated.





## APPOINTMENTS AND PROMOTIONS



**Gregory Fernandez**  
*Psychiatrist*  
Appointed as Associate Clinical Member; Department of Psychiatry & Behavioral Sciences, Psychiatry Service



**Leontine van Elden**  
*Pulmonologist*  
Appointed as Associate Clinical Member; Department of Medicine, Division of Subspecialty Medicine, Pulmonary Service



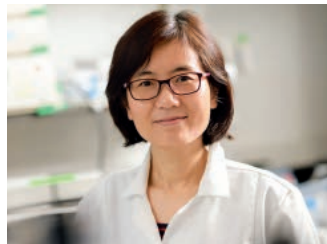
**David Della Rocca**  
*Surgeon*  
Appointed as Associate Clinical Member; Department of Surgery, Ophthalmic Oncology Service



**Alina Dulu**  
*Critical Care Medicine Physician*  
Appointed as Associate Clinical Member; Department of Anesthesiology & Critical Care Medicine, Critical Care Medicine Service



**Bo Zhao**  
*Medical Physicist*  
Appointed as Associate Clinical Member; Department of Medical Physics, Radiotherapy Physics Service



**Danwei Huangfu**  
*Developmental Biologist*  
Promoted to Member; Developmental Biology Program, Sloan Kettering Institute



**Chaya Moskowitz**  
*Biostatistician*  
Promoted to Member, Memorial Hospital; Department of Epidemiology & Biostatistics, Biostatistics Service



**Alessia Pedoto**  
*Anesthesiologist*  
Promoted to Clinical Member; Department of Anesthesiology & Critical Care Medicine, Anesthesiology & Pain Service



**Luis Tollinche**  
*Anesthesiologist*  
Promoted to Clinical Member; Department of Anesthesiology & Critical Care Medicine, Anesthesiology Service

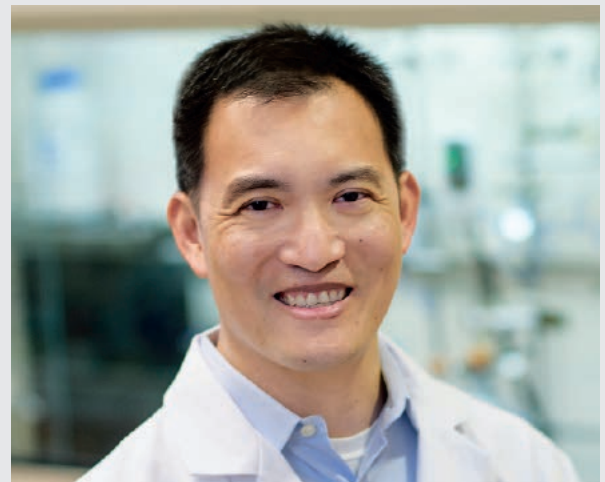


**Barbara Egan**  
*Hospitalist*  
Promoted to Clinical Member; Department of Medicine, Hospital Medicine Service

## ENDOWED CHAIRS



**Stephen Solomon** was appointed Incumbent of the Enid A. Haupt Chair in Clinical Investigation.



**Derek Tan** was appointed Incumbent of the Eugene W. Kettering Chair.

## CAROL BROWN APPOINTED CHIEF HEALTH EQUITY OFFICER

In September, Carol Brown was appointed Senior Vice President and Chief Health Equity Officer. In her new role, Dr. Brown will establish MSK's Office of Health Equity and work to address cancer disparities that exist due to racial, ethnic, cultural, or socioeconomic barriers. She will be responsible for leading patient care and research activities of the Office of Health Equity and will help develop new clinical and translational studies to address disparities in cancer outcomes.

Dr. Brown, a gynecologic surgeon, will also assist the Office of the Physician-in-Chief, MSK's Graduate Medical Education programs, and MSK's residency and fellowship directors to ensure that MSK builds a more diverse and equitable clinical, educational, and research enterprise.

She takes on this important role after more than two decades of working at MSK to improve cancer care for underserved populations and address the inequalities that exist for many in the healthcare system. ●



## CRAIG THOMPSON AWARDED COLUMBIA BUSINESS SCHOOL'S DEMING CUP FOR OPERATIONAL EXCELLENCE

**Craig B. Thompson, President and CEO of MSK, was awarded Columbia Business School's Deming Cup for Operational Excellence.** Dr. Thompson and MSK were recognized with this prestigious award for leadership during the ongoing COVID-19 pandemic. "Thanks to teamwork, a strong operational foundation, and their own personal commitment to our mission, our MSK employees have continued to deliver exceptional care to our patients every single day of this ongoing pandemic," said Dr. Thompson. ●

## INGO MELLINGHOFF NAMED CHAIR OF DEPARTMENT OF NEUROLOGY

In October, Ingo Mellinghoff was appointed as Chair of the Department of Neurology.

As a renowned physician-scientist, Dr. Mellinghoff's focus is on the characterization of signaling pathways altered in primary brain tumors and early-phase clinical trials for new drugs targeting these pathways.

Since fall of 2018, Dr. Mellinghoff had served alongside Edward Avila as the acting co-chair of the department. ●

## LORENZ STUDER RECEIVES INAUGURAL \$8.95 MILLION GRANT FROM ALIGNING SCIENCE ACROSS PARKINSON'S INITIATIVE

**Lorenz Studer, Director of the Center for Stem Cell Biology at MSK, was awarded an \$8.95 million grant to continue his research into the causes and progression of Parkinson's disease.**

The award is given by the Aligning Science Across Parkinson's initiative in partnership with the Michael J. Fox Foundation. It will be shared among five institutions, with MSK being the lead grant recipient. ●

### MSKNews

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MSK Before You Go

# Everyone should get a flu shot.

**According to the Centers for Disease Control and Prevention, influenza activity begins in October and peaks between December and February.**

While the best time to get a flu shot is in September or early October, no one should skip the vaccine because they think it's too late.

Memorial Sloan Kettering infectious disease specialist Monika Shah (pictured right) answers common questions about the flu and its vaccine.

## **Is the flu really just a bad cold?**

The flu is more dangerous than a cold. In the United States, hundreds of thousands of people are hospitalized with the flu each year and thousands die.

## **Can I get a flu shot even if I have cancer?**

The best way to protect you and your family is to get a flu shot every year. It reduces your risk of getting the flu and can reduce the severity of symptoms if you do become infected. The flu vaccine is recommended for most people with cancer. It's even more important this flu season because of COVID-19. Although much is still unknown about what happens if you get infected with both viruses simultaneously, people with cancer may be at higher risk for complications.

## **Can I get the flu from a flu shot?**

No. The vaccine is made from an inactivated form of the flu virus.

## **Where should I go to get a flu shot?**

Contact your doctor's office or seek out one of the many local pharmacies that offer flu shots.



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