Moving the Ball Forward
How translational research at MSK is speeding up discoveries to help patients like Mark Denisiuk
Dear MSK Community,

Breakthrough cancer discovery can start anywhere: a patient with a unique case, a researcher with a hunch, or an unexpected result that connects seemingly disparate findings. An investigation into a new treatment can begin with the patient, move to the lab, and circulate back and forth from the bench to the bedside.

This modern approach to research improves on the traditional process, which generally has been one-directional and categorized into three distinct phases: basic — to understand the behavior of cells; translational — to apply that knowledge to create new drugs for patients; and clinical — to test therapies in patients.

This issue of MSK News focuses on the growing importance of that middle phase, translational research, powered by new technologies and our increasing knowledge about how cancer develops and spreads. Thanks to a generous gift from Fiona and Stanley Druckenmiller, MSK will be able to advance the most brilliant ideas into early-stage translational research — just the beginning. It will rapidly seed the most creative and promising ideas and multidisciplinary approaches.

MSK has invested in this approach on a more modest scale over the past few years, and found it helps accelerate transformational technologies, including the development of CAR T cell therapy, tools to address and act on patient-reported outcomes, and theranostics (see page 4).

The Fiona and Stanley Druckenmiller Presidential Innovation Fund will provide a mechanism for scientists, physicians, and nurses to apply for funding for novel translational projects. In funding projects, emphasis will be given to non-incremental ideas and multidisciplinary approaches.

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The Fiona and Stanley Druckenmiller Presidential Innovation Fund is just the beginning. It will rapidly seed the most creative and promising projects in translational cancer medicine that might otherwise not be funded. It will ensure that the most brilliant people in translational cancer research have the resources they need to make the biggest impact. As science progresses and unexpected discoveries are made over the next decade, the Fiona and Stanley Druckenmiller Presidential Innovation Fund will respond quickly to evolving research needs in real time, allowing MSK to stay at the forefront of the field.

Sincerely,

Craig B. Thompson
President and Chief Executive Officer

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A Smart Bomb for Cancer

Testing a vaccine. A pioneering clinical trial in an early phase of research. For a small group of patients in New York City, investors are reason for optimism. Barbara Brigham is among the first in the field of theranostics, which combines imaging and therapy for a search-and-destroy mission.

Theranostics: A Smart Bomb for Cancer

When Dave Norkin was diagnosed at 39 with a rare cancer, he was told he had just months to live. Now, a decade later, he’s surviving — thanks to the emerging field of theranostics, which combines imaging and therapy for a search-and-destroy mission.

Takina Aim at Pancreatic Cancer: Reasons to Be Optimistic

Pancreatic cancer will soon become the nation’s second leading cause of cancer death, but there is reason for optimism. Barbara Brigham is among a small group of patients in a pioneering clinical trial testing a vaccine.

Translating Science Into Cures: Bringing Fresh Hope to the Denisiluk Family

Mark Denisiluk was diagnosed with acute myeloid leukemia in the spring of 2021. He found hope when he enrolled in an early trial of an entirely new kind of drug that’s based on lab research conducted at MSK.

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Unlocking a Mystery: What’s Behind the Rise in Colorectal Cancer Among Young People

Doctors and scientists at MSK are desperately trying to figure out why more young patients like Rebecca, 33, are getting colorectal cancer — and how best to treat them.

Decoding the Biology of Brain Tumors

Brain cancer is deadly because it’s so difficult to study. Scientist Luis Parada has developed an innovative model to analyze how brain tumors form and respond to treatment.

Owen and Stacia: A Love Story

After Owen Strong died of a glioblastoma at age 30, his girlfriend set off on a 1,100-mile bike ride to raise money for research, powering through her grief to make a difference for other families.

Donors on a Mission to Fast-Track Cancer Therapies at MSK

Fiona and Stanley Druckenmiller know the value of a good investment. That’s why they have their sights set on a new venture: supporting translational cancer research at MSK.

Congratulations

These honorees are among the most prestigious in science.

Luiz Alberto Diaz, Jr., MD, was chosen by US President Joe Biden to serve on the National Cancer Advisory Board.

Dana Pe’er, PhD was named a Howard Hughes Medical Institute investigator.

Justin Perry, PhD, was named a 2021 Pew Scholar and was also selected for the 2021 National Institutes of Health Director’s New Innovator Award.

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Read more stories online: mskcc.org/winter-2021-22
Dave Norkin remembers very clearly the first time he met with MSK physician Diane Reidy-Lagunes. It was his daughter’s birthday. She had just turned 3.

But when he saw Dr. Reidy-Lagunes, she saw hope.

“I remember thinking, based on her attitude when I saw her at the time, that there might be more hope than I was originally led to believe,” Dave says, a decade after his grim diagnosis.

An expert in treating neuroendocrine tumors, Dr. Reidy-Lagunes knew that Dave would be a good candidate for an emerging type of exquisitely targeted therapy called theranostics.

A mash-up of the words “therapy” and “diagnostics,” theranostics combines imaging techniques and targeted therapy into one very precise package. Like other forms of targeted therapy, theranostics involves a drug that circulates through the blood and binds to a specific target on cancer cells. But in this case, the drug is linked to a radioactive element that releases radioactivity to zap and kill the cancer cells.

Unlike other targeted therapies, doctors can predict exactly where it will go.

**Seeing Is Believing**

“We have a theranostic motto, which is ‘We see what we treat, and we treat what we see,’” says nuclear medicine physician Lisa Bodei, who is Director of Targeted Radionuclide Therapy at MSK and who administered Dave’s treatments.

The emphasis on seeing is a key part of what distinguishes theranostics from other forms of precision medicine, and even chemotherapy.

Typically, when a patient receives a chemotherapy drug, for example, there’s no way of knowing how much of the medicine is getting to the cancer. With theranostics, it’s very different. There’s a visualization step at the beginning and at the end.

First, doctors administer a version of the drug carrying a diagnostic radioactive element, known as an isotope. This isotope emits a very low level of radiation that does not damage cells but can be easily visualized with a PET scan. This “tracer” allows the doctors to see where the drug is collecting.

Then, during the therapeutic phase, they switch to a version of the drug carrying a therapeutic isotope, which emits enough radiation to kill cancer cells. Doctors know exactly where it will go: the same place that the diagnostic tracer did. Moreover, they can do a follow-up scan to confirm. The end result is that doctors can see precisely where the drug went to kill cancer cells.

Dr. Bodei uses a military metaphor to describe the approach. “It’s like having a tank that is outfitted with both radar to survey the territory and a missile launcher. The tank operator detects the enemy and then attacks the enemy with the same tank,” she says.

The arsenal comes from around the world, according to MSK radiopharmacist Serge Lyashchenko, who oversees the manufacturing process of these powerful drugs. For each patient, he orders a particular radioactive isotope produced by a nuclear reactor. “Depending on the isotope needed, the reactor might be in Belgium, South Africa, Germany, or Turkey,” says Dr. Lyashchenko.

Under strict safety protocols in the basement of MSK’s Schwartz building near Memorial Hospital, he and his team create these drugs deploying radioactivity. “Basically, the radiation emitted by these drugs rins molecules apart,” Dr. Lyashchenko explains. “When it comes to cancer, the molecule you want to break is DNA, so that the cancer cells can’t reproduce, and they die.”

The process is so precise, the surrounding healthy tissue can be spared.

Though the idea of being exposed to radiation might sound scary, the directed nature of the treatment means that it is very safe. And compared with some other treatments that Dave Norkin has had, he says it’s been relatively painless.
“You just sit for three to four hours while they administer the medication,” he explains. “You really don’t feel anything.”

Dave received the first of several theranostics treatments while participating in a clinical trial, led by MSK physicians. It involved a radioactive version of a hormone called a somatostatin receptor (SSTR) antagonist. This hormone receptor is found in many neuroendocrine tumors and serves as the target for the theranostic agent.

Dr. Reidy-Lagunes notes that the trial showed that the treatment was safe and effective. “This therapy was a game changer for many of our patients,” she says. “Dave was our last patient enrolled, and it kept his tumor controlled for close to two years.”

That was especially striking to Dr. Reidy-Lagunes because no other therapy Dave had received had been able to achieve such good results.

“What’s Old Is New Again
Theranostics has been in the news a lot recently, in part due to a recent FDA-approved theranostic imaging agent for prostate cancer and a treatment version that is currently being tested in clinical trials.

But Dr. Bodei points out that theranostics itself isn’t new. In fact, 2021 marks the 80th anniversary of the very first theranostic agent — radioactive iodine for the treatment of thyroid cancer. This is still the standard treatment for that disease.

Today, the cancers most commonly treated with theranostics are thyroid cancer, prostate cancer, and neuroendocrine cancers. But, in theory, it can be used against all kinds — provided scientists can identify good targets on cancer cells.

In recent years, researchers have gotten better and better at identifying unique targets on cancer cells and at devising small molecules or antibodies to deliver their toxic payload with greater precision and power.

The Next Wave
The most exciting development in theranostics is the use of a type of radioactivity called alpha emitters that are 100 times more powerful, according to Jason Lewis, Chief of MSK’s Radiochemistry and Imaging Sciences Service and the Emily Tow Jackson Chair.

“And when they deposit their lethal energy, it’s in the range of a low cell so we can spare healthy tissue,” says Dr. Lewis. “Alphas are really taking theranostics to the next level.”

Dr. Lewis is an expert in the development of radiopharmaceuticals for targeted diagnosis and the treatment of cancer. His research has been generously supported by the Tow Foundation and Marie-Noelle Meyer and her late husband, Fred J. Meyer.

In part due to Dr. Lewis’ expertise and persistence, MSK just got the green light to build a new facility so that these powerful agents can be made right on-site.

“We’re likely to be the first academic site in the US to have a laboratory dedicated to the clinical production of these agents,” he says. “That will help MSK both meet patient demand and also help place ourselves at the cutting edge of developments in this important area.”

Heiko Schöder, Chief of the Molecular Imaging and Therapy Service at MSK, emphasized what distinguishes MSK in the field: the focused collaboration of basic science researchers and clinicians to develop novel theranostics for more cancers.

Looking Ahead
Dave Norkin has far outlived his original doctors’ expectations. It will be 10 years in March since he was diagnosed.

“I know that when I get a certain treatment, it’s not going to last forever and that the cancer is going to recur,” Dave explains. “But hearing about all the new things they’re doing is really uplifting. I hope anyone reading this will be comforted knowing there are a lot of really good people trying their hardest to make sure we can live with this and enjoy our best lives.”

“I hope anyone reading this will be comforted knowing there are a lot of really good people trying their hardest to make sure we can live with this and enjoy our best lives.”

—Dave Norkin

Jason Lewis (left) and Serge Lyashchenko

Nuclear medicine physician Lisa Bodei demonstrates the location of a theranostic tracer on a PET scan.

The small dark spots on this PET scan reveal the theranostic agent, piflufolastat F18, treating metastatic prostate cancer in bones and lymph nodes.

“You just sit for three to four hours while they administer the medication,” he explains. “You really don’t feel anything.”

—Lisa Bodei
She got the awful news from her doctor, Vinod Balachandran, who had been monitoring a pancreatic cyst that was discovered three years earlier. She had her regular imaging test and expected another clear report. But the next morning, she found out she had stage 2 pancreatic cancer — unrelated to the cyst, in a different part of the pancreas.

The outlook seemed grim. Pancreatic cancer is among the deadliest forms of the disease. Even people who are diagnosed and treated at the earliest stage have a 50% chance that the disease will come back.

But Dr. Balachandran suggested that in addition to surgery and chemotherapy, Barbara try something new: a small, preliminary clinical trial testing a vaccine using messenger RNA (mRNA) technology — the same technology used to create the COVID-19 vaccine. There are essentially two kinds of vaccines — those given as a precaution to prevent infection and those that are therapeutic and given after someone is sick. Barbara was given a therapeutic mRNA vaccine to train her immune system to be on the alert for cancer cells. It might reduce the risk that her cancer would return.

“I don’t think there was any hesitation about joining the trial,” Barbara says. “I had complete confidence in Dr. Balachandran. He said I would be a great candidate, and my son, who was with me, agreed it was the best way to go.”

Learning From Long-Term Survivors

In 2017, Dr. Balachandran’s laboratory had made an important finding about why some people beat the odds and survive pancreatic cancer after their tumors are removed. Researchers analyzed samples from these lucky few and found that the tumors contained proteins, called neoantigens, which immune cells recognize as being especially foreign. These conspicuous targets provoked the immune system to attack, keeping the cancer at bay.

When his team published the findings in the journal *Nature*, Dr. Balachandran was contacted by Uğur Şahin, the CEO of the German biotechnology company BioNTech (which later worked with Pfizer in 2020 to develop the first COVID-19 vaccine). Dr. Şahin said he had read the paper and was interested in working with Dr. Balachandran on an mRNA vaccine for pancreatic cancer. Shortly after, Dr. Balachandran and his team flew to Germany to meet with BioNTech and explore the idea.

For Barbara Brigham, being diagnosed with pancreatic cancer in the fall of 2020 was a devastating blow in an already rough year. She had just lost her mother and husband after long illnesses, both needing extensive care. The 74-year-old semiretired librarian from Long Island was finally starting to focus on her own health needs.

Vinod Balachandran is leading a clinical trial testing whether mRNA vaccines — the same technology used to create COVID-19 vaccines — can prevent pancreatic cancer from returning after surgery.
Research by Luis Diaz has helped identify pancreatic patients who would benefit from immunotherapy drugs.

The collaboration progressed quickly. By 2019, BioNTech and Dr. Balachandran had created a vaccine and set up a clinical trial for 20 patients, including Barbara, to test if it was safe. She and the other patients had their tumors removed and genetically sequenced to look for mutations that produce the neoantigens that would be the most easily targeted by the immune system. Each patient received a vaccine based specifically on their tumor’s molecular fingerprint.

“The vaccine is designed to replicate the success of long-term survivors in a broader group of people,” Dr. Balachandran says. “It’s a great example of MSK’s forward-thinking vision in cancer care — to bring the most exciting medicines to cancer patients.”

“A Very Exciting Time for the Field”

Pancreatic cancer is projected to become the nation’s second leading cause of cancer death within 10 years, but there are good reasons for optimism thanks to this kind of translational research discovery by investigators at the Sloan Kettering Institute (SKI) and across MSK.

Experts in pathology, cancer genetics, computational biology, and clinical oncology are closely collaborating within the David M. Rubenstein Center for Pancreatic Cancer. Overseen by physician-scientist and David M. Rubenstein Chair Christine Iacobuzio-Donahue.

“MSK is extraordinary in terms of the infrastructure, the resources, and the talent across different specialties for any aspect of pancreatic cancer,” she says. “As a pancreatic cancer researcher, it’s a very exciting time for the field. I think it’s just a matter of time until we crack this.”

Lab Discoveries Drive Progress

Decades Later

The mRNA vaccine is just one example of progress in fighting pancreatic cancer. It’s also a striking example of how basic research discoveries into cell behavior can translate into applications for patients.

In a compelling case of scientific happenstance, a seemingly unrelated basic research finding is bearing fruit many years later. In the early 1990s, Maria Jasin, a member of the Developmental Biology Program and William E. Snee Chair in SKI, made groundbreaking discoveries about how DNA repairs itself when it becomes damaged by things like sunlight, smoking, or radiation. When the repair process doesn’t work correctly, damage in the genome can accumulate and eventually lead to cancer.

Dr. Jasin’s work helped researchers understand the role of the BRCA1 and BRCA2 genes. When defective versions of these genes are inherited, they are linked to breast, ovarian, and other cancers, including pancreatic. Based on her findings, scientists began developing a class of tumor-fighting drugs called PARP inhibitors for patients with a BRCA mutation. In 2019, nearly three decades after Dr. Jasin’s initial discovery, the FDA approved the PARP inhibitor olaparib (“Lynparza”) for people with metastatic pancreatic cancer who have an inherited BRCA mutation.

“You can see the thread leading from Maria’s major body of work to this class of drugs, from her laboratory bench to the patients’ beds,” Dr. Balachandran says.

Immunotherapy Helps Some Patients

Another way to target pancreatic cancer cells is through a genetic abnormality called a mismatch repair (MMR) deficiency. Research first led by MSK medical oncologist and Grayor Family Chair Luis Diaz when he was at Johns Hopkins discovered that patients with MMR-deficient cancers respond well when treated with the immunotherapy drug pembrolizumab (“Keytruda”).

Now patients found to have MMR-deficient tumors can receive pembrolizumab as a standard treatment.

“Even though pembrolizumab has helped only a small fraction of people with pancreatic cancer, it proved that immunotherapy can actually work for this disease,” Dr. Balachandran says.

The Lethal Cascade of Genetic Mutations

There is other progress, too. Dr. Iacobuzio-Donahue says that the pancreatic research community tends to agree that most of the important pancreatic cancer genes — and the mutations within them — have been identified. With advances in technology, she has shifted her research lens to look in more granular detail.

“My team is now focused on the timing of genetic mutations: which ones initiate the cancer, which ones occur after the tumor forms, as well as factors in the tumor microenvironment — the tissues, blood vessels, immune cells, and other noncancerous components surrounding a tumor,” she says.

Her lab is collaborating with the lab of SKI computational biologist and Alan and Sandra Gerry Chair Dana Pe’er to dig deeper. The two scientists are principal investigators of a large grant awarded to MSK from the Human Tumor Cancer Atlas Network, a National Cancer Institute-funded Cancer Moonshot initiative.

“Dr. Pe’er is an expert in single-cell analysis, which uses new technologies to study cancer one cell at a time in exquisite detail,” she says. “This enables researchers to look at RNA within individual cells to determine which genes are expressed, or ‘turned on.’”

“Doing the single-cell RNA sequencing with Dana is giving us data that is profound — it’s fascinating looking at the disease in a completely different way after my years of focusing on DNA,” Dr. Iacobuzio-Donahue says.

She says there is intriguing evidence that the tumor microenvironment plays a critical role in selecting which cancer cells grow and multiply based on their genetic makeup. Some tumors will spread, while others will stay in the pancreas.

“Agressive primary tumors have distinct genetic patterns, and we’re really trying to understand how that affects the process at the molecular level.”

If researchers can classify tumors based on these genetic patterns, they would know, for example, which tumors are likely to spread and which are not.

“I’m excited about it because it is interesting science, and it has direct clinical relevance,” Dr. Iacobuzio-Donahue says. “As a pancreatic cancer researcher, it’s a very exciting time for the field.”

Dr. Balachandran completed the trial in 18 months, a full year ahead of schedule despite the COVID-19 pandemic.

“Dr. Balachandran’s early vaccine trial offers the most promise for Barbara. Her tumor was removed in October 2020 and used to make an mRNA vaccine personalized for her. She received nine vaccine doses, in addition to chemotherapy and a single dose of immunotherapy — most of it at MSK Commack, an outpatient center on Long Island. Her treatment was completed by September 2021. Like the other people in the vaccine trial, she has a CT scan every three months to see if the cancer returns.

“I feel very well so far, and for now there is no detectable cancer,” she says. “I had a unique support system from my family, who have helped me through this and who drove me to many appointments, including my three sons, my in-laws, my niece and nephew, and my brothers.”

Research by Luis Diaz has helped identify pancreatic patients who would benefit from immunotherapy drugs.

Barbara’s Best Hope

Today, Dr. Balachandran’s early vaccine trial offers the most promise for Barbara. Her tumor was removed in October 2020 and used to make an mRNA vaccine personalized for her. She received nine vaccine doses, in addition to chemotherapy and a single dose of immunotherapy — most of it at MSK Commack, an outpatient center on Long Island. Her treatment was completed by September 2021. Like the other people in the vaccine trial, she has a CT scan every three months to see if the cancer returns.

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Barbara says. “I could absolutely see how sorting out this question could benefit patients within five years.”

MSK Board Member David M. Rubenstein, Alan and Sandra Gerry, and the Ben and Rose Cole Charitable PRIA Foundation have provided vital support for pancreatic cancer research at MSK.
In the spring of 2021, Mark Denisiuk began feeling unwell. He had a sore throat and was always congested. His doctor diagnosed a sinus infection. Then Mark started having night sweats and extreme fatigue.

“In the past, I had always powered through any illness I had, but the night sweats worried me,” says Mark, a 46-year-old civil engineer who lives in Madison, New Jersey. When he suddenly grew too tired to get out of bed, his wife, Lauren, insisted he go back to the doctor. His doctor ordered blood work and the next day immediately referred him to a hematologist. A bone marrow biopsy at a local hospital revealed that Mark had acute myeloid leukemia (AML), an aggressive blood cancer that usually affects older people.

Lauren, who works in the pharmaceutical industry, began calling every doctor she knew for advice. Just four days after his diagnosis, Mark was admitted to Memorial Sloan Kettering Cancer Center, under the care of hematologic oncologist Aaron Goldberg.

Mark ultimately ended up enrolled in a phase 1 clinical trial of a drug created based on translational research conducted at MSK. His case is a dramatic example of the critical and growing importance of translational research — where basic scientific discoveries about the behavior of cells are translated into experiments aimed at developing new therapies for patients.

Major Research Grant Recognizes MSK’s Expertise

In September 2021, MSK’s leukemia team received a prestigious SPORE (Specialized Programs of Research Excellence) grant from the National Institutes of Health (NIH) to expand its translational research program. The grant is overseen by physician-scientist Omar Abdel-Wahab, Director of MSK’s Center for Hematologic Malignancies (CHM) and Edward P. Evans Endowed Chair for MDS, and hematologic oncologist Martin Tallman, Leukemia Service Chief and Cassidy Family Endowed Faculty Chair.

Efforts funded by the grant will focus largely on AML, the most common type of leukemia in adults, which affects about 20,000 people in the United States every year.

“Despite advances in recent years, AML is still a really tough disease,” Dr. Abdel-Wahab says. “We are directing our efforts there because it’s where we feel we have the opportunity to make a big difference.”

The SPORE grant will allow investigators to accelerate a number of initiatives, including developing new cell-based treatments for AML. They are also looking for ways to overcome resistance to targeted therapies.

A Trial for a New Class of Drugs

Before Mark could begin treatment for his cancer, he needed surgery to alleviate swelling in his sinuses caused by the leukemia. The procedure was performed by MSK surgeon Marc Cohen. Then Dr. Goldberg started Mark on cocktail of chemotherapy drugs.

The treatment was intense. Mark spent 42 days in the hospital and lost 15 pounds. He initiated a clinical trial of a drug called enasidenib, which targets a specific mutation found in AML.

“An opportunity to treat a patient with something new and potential to improve on what was already there was really exciting,” says Dr. Goldberg.

Mark’s case is a dramatic example of the value of translational research. At MSK, scientists and clinicians work closely together to develop new treatments based on basic scientific discoveries. This partnership is crucial in advancing the field of cancer treatment.

“Translating Science Into Cures

Bringing Fresh Hope to the Denisiuk Family

Mark Denisiuk with his wife, Lauren, and their son, Benjamin, at their home in New Jersey

Acute myeloid leukemia affects about 20,000 people in the United States every year.
35 pounds. Unfortunately, another bone marrow biopsy revealed he still had a high number of leukemia cells in his body. Dr. Goldberg tried another difficult chemotherapy regimen, and Mark spent another 22 days in the hospital. But the results were only slightly better.

Then came a new ray of hope. Dr. Goldberg recognized that Mark’s leukemia had a chromosome abnormality called an MLL rearrangement, which might respond well to a specific targeted therapy. He referred Mark to Eytan Stein, who leads MSK’s Program for Drug Development in Leukemia, for treatment on a clinical trial of an experimental drug called SNDX-5613.

It’s in a new class of drugs called menin inhibitors. In MLL-rearranged leukemias and leukemias with a mutation in a gene called NPM1, there is a protein called menin that causes the disease to develop and grow. Research at MSK led by physician-scientist Scott Armstrong, now at Dana-Farber Cancer Institute in Boston, showed that menin could be blocked with drugs, thwarting the growth of leukemia cells.

Knowing Mark loves to garden, Dr. Stein explained it using this analogy: “Imagine your blood and bone marrow are like a garden. If you have leukemia, there are a lot of weeds mixed in with the flowers. With chemotherapy, you use an herbicide that kills everything, and hope that only the flowers will grow back. But this drug can cause leukemic cells to become normal cells, and then you make the weeds bloom into flowers.”

The medication is a simple pill Mark took at home. Unlike the harsh side effects from previous treatments, Mark says, “I felt like I kept getting stronger and stronger as time went on.”

“I felt like I kept getting stronger and stronger as time went on.”
—Mark Denisiuk, on his experience taking the experimental drug SNDX-5613

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The medication is a simple pill Mark took at home. Unlike the harsh side effects from previous treatments, Mark says, “I felt like I kept getting stronger and stronger as time went on. I really had no side effects.” Three months later, his leukemia was in remission.

In December 2021, Dr. Stein presented the first results from the trial that Mark participated in at the American Society of Hematology annual meeting. He reported that 55% of patients responded to the menin-blocking drug. Some of them were still doing well after six months.

Collaboration Drives Translational Advances

The kind of translational research that has led to the success of drugs like menin inhibitors is possible thanks to wide-ranging collaborations across MSK. The Center for Hematologic Oncology & Pathogenesis Program includes lab researchers from both the Human Oncology & Pathogenesis Program and the Sloan Kettering Institute (SKI), in addition to clinical investigators. Scientists including SKI cancer biologists Scott Lowe, a Howard Hughes Medical Institute Investigator, and Michael Kharas can work directly with doctors to focus on developing new treatments. Much of the clinical research is overseen by Marcel van den Brink, Head of the Division of Hematologic Malignancies and Alan N. Houghton Chair.

Researchers rely heavily on the Hematologic Oncology Tumor Bank, directed by physician-scientist James Young. “Most people with hematologic cancers who come to MSK for treatment are happy to donate their blood and/or tissues for research,” Dr. Young says.

The bank holds thousands of samples from patients treated for a range of hematologic cancers, as well as samples from bone marrow transplant patients and their donors.

Grateful for a Second Chance

After Mark recovered from chemotherapy and lengthy hospital stays, he was able to walk his 7-year-old son, Benjamin, to school and play soccer in the backyard. Then came more encouraging news: Because the menin inhibitor had put his leukemia into remission, Mark learned that he qualified for a bone marrow transplant, which could cure his disease. While his genetic makeup made it challenging to find a match, Juliet Barker, Director of MSK’s Cord Blood Transplantation Program, found a donor through a public cord blood bank. (These banks contain umbilical cord blood that parents donate after their babies’ births.)

“Cord blood has the advantage that a perfect match between the donor and the patient is not required,” Dr. Barker says. Mark received his transplant in November 2021 and was discharged from inpatient care in mid-December. “I’m really grateful to Dr. Stein, Dr. Goldberg, Dr. Barker, and MSK’s exceptional nursing staff, as well as the rest of the team involved in this clinical trial. It gave me a second chance at life when there were not many options left,” Mark says. “I also could not have gone through the treatments so successfully without my wife, Lauren, who has been there for me and our son every step of the way.”

The following donors have made significant gifts that have been instrumental in advancing blood cancer research at MSK:

Peter and Susan Solomon
Edward P. Evans Foundation
Comedy vs Cancer, founded by Niccole and Jeremy Kroll, Jennifer Rogers, and Robert Carlock
Steven A. Greenberg Charitable Trust
Mr. and Mrs. Donald G. Calder
George L. Ohrstrom, Jr. Foundation
Paul E. Singer Foundation
Melvin Berlin Family
Nassef Sawiris
Nonna’s Garden Foundation

Colleen Ranaghan (middle) and registered nurse Nicole Banu.
Unlocking a Mystery

What’s Behind the Rise in Colorectal Cancer Among Young People

Rebecca Lerner receives a chemotherapy infusion at MSK. She was diagnosed with colorectal cancer just before she turned 33.

A disturbing question lies at the heart of a common and deadly cancer. Why is colorectal cancer striking more people as young as their 20s and 30s — and even teenagers?

Most of these young people have no family history of the disease. They also have few of the risk factors associated with colorectal cancer, which typically develops in people 60 and older.

In fact, many of the clues that medical investigators rely on have led to dead ends.

First Center in the World

To find answers, Memorial Sloan Kettering Cancer Center established the first center in the world devoted to the specific needs of people under 50 with these cancers.

The Center is also a focal point for a massive research effort that flows back and forth from MSK patient beds and clinical trials to laboratories and sophisticated artificial intelligence tools at the Sloan Kettering Institute (SKI).

The goal of this collaboration is to translate MSK’s unparalleled expertise into advances that will save lives.

A Terrible Trend

The statistics are startling: For the past few decades, the number of people below age 50 who are diagnosed with colorectal cancer has been steadily rising.

In fact, cases of the disease among younger adults are expected to nearly double by 2030.

Even worse, the death rate from colorectal cancer for younger people is ticking upwards, after previously declining for years.

A More Aggressive Cancer?

Medical oncologist Andrea Cercek is Co-Director of MSK’s Center along with gastroenterologist Robin Mendelsohn. Dr. Cercek says, “One of the most urgent questions we needed to answer is how we should treat these younger patients.”

She explains, “Does the rise in colorectal cancer in younger people signal that the disease is more aggressive in these patients and should be treated more aggressively too? Is this a new kind of colorectal cancer?”

Dr. Cercek adds that “many doctors decided that since younger patients are usually stronger than older patients, it made sense to treat them with stronger chemotherapy regimens.”

‘Happening Earlier’

However, important new translational research at MSK suggests a new way forward.

In a paper published in August 2021, Dr. Cercek and her research group, including MSK’s computational biology team, performed the largest and most comprehensive comparison ever of colorectal patients below 50 — and as young as their teens — with patients over 50.

The comparison of 1,446 MSK patients looked at the genomic makeup of patient tumors, the different areas in the colon and rectum where the tumors developed, the treatments that were given, and the outcomes of each age group, including overall survival rates.

“We found there are really no differences, across the board, no matter how old or young a patient is,” says Dr. Cercek. “This is the same disease biology in younger patients — it’s just happening much earlier in their lives.”

Dr. Cercek adds: “Importantly for younger patients, we also found that their responses to chemotherapy are the same as older patients and so are their survival and outcomes.”

What that means, she says, is “we should not treat these patients differently just because they’re young, because it won’t improve their outcomes. They will just have more toxicity without any benefits.”

She concludes, “Since our research suggests this disease is the same across all age groups, the next question we’re trying to answer is, ‘Why is this happening to younger people?’ “

The hunt for clues is taking place in clinics and labs across MSK, including a collaboration between Dr. Cercek and MSK medical oncologist Rona Yaeger, a physician-scientist. Together with other colleagues, one aspect they are investigating is the genetic evolution of colorectal cancer in young people.

Translating Cancer’s Cross Talk

Another place searching for answers is the SKI laboratory of Josie Roberston Investigator Karuna Ganesh. She is a physician-scientist who cares for patients with gastrointestinal cancers and is a member of the Molecular Pharmacology Program at SKI.

She stresses that at SKI, researchers are investigating cancer from every angle. “We are looking not just at the tumor in isolation but at systemic factors, meaning things that are happening in the whole body that influence how the tumor can survive.”

She explains that systemic factors “include the immune system, hormones, and signals from nerves and how these interact with cancer cells, as well as the microbiome” — the enormous community of bacteria and other organisms living in our bodies that play a significant role in our health. “We also look at how all of these factors are influenced by diet and exercise, age, and medications a person is taking.”

The goal, she says, is to understand the “cross talk that happens among these systemic factors and cancer cells, so we can tease apart the mechanisms by which cancer arises and grows.”

Rise of the Organoids

A powerful new method to eavesdrop on this cross talk is called an organoid. Dr. Ganesh explains an organoid as a “mini gut, where cells from a patient’s tumor are grown in a dish in three dimensions, so you see all of the different cell types, just like in an intact tumor.”

The organoid “can also evolve and change to respond to different stresses and environmental signals, just like a primary tumor or metastatic cancer cells that have spread.”

This ability for cancer cells to adapt to changing environmental cues is called plasticity, and it’s an important reason that many cancer treatments lose their potency over time in some patients, as tumor cells evolve to outwit the therapy.

By introducing a patient’s own microbiome and immune cells into the organoid, Dr. Ganesh and her team can see how all the cells interact with the tumor.

Andrea Cercek is Co-Director of the Center for Young Onset Colorectal and Gastrointestinal Cancer.
Dr. Ganesh says the insights that have been gained prove the value of translational research at MSK. “Unlike traditional cancer models, studying patient samples and organoids enables us to capture the diversity and plasticity of tumor and environment interactions that we see in our patients. Ultimately, our goal is to use these insights to develop more effective drugs to treat cancer. This is why the translational research effort that spans the clinic and the lab is so important.

Dr. Ganesh is also quick to point out that “trying to understand the interplay of so many different factors probably would not be possible, to be honest, without the collaboration of our SKI colleagues in computational biology, like Dana Pe’er and Christina Leslie.”

360-Degree View of Cancer

This 360-degree view of cancer is also the bedrock of the Center for Young Onset Colorectal and Gastrointestinal Cancer, which aims to help people with the specific issues they face at a particularly vulnerable stage of life.

Rebecca Lerner found out she had colorectal cancer in early 2021, just weeks before her 33rd birthday. She had insisted on a colonoscopy after years of persistent stomach issues.

Neither she nor her healthcare providers thought someone so young and healthy could have colon cancer — a common obstacle to early diagnosis for young people who develop the disease.

“There’s nothing like being told you have cancer,” she recalls. “You don’t know how to function.” When she learned she had stage 3 colon cancer, she says, “I went to the darkest places my mind has ever been.”

Swinging Into Action

After surgery at a major hospital near her home in New Jersey, Rebecca came to MSK for chemotherapy. Her age and diagnosis meant the Center was alerted as soon as she made an appointment. Behind the scenes, specialists at the Center who had treated many young people like Rebecca swung into action.

“I met with Dr. Cercek for the first time on March 3 of 2021. I told her my fiancé and I had set our wedding date for the next week — was that OK? She said, ‘It’s perfectly OK.’ ” She continues, “Then Dr. Cercek and the Center immediately began to help me with fertility preservation so I could freeze my eggs before starting chemo. My husband, Ian, and I both hope for a family of our own, so we froze embryos as one option for having children. I was so relieved all of this was just automatically part of the plan for a younger person like me. I don’t think it would be like this at other hospitals.”

Best Care

After Rebecca’s first appointment, the Center’s dedicated social worker — Hadley Maya — reached out to Rebecca, as she does with all the Center’s patients.

“She saved me,” Rebecca says. “I wanted her to be my best friend. I think she is my best friend,” Rebecca admits with a laugh — “she just doesn’t know it.”

Rebecca credits Hadley with helping her through a challenge that may be unique to younger cancer patients. “I got married in the middle of all this, and while I’m fortunate to be very close with my parents, it created some difficult dynamics. I needed to do this with my husband — he had to be my caregiver — without hurting my parents’ feelings. Hadley helped me navigate the relationship with my parents, so that everyone felt heard.”

Today, Rebecca has no evidence of disease. And she remains in close touch with her care team at MSK, explaining, “They do all of the things that you need, and the things you don’t know you need. I feel like I got the best care possible because of it.”
Finding a treatment for brain tumors like glioblastoma (GBM) has been a heartbreaking challenge. The five-year survival rate is less than 10% for patients 45 and older. Because these tumors are relatively rare and located in such a sensitive and well-sheltered part of the body, researchers have lacked a reliable source of tumor tissue to understand their underlying biology.

Luis Parada, who has spent much of his scientific career trying to study the elusive biology of these tumors. Dr. Parada, who holds the Albert C. Foster Chair, came to Memorial Sloan Kettering in 2015 with the explicit goal of developing a better way.

Dr. Parada’s protocol for creating a patient-derived xenograft (PDX) is a laboratory model in which cells from a human tumor are transplanted into a research animal, such as a mouse. The human cells grow into a new tumor in the animal and can then be studied on the microscopic level to better understand their properties and also be used to test potential drugs.

Decoding the Biology of Brain Tumors

As Director of MSK’s Brain Tumor Center (BTC), Dr. Parada collaborates with clinicians and scientists throughout the institution, breaking down silos to advance their understanding. As a result, the Center now has stored more than 100 verified PDX models, ready to be studied by researchers at MSK.

Dr. Parada’s protocol for creating these models is among the most stringent compared with programs at other institutions. The human tumor cells for his models come directly from patients who are having surgery at MSK. Neurosurgeons and affiliated faculty members of the BTC, Viviane Tabar, who holds the Theresa Feng Chair in Neurosurgery; and Cameron Brannan perform most of these surgeries at Memorial Hospital.

Once the tumor tissue is removed from the patient, it is quickly whisked away by Dr. Parada’s team to be surgically implanted directly into the brain of a mouse. The tumor cells never touch a culture dish or other chemicals that might alter their activity. Moreover, they are grown in the same organ from which they were derived — the brain. Then, Dr. Parada’s team monitors them through MRI scans to make sure that they have taken root in the mouse brains.

Once three successive generations of mice have been grown with the transplanted tumors, the researchers sequence the tumor’s DNA to make sure that the PDX models are as close as you can get to actually experimenting on human brain tumors. “That’s unprecedented,” Dr. Parada says. “These PDX models are as close as you can get to actually experimenting on human brain tumors.”

Neuro-oncologist Ingo Mellinghoff specializes in the treatment of primary brain tumors. "These PDX models are as close as you can get to actually experimenting on human brain tumors." Dr. Parada suspects that there isn’t one glioblastoma, but rather five or six subtypes, based on preliminary evidence. His goal is to identify unique vulnerabilities of each subtype and develop specific treatments for each of them. One day, the team at MSK’s Brain Tumor Center hopes their work will improve patients’ odds of surviving this deadly disease.

Of course, none of this hope would be possible without the philanthropic investments that made this unique PDX program possible — and keep it running. In particular, Dr. Parada is grateful to the Mortimer B. Zuckerman Family Foundation, Richard A. and Susan P. Friedman, and the Richard H. Schneider Foundation, Richard H. Schneider Family Fund for making transformational gifts to support brain cancer research initiatives at MSK. •

Mice as Surrogates for Patients

Researchers are using the PDX models to establish various subtypes of glioblastoma based on their genetic makeup. Then, these tumors in mice are treated with drugs in what they call a “preclinical trial” — similar to what you would do with patients, but with mice instead.

“This is unprecedented,” Dr. Parada says. “These PDX models are as close as you can get to actually experimenting on human brain tumors.”

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Owen and Stacia's Love Story

Bright, athletic, gregarious, and kind, Owen Strong was enjoying a quintessential life in Manhattan. Living with college friends from Tufts, he was working in the family real estate business and recording songs with his band, the Evening Fools. Then, in February 2018, at age 28, Owen was beset by blinding, inexplicable headaches. Without mentioning anything to his family, he sought help from his trusted pediatrician, who referred him to a neurorologist. An MRI revealed a deadly mass in his brain.

Owen's sister, Leda, and their parents, Ed and Laurel Strong, were on vacation when they got the news. “I think of it as a roadside bomb,” says Ed. “It was just so unexpected.”

Cecily Strong, a cast member on Saturday Night Live, is Owen’s cousin. She wrote in her memoir, This Will All Be Over Soon: “I didn’t know how long I sat frozen on my bed making those guttural wailing noises. I kept saying, ‘No, no, no, no, no, no, not my little Owen.’”

Owen, on the other hand, had joked, “Of all the things I was getting brain tumors, I am the one who actually has one.” That he maintained his sense of humor was no surprise. “He was funny and kind,” says Leda. “He put everyone at ease.”

A Devastating Diagnosis

The family came to Memorial Sloan Kettering Cancer Center in March 2018, where neurosurgeon Cameron Brennan removed the tumor — a glioblastoma, the deadliest of all brain tumors. Owen underwent six weeks of radiation and several months of chemotherapy under the care of neuro-oncologist Adrienne Boire, who also conducts research supported by Alan and Sandra Gerry through the Gerald and Stephanie Smart, member of the Owen’s care team were outside waiting for her. Photos were taken; teary hugs exchanged. “The last time I had seen Stacia was at Owen’s memorial service,” says Dr. Boire. “It was good to see her moving on with her life, surrounded by people who love her.”

Reconnecting with Owen’s MSK team was “so healing,” says Stacia. “It meant a lot to me that I could see them in a positive situation. It gave me the fuel to keep going. They’re fighting for thousands of people, so supporting them means supporting all patients.”

Stacia says she felt Owen’s presence every day. Even when thunderstorms were predicted, the ride was not once interrupted by rain. “I had sunshine following me down the East Coast,” she says. Upon arrival at Owen’s high school, Andrew’s School of Delaware, crowds cheered and a bald eagle circled overhead. Owen, who had always loved birds, was clearly with them, says Stacia.

The Start of Something Big

Stacia crossed the finish line one month and 1,100 miles after her start. She raised more than $56,000 for brain tumor research at MSK.

Leda imagines her brother’s reaction would be: “You didn’t have to do all that for me.”

Of course, the ride was not just for Owen; it was for all brain cancer patients in the future. “Philanthropy is especially important in this field because the government and pharmaceutical companies can be reluctant to fund out-of-the-box experiments. But out-of-the-box thinking is essential in discovering a treatment that works against such a devastating cancer.”

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For the next eight months, Owen continued life as a 20-something: working, seeing friends, attending weddings. For Halloween, Owen went to a party dressed as the Big Friendly Giant, a character from a Roald Dahl children’s book. There, his eyes fell upon 25-year-old Stacia Smart. They began dating, and Owen told her he had brain cancer.

“Of course, I was completely shattered,” she recalls. “But, I thought, ‘OK, I’m here and the universe wouldn’t put me in a situation I didn’t know how to handle.’”

Stacia and her family were well-versed in the grief of glioblastoma; Stacia’s uncle had brain cancer.

When Owen broke the news to her, she says: “I decided then and there that I wouldn’t leave his side. I was all in, and we were going to go through this together.” And so they did, falling quickly in love.

Remaining with Owen’s MSK team was “so healing,” says Stacia. “It meant a lot to me that I could see them in a positive situation. It gave me the fuel to keep going. They’re fighting for thousands of people, so supporting them means supporting all patients.”

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Now, the Druckenmillers have set their sights on a new venture: supporting translational cancer research at Memorial Sloan Kettering Cancer Center. With a transformational gift of $100 million from the Druckenmillers, MSK established the Fiona and Stanley Druckenmiller Presidential Innovation Fund in late 2021. The fund is designed to fuel the most creative and impactful early-stage translational research and to channel advances in cancer biology directly into potential treatments. Translational research serves as a bridge between the laboratory and the clinic, often resulting in the development of novel diagnostics and therapies.

“We wanted to create more opportunities to support research endeavors that could lead to lifesaving treatments for many people with cancer. We’re confident that the fund will have a transformative effect on cancer outcomes over the next 10 years,” says Mrs. Druckenmiller.

The Druckenmillers have long been champions of MSK’s approach to cancer medicine, which fosters close collaboration between doctors and scientists to deliver world-class care. Mr. Druckenmiller has been a member of MSK’s Boards of Trustees and Governing Trustees since 1997, and the couple has supported a wide range of programs across the institution. In 2015, they made a gift to establish the Fiona and Stanley Druckenmiller Center for Lung Cancer Research, with the goal of providing more effective therapies for people with lung cancer. In a few short years, physician-scientists and surgeons working side by side have initiated high-impact projects that have identified new strategies to treat people with lung cancer.

“Time and time again, we have witnessed the incredible advances that come from placing resources in the hands of talented doctors and scientists,” says Mr. Druckenmiller. “I can’t think of another institution better positioned to shape the future of cancer care than MSK.”

Philanthropy provides the necessary support for MSK researchers to study cancer in innovative ways. The Druckenmillers’ generosity ensures that the most brilliant people working in translational cancer research have the resources they need to make the most significant discoveries.

“All of us at MSK are deeply grateful to the Druckenmillers for their leadership and support of this crucial initiative, which will launch pathbreaking research and clinical care efforts and bring hope to so many people with cancer,” says Craig B. Thompson, President and Chief Executive Officer of MSK. “It is an honor to partner with them in this visionary endeavor.”

Visit mskcc.org/druckenmiller-news to read more about the Fiona and Stanley Druckenmiller Presidential Innovation Fund.