Division of Hematologic Malignancies 2020 ANNUAL REPORT

Memorial Sloan Kettering Cancer Center

Table of Contents

Letter from the Division Head

We are happy to share the progress of the Division of Hematologic Malignancies at MSK over the past year. You will find highlights for each of the services that make up the Division, as well as the accomplishments of our faculty, nurses, nurse practitioners, physician assistants, pharmacists, fellows, and others. This year, we interviewed eight members of our division, who all in their own individual way contribute to the continuing success of the Division.

As COVID-19 continues to dramatically impact our daily lives, I am inspired by the persistent dedication of our faculty, nurses, and staff to our patients and mission. Our team is a highly collaborative group of professionals with diverse knowledge and experience. The 2020 Annual Report aims to acknowledge their tireless efforts and extraordinary devotion demonstrated during this once-in-a-lifetime pandemic.

Sincerely,

Marcel van den Brink, MD, PhD
Alan Houghton Chair in Immunology
Head, Division of Hematologic Malignancies
Memorial Sloan Kettering Cancer Center

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Scott James


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Brian Shaffer


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Jodi Mones


Rekha Parameswaran


Gerald Soff


Cy Wilkins

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Omar Abdel-Wahab


Ellin Berman


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Anthony Daniyan


Andrew Dunbar

Mark Geyer

Jacob Glass

Aaron Goldberg

Virginia Klimek

David Knorr

Ross Levine

Peter Maslak

Anthony Mato

Michael Mauro

Kamal Menghrajani

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Raajit Rampal

Lindsey Roeker

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Eytan Stein

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Philip Caron

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Lorenzo Falchi

Audrey Hamilton

Paul Hamlin

Steven Horwitz

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Erel Joffe

William Johnson

Niloufer Khan

Anita Kumar

Christina Lee

Matthew Matasar

Alison Moskowitz

Ariela Noy

Colette Owens

Lia Palomba

Ildefonso Rodriguez-Rivera

Gilles Salles
Service Chief, Lymphoma

David Straus

Santosha Vardhana

Gottfried von Keudell

Anas Younes*

Andrew Zelenetz

Myeloma

Hani Hassoun

Malin Hultcrantz

Neha Korde

Ola Landgren*

Alexander Lesokhin
Interim Service Chief, Myeloma

Sydney Lu

Sham Mailankody

Francesco Maura*

Urvi Shah

Eric Smith*

Carlyn Tan

*transitioned from the division in 2020

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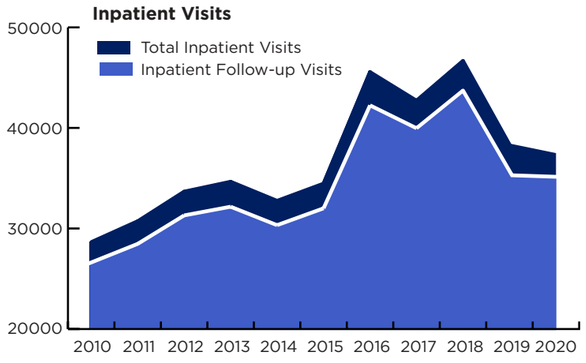
Senior Director, Hospital Administration

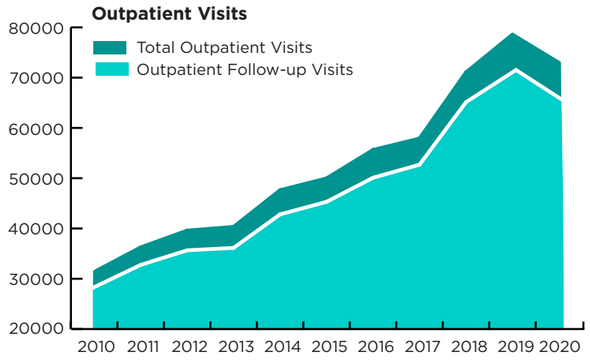
Kristen Hakuta
Director, Medicine

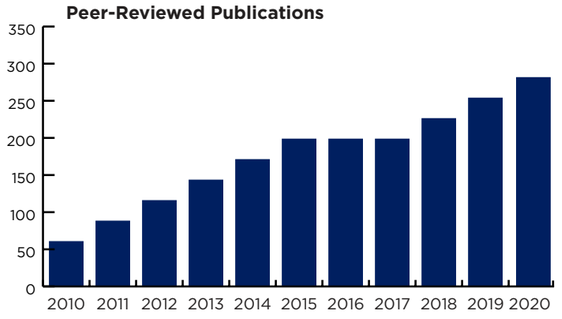
Chelsea Brooklyn
Manager
BMT & Supportive Care

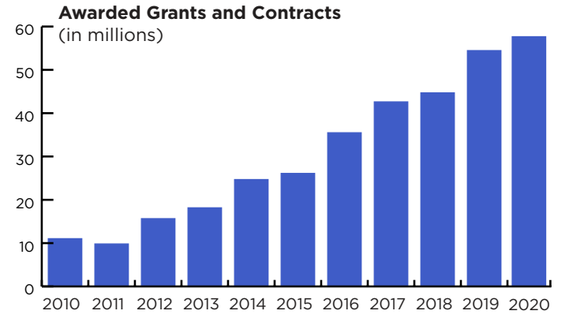
David Pagel
Manager
Hematology, Leukemia, Lymphoma, & Myeloma

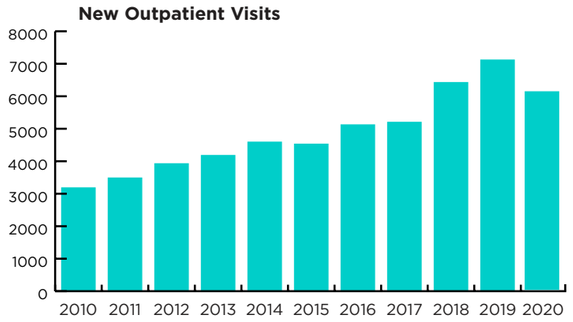
2020 Metrics

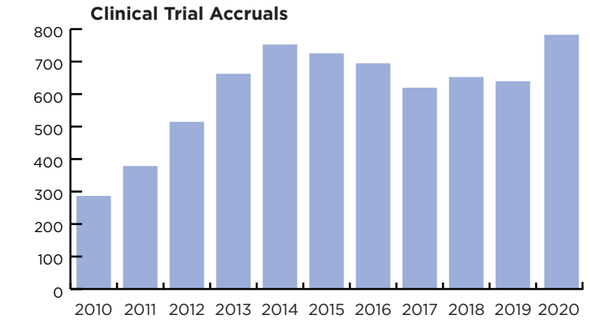


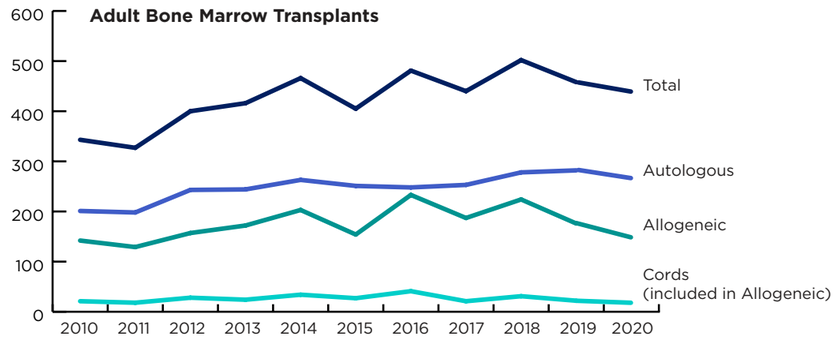












COVID-19

Gilles Salles, MD

COVID-19 and the Division of Hematologic Malignancies

This year, Memorial Sloan Kettering and the Division of Hematologic Malignancies adapted to the challenges that COVID-19 presented and safely provided exceptional cancer care.

During this time, when it was safest to limit patients' office visits, telemedicine ensured that patients were receiving quality care by giving them the ability to connect with MSK providers remotely. The Division quickly built up telemedicine capacity, which reduced crowding in MSK facilities by allowing patients to access follow-up care remotely from the comfort of their homes. We also made it possible for patients with in-person appointments to have "virtual visitors."

The Division went from performing about 40 telemedicine visits per day in early March to more than 1,200 per day in December 2020, with plans for continued growth. This integral tool used to mitigate COVID-19 in the healthcare setting is becoming an established industry-wide best practice.

MSK continues to be a leader in COVID-19 testing in an effort to keep patients, staff, and the community safe and healthy. At the beginning of the outbreak in New York City, MSK's scientists developed a highly effective COVID-19 diagnostic test, and MSK was one of the first hospitals in New York authorized for COVID-19 diagnostic testing. MSK provides regular COVID-19 diagnostic testing to patients and staff as well as antibody testing to detect prior infections.

Hundreds of MSK employees who have recovered from COVID-19 have stepped forward to donate their plasma to treat patients through a clinical trial. Plasma from people who have recovered from a viral infection has long been known to have potentially therapeutic benefits for patients.

As leaders in the field, MSK researchers have spent decades studying hematologic malignancies, bone marrow transplantation, and how the immune system responds to cancer. During the COVID-19 pandemic, many of them applied their insights toward gaining a deeper understanding of how the immune system reacts to the coronavirus that causes COVID-19.

COVID-19 has created new and unprecedented challenges, but MSK staff continued their work as healthcare providers, researchers, teachers, and leaders. In 2020, members of the Division remained productive — as evidenced by their 269 published papers, with more than 40 of them related to COVID-19. **Many of these studies are highlighted in the following pages (using this symbol: ⚛).**

Our physicians rose to the occasion, supporting hospitals in the surrounding community. Faculty members including Roni Tamari, Gunjan Shah, Santosh Vardhana, Matthew Matasar, and Ariela Noy volunteered externally at hospitals and clinics in the community. This report will highlight staff contributions across the board, including support from our nurses, advanced practice providers, administrative staff, and fellows.

Cancer Doesn't Stop in a Pandemic

As the height of the COVID-19 outbreak in New York City and the Tri-State area begins to subside, oncologists at MSK are urging patients to schedule cancer screenings and treatments now — as the long-term toll of missed diagnoses and delayed treatments could be devastating for patients and their loved ones across the region and the country.

MSK's inpatient and outpatient facilities in New York City, Long Island, Westchester, and New Jersey are open, and appointments are available for new and existing patients.

We have adopted enhanced safety measures, including providing patient screenings, reducing density in facilities, enacting safe visitor policies, curbside check-in wherever possible, fostering clean and safe environments, conducting staff health checks and testing, providing telemedicine services, and virtual express check-out.

If you have recently been diagnosed with cancer or need to continue ongoing cancer treatment, please visit www.mskcc.org/experience/become-patient/appointment to make an appointment.

The following trials were conducted by physician-⚛ scientists in the Division:

- IRB#20-144: Expanded Access to Convalescent Plasma for the Treatment of Patients with COVID-19; PI: Essie Papadopoulos
- IIRB#20-168: Phase II Study of N-acetylcysteine in Severe or Critically Ill Patients with Refractory COVID-19 Infection; PI: Santosha Vardhana
- IIRB#20-185: A Phase II Study of IL-6 Receptor Antagonist Tocilizumab to Prevent Respiratory Failure and Death in Patients with Severe COVID-19 Infection; PI: Boglarka Gyurkocza
- IIRB#19-168: A Phase II Study of IL-1 Receptor Antagonist Anakinra to Prevent Severe Neurotoxicity and Cytokine Release Syndrome in Patients Receiving CD19-Specific Chimeric Antigen Receptor (CAR) T Cells and to Treat Systemic Inflammation Associated with COVID-19; PI: Jae Park

PhD candidate Laura Menocal made sure necessary work at the lab kept going in the face of COVID-19.

The Path Ahead: How MSK Responded to COVID-19

"It felt like watching a terrifying storm moving toward us in slow motion." That is how Memorial Sloan Kettering lymphoma doctor Matthew Matasar describes watching the COVID-19 pandemic unfold.

MSK doctors, researchers, and staff never wavered in their commitment to continue to provide care for people with cancer, even as much of the world stood paralyzed. The story of that response has important lessons about resilience and creativity as well as insights into what lies ahead in the new normal as the threat from the virus persists.

Getting Testing Right

Infectious disease expert Monika Shah says it was unnerving that so little was known about COVID-19 in March 2020. "In medicine," she says, "we're used to practicing in an evidence-based fashion, meaning that we rely on data and prior experience. But there was no evidence for us. We had to gather our own data and learn from our own experiences as we went along, even as we worked to help keep people safe."

Like many hospitals, MSK faced possible shortages of testing supplies. To increase efficiency, MSK developed its own system to test for the virus. "I remember coming in one weekend, and we started to put together a plan to ramp up testing," says Dr. Shah. "Very quickly we went from doctors like me ordering individual tests to a system that could get a test for any patient or any one of our thousands of employees."

The new system worked well and also helped streamline the organization. "I have a patient who has been coming to MSK for more than 25 years," says Dr. Shah. "He lives in a Brooklyn neighborhood that had a high rate of COVID-19. When he grew concerned about some symptoms, I had him come in for testing."

The man tested positive for COVID-19 but did not need to be hospitalized. "He was amazed by how well organized everything was, from the time he called us to the separate screening area where he was tested to the phone calls he received to ensure he was recovering appropriately," says Dr. Shah.

"A lot of other cancer centers had to pause research during their initial COVID-19 response," says medical oncologist Matthew Matasar. At MSK, many clinical trials were able to continue.

Care Closer to Home

MSK's regional care locations have been crucial for patient care during the pandemic.

"I'm so grateful that MSK invested in our regional care network," says Dr. Matasar, who is the Medical Site Director at MSK Bergen. "The overwhelming preference of patients is to get the care they need closer to home, especially if they live outside New York City. We never closed MSK Bergen or any of our regional locations across New York and New Jersey, and that's so important."

MSK also brought care right into people's homes, thanks to a massive scaling up of telemedicine visits, when doctors and patients see and talk to one another using computers or smartphones. By late June, two out of every three outpatient appointments were telemedicine visits. "People have been talking about telemedicine in cancer care for a long time," says Dr. Matasar, "but in a 'wouldn't that be cool' kind of way, as if it's something out of a Star Trek episode."

Medical oncologist Nitya Raj says replacing office visits with telemedicine has been transformative. "Going forward," she says, "telemedicine is really going to make medicine better for doctors, nurses, and especially patients and their families who won't have to travel to get great MSK care."

The Research Lens

As doctors and nurses adapted for patient care, MSK's researchers responded to the COVID-19 pandemic with their own creativity and determination.

In March, researchers organized the Laboratory Emergency Task Force to identify and facilitate the complex logistics required to pause research across MSK.

Laura Menocal, a PhD student who works in the lab of Andrea Schietinger, joined a team that checked in on Sloan Kettering Institute labs, even at the height of the pandemic. "Once or twice a week, I came into the lab alone and stayed for an hour or two to take care of things that were absolutely necessary," Ms. Menocal says. Her efforts meant colleagues could avoid exposure to COVID-19. Ms. Menocal knew all too well how dangerous the virus could be: "My cousin, a doctor in Mexico, died of COVID-19. Of course, it was a very difficult time for me both personally and professionally."

Because of the dedication of researchers like Ms. Menocal, MSK's labs have resumed their work. "It was very smooth picking up my work again," she says. "I'm very excited about what's ahead in cancer research because we are making so many important discoveries."

> **"A lot of other cancer centers had to pause research during their initial COVID-19 response."**
>
> **Matthew Matasar**
> **medical oncologist**

The Future of Clinical Trials

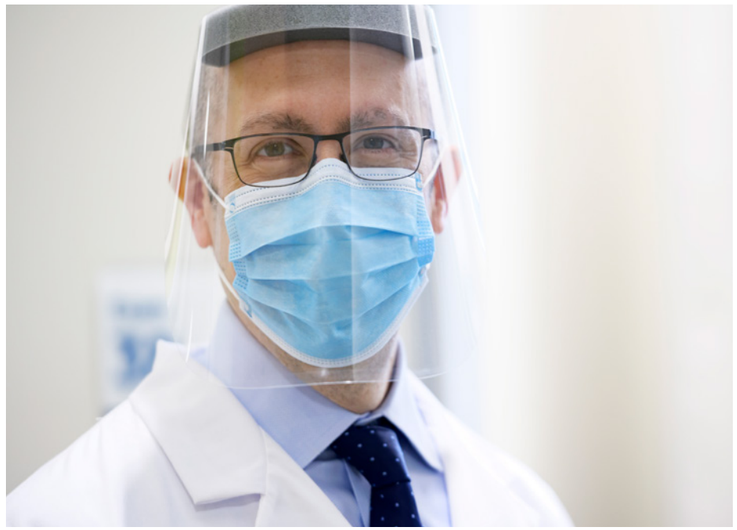
Clinical trials are a vitally important part of cancer research, as they investigate possible new therapies. "A lot of other cancer centers had to pause research during their initial COVID-19 response," notes Dr. Matasar. "However, MSK kept many of our clinical trials going because we know for some patients, that's the very best type of cancer care."

To continue the trials and stay on schedule, MSK relied in part on telemedicine, which until the COVID-19 pandemic was virtually unheard of in clinical trials. For the first time, many patients receiving novel therapies were no longer heading into their doctor's office but instead were comfortable at home. "Our goal was to have people come to see us only when they were actually receiving treatment and do checkups through telemedicine," explains Dr. Raj.

For some clinical trial patients, providing treatment required extra ingenuity. "A colleague told me about an MSK clinical trial patient from Latin America who had to fly into New York City regularly for treatment," says Dr. Matasar. "During the pandemic, MSK figured out how to fly the investigational drug to the patient and had it administered by a local oncologist there."

That kind of commitment sets MSK's care apart. "We've heard often to never waste a crisis. And MSK learned a lot from this one," says Dr. Matasar. "From testing to patient care and clinical trials, when we look back at what we've done and how we've improved, we're going to be shocked and proud of what we've accomplished."

www.mskcc.org/msk-news/fall-2020/path-ahead-how-msk-responded-covid-19



Medical Oncologist Matthew Matasar

Exploring the Potential of Convalescent Plasma for COVID-19

Esperanza Papadopoulos, PI on the convalescent plasma trial

As the world struggles with the epic challenge of the COVID-19 pandemic, employees at MSK have risen to the occasion in countless ways. In addition to providing extraordinary care and comfort for patients with COVID-19, our staff are contributing to our collective understanding of a new treatment approach using convalescent plasma — both by studying it and donating it.

Plasma from people who have recovered from a viral infection has long been known to have potentially therapeutic benefits for patients. Today, hundreds of MSK employees who have recovered from COVID-19 have stepped forward to donate their plasma to treat patients through a clinical trial led by Principle Investigator (PI) Esperanza Papadopoulos, Clinical Director of the Adult Bone Marrow Transplantation Unit. Genovefa Papanicolaou, Infectious Diseases Specialist, Cheryl Goss, an associate attending in Laboratory Medicine, and benign hematologist Cy Wilkins round out the leadership team for the initiative, working closely with staff from Clinical Research, Infectious Diseases, Nursing, Laboratory Medicine, Hematology-Oncology, Health Informatics, and more.

A National Emergency

On March 21, 2020, Sergio Giralt, Deputy Division Head, Division of Hematologic Malignancies, and Paul Hamlin, Medical Director, David H. Koch Center for Cancer Care at Memorial Sloan Kettering Cancer Center, took part in the first conference call of the National COVID-19 Convalescent Plasma Project. The virtual meeting included more than 100 participants from academic institutions who had come together to investigate the use of plasma as a treatment for patients with COVID-19. After the meeting, Dr. Hamlin reached out to Drs. Papadopoulos, Papanicolaou, Goss, and Wilkins and asked them to lead MSK in this national grassroots effort, which now involves 57 institutions from 46 states.

"We immediately started to pull a team together," says Dr. Papadopoulos. The task was mammoth: As quickly as possible, they had to launch a clinical investigation that would explore questions surrounding 1) access, 2) safety, and 3) healthcare utilization related to plasma donation. And they had to do it during a national health emergency while MSK was grappling with an altered workplace, one defined by a greater proportion of employees who were working remotely or were out sick.

The FDA took steps to allow institutions across the nation to enroll multiple patients, significantly speeding up the delivery of convalescent plasma to COVID-19 patients, and allowed researchers to launch clinical trials at a faster-than-usual rate.

"At this phase, we are investigating if we can get the plasma to patients who need it and whether there are any adverse effects," says Dr. Papadopoulos. "The true efficacy of convalescent plasma will be explored in future trials."

One early logistical question was where to get convalescent plasma. "Most hospitals in New York City have to rely on the New York Blood Center or the Red Cross for blood products, including plasma, because they don't have donation facilities," says Dr. Goss. "We're fortunate at MSK to be one of only two healthcare institutions in the city with our own donor room."

MSK's donor room, located on the ground floor of the Schwartz building, offers a full range of services for the collection, processing, and testing of standard blood components. Given that, as well as the presence by early April of more than 1,000 employees who had tested positive for COVID-19, it made sense to keep collection efforts in-house and rely on plasma from MSK's recovered employees, obtained in our own donor room.

Putting Plans into Action

A frenzy of preparation soon began.

"We don't typically collect large amounts of plasma," explains Dr. Goss. "We mostly collect platelets and red blood cells for our patients, so large-scale plasma collection required a huge ramping-up of the donor room. It wouldn't have been possible without the incredible efforts of the staff."

Joann Tonon, Senior Manager, Transfusion Medicine and Cellular Therapy, who manages the Blood Bank, created entirely new workflows to handle specialized inventory and order processes. Eileen Walsh, Nurse Leader in Laboratory Medicine, wrote and implemented multiple SOPs (standard operating procedures) for the new required workflows. Collection instruments were reprogrammed for plasma collection, and new large-volume collection kits were purchased.

> **"I feel so grateful for the remarkable care and support I received from the MSK community."**
>
> **Yu Chen**
> **MSK physician-scientist**

At the same time, work was underway to identify employees who were willing to donate. The research team spread the word about the need for donors, using OneMSK and other internal channels, including word-of-mouth. They also worked with Health Informatics to create an eligibility form that captured basic information about prospective donors.

"Once employees heard about it, we had an overwhelming response," says Dr. Papanicolaou.

As donors started to appear, Theresa Elko and Lauren Levy, physician assistants in Clinical Research, screened hundreds of donors and made thousands of phone calls, and Joseph Licata, Manager of the Blood Donor Program, worked tirelessly to schedule donors.

Between March 21, the date of the first conference call of the Convalescent Plasma Project, and April 13, when staff in the donor room collected the first plasma donation, more than 500 MSK employees who had recovered from COVID-19 came forward to donate. Donors must meet a high bar for donation: They must have recovered from COVID-19, test negative for the virus, and have been without symptoms for at least two weeks. They must also meet the standard eligibility criteria for blood donation.

Despite the challenges, the team's quest for plasma was successful: Since April 13, they have already collected 60 donations. Most important, 49 MSK patients with COVID-19 have received convalescent plasma.

One of those who donated is Lisa Toth, Clinical Nurse II in the 4th Floor Chemotherapy Suite in Rockefeller Outpatient Pavilion (53rd Street). Ms. Toth had the virus, recovered at home, and returned to work in mid-April.

"When I heard about the plasma donation opportunity, it wasn't even a question if I would donate. I really wanted to do anything I could to help my colleagues and the patients fight this virus. I'm grateful I was given the opportunity to donate."

A Grateful Recipient

One of the first patients to receive the new therapy was Yu Chen, an MSK physician-scientist who specializes in the treatment of prostate and bladder cancer.

"I feel so grateful for the remarkable care and support I received from the MSK community," says Dr. Chen, who continued his recovery at home after being released from Memorial Hospital on April 23.

Dr. Chen remembers "images of my colleagues hovering over me" while he was lying in the ICU, his status declining by the day. Tobias Hohl, Chief, Infectious Diseases Service — and Dr. Chen's MD and PhD classmate from Weill Cornell — suggested he try convalescent plasma therapy. As his condition worsened, and while "praying not to be intubated," Dr. Chen was infused with plasma from a donation received the day before. He experienced rapid improvement in his

Lisa Toth donates plasma with help from Anli Chang

symptoms, left the ICU three days later, and was discharged from the hospital five days after that, grateful for the "selfless and lasting gift" he had received.

Reflecting on his experience, Dr. Chen says, "I want to thank my donor from the bottom of my heart. I know when I'm cleared for work, donating myself will be my first task."

The Prize: Antibody-Rich Plasma

Researchers don't yet understand why convalescent plasma seems to help some patients and not others, but they believe it may be connected to the level of antibodies in the plasma, which can vary greatly. Another puzzle is why one donor's plasma has a high "titer," or concentration of antibodies, and another's is so low that it barely registers. In the fight against COVID-19, plasma with high titer is the weapon everybody wants.

Knowing whether donated plasma has any antibodies only became possible at MSK when the Department of Laboratory Medicine, chaired by Melissa Pessin, released an antibody test the week of April 27. Lab Medicine evaluated three different tests from outside vendors before determining that one submitted by Abbott Diagnostics was the best for use at MSK.

"It was an extensive evaluation process," says Dr. Pessin, who asked Ellinor Peerschke, Vice Chair of Lab Medicine, and Lakshmi Ramanathan, Chief, Clinical Chemistry Service, to lead the effort. "We took samples of pre-COVID blood that were collected last year and put them through the tests to ensure that the results didn't cross with other coronavirus strains. We also reached out to Deborah Korenstein [Chief, General Internal Medicine Service] to help us get samples of serum from recovered employees to confirm that the tests worked as they were supposed to."

Dr. Pessin says that Lab Medicine is now working to see if the test can be modified to provide the actual levels (titers) of those antibodies.

Going Forward

There's no end date for the convalescent plasma trial. But as antibody testing improves and researchers can determine the level of antibodies a patient is receiving, additional trials may launch to explore whether convalescent plasma is an effective treatment.

Meanwhile, the team continues to collect plasma from staff, thankful for the chance they've been given to help COVID-19 patients.

"I have been staggered by the strength of my colleagues and patients — who are sometimes one and the same — and I am so grateful for this opportunity to explore new therapies for our patients," says Dr. Papadopoulos.

As the PI on the trial, she participates in regular meetings of the COVID-19 Convalescent Plasma Project, often involving 200 to 300 people, and fields requests from her MSK colleagues wondering if their patients might be eligible for the trial. She and the rest of the team are mindful of the unique roles they are playing in this unprecedented time — and the opportunities it has presented.

"I've been at MSK for more than 30 years, and I've never been exposed to such a broad cross-section of the institution or met as many people as I have since this trial started. It's been exhilarating and humbling all at once."

MSK Experts Draw on Expertise to Unmask Secrets of COVID-19

This article was published in Fall 2020.

In March 2020, medical oncologist Santosha Vardhana was faced with a new challenge: Many of his patients with lymphoma were becoming infected with the COVID-19 virus. As he saw more cases, Dr. Vardhana noticed a troubling pattern begin to emerge. Patients were managing well through the initial stage of infection but then got progressively worse. Many of them suffered irreversible lung damage.

"The longer they were sick with COVID-19, the harder it was for the immune system to fight back at all," says Dr. Vardhana, who also conducts research in the lab of Memorial Sloan Kettering President and CEO Craig B. Thompson. "There was a desperate need to find a way to help them get better."

Dr. Vardhana wondered if people with lymphoma were especially susceptible to the virus. Lymphoma is a disease of the body's immune system — it cripples the very thing that fights off an infection such as COVID-19.

He looked for clues in his patients' blood tests. What he found was that while the cancer was suppressing one arm of the immune system, COVID-19 was depleting another part of it. This perfect storm is what was allowing the virus to persist, causing extreme damage to the lungs. Meanwhile, MSK immunologist and medical oncologist Jedd Wolchok was thinking about this problem and how it intersected with MSK's long-term commitment to studying immunotherapy and immunology.

"We quickly began to strategize about how we could use our knowledge of the immune system and medicines that affected it to try and enhance the response to COVID-19," Dr. Wolchok says.

The pair brainstormed and came up with an inspired solution: a drug called N-acetylcysteine, which is used to treat people with cystic fibrosis, a disorder of the lungs and digestive system. They thought that if the drug could help restore lung tissue in those patients, it might be able to help people with COVID-19 too.

They swiftly designed a clinical trial at MSK to test their theory.

"Everyone here worked together to get this trial going quickly, from the Institutional Review Board that approved the study to the nursing staff that learned how to administer the drug," Dr. Vardhana says.

Today, MSK continues to play a crucial role in the global effort against COVID-19. Doctors and researchers from across the institution have drawn on their vast experience in fields from biology and immunology to chemistry and more to achieve one simple goal: learn how the virus affects the body so they can better care for patients.

Don't Delay

As the pandemic surged in New York City in March, Drs. Vardhana and Wolchok were right to be concerned about their patients. Cancer therapies, especially chemotherapy, can lower a person's immune defenses and make them susceptible to infections.

"For many of our patients, cancer care was suspended," says MSK Chief Medical Epidemiologist Mini Kamboj. "And rightly so, given the uncertainty of the situation."

But cancer care can't wait. MSK doctors felt the urgency to get answers about COVID-19 and safely resume treatments as soon as possible.

"It was so palpable how little we knew in March going into April," says Ying Taur, an infectious disease

Medical oncologist Santosha Vardhana says a clinical trial "wouldn't have happened this fast if MSK didn't make it a priority due to an intense focus on COVID-19."

specialist. Colleagues at MSK and other institutions were phoning him for advice: When would it be safe to have patients come in for treatment? With each call, he gave an honest answer: He didn't know. But he also knew that wasn't good enough.

Drs. Kamboj and Taur set out to get a clearer picture of the actual treatment risks. They launched a study looking at more than 400 MSK patients in active cancer treatment who were diagnosed with COVID-19 between March 10 and April 7. One key aspect of the research was that they followed the patients for 30 days after their COVID-19 treatment ended.

What they found was encouraging: For most adults, chemotherapy didn't seem to make COVID-19 any worse.

"If you're an oncologist and you're trying to figure out whether to give patients chemotherapy, or if you have cancer, these findings should be very reassuring," Dr. Taur says. "People should not delay cancer treatment."

The study was published in June in Nature Medicine.

Drs. Kamboj and Taur caution that there are still some questions. There was some evidence in their research that people treated with checkpoint inhibitors (which work by releasing the brakes on the immune system to attack cancer) had an increased risk of severe breathing problems. There is also a need for a deeper dive into patient outcomes for individual cancers.

Unique Expertise

A COVID-19 infection still is complicated for people with cancer. It can cause a wide range of symptoms, from fever to inflammation to difficulty breathing. But MSK doctors are tackling these problems by applying lessons already learned from addressing similar symptoms caused by cancer or its treatments.

"Our experience in caring for people with cancer — and in how the immune system behaves — has given us ideas for how to overcome some of these challenges," Dr. Vardhana says.

It's understood in the medical community that some of what makes COVID-19 so damaging to the body is not just the infection itself. An overzealous immune system is also to blame — it works too hard and starts damaging the body. MSK specialists are familiar with this phenomenon: They've seen it occur in some people who receive a type of immunotherapy called chimeric antigen receptor (CAR) T cell therapy.

CAR T cell therapy was pioneered at MSK, so doctors here are especially proficient at minimizing and treating an extreme immune system response, even in the most severe cases. "This expertise has helped enormously as we try to prevent similar damage in COVID-19 patients," says MSK medical oncologist Jae Park.

Blood cancer specialists Boglarka Gyurkocza and Ann Jakubowski are leading a new effort to tamp down the excessive immune response. They started a clinical trial at MSK that tests whether a drug called tocilizumab (Actemra®) can minimize damage to the lungs and other organs in COVID-19 patients. Tocilizumab is an immunosuppressive drug, meaning it slows down immune system activity and prevents it from going into overdrive. It is approved by the FDA to treat several forms of arthritis.

"This drug targets a specific inflammatory molecule that is detected at high levels in people with COVID-19 infections," Dr. Gyurkocza says. "We think therapies like this, combined with other approaches that can enhance tissue repair or target the virus directly, could bring substantial improvements for patients."

Moving Forward

But what about a vaccine? That's the real hope for bringing COVID-19 under control.

To develop a vaccine against COVID-19, the worldwide scientific community first needs a clear picture of how the immune system responds to the virus. That response is often understood through antibody testing.

To an average person, a COVID-19 antibody test tells them whether they previously had the virus. To a scientist, antibody test results tell a deeper story.

It's like the difference between looking solely at a baseball team's win-loss record, versus scrutinizing individual batting averages, home run totals, and strikeout rates in order to understand why the team didn't make the playoffs.

At MSK, physician-scientist Michael Glickman and structural biologist Christopher Lima are committed to that deeper story behind a COVID-19 antibody test. They work with MSK's Antibody & Bioresource Core Facility and Immune Monitoring Core Facility and started creating a COVID-19 antibody test in February.

As of mid-August, there were more than 130 publications related to COVID-19 from MSK researchers.

Their test detects and measures three antibody types, one of which frequently blocks a virus from entering healthy cells. This is known as a neutralizing antibody. The most effective vaccines, such as those for polio and measles, stimulate the body to produce these types of antibodies, according to Dr. Glickman.

"A COVID-19 vaccine, when it's created, will likely work by causing the body to produce neutralizing antibodies, as well as other types of immunity," he says. "An antibody test like the one created by MSK could provide clues into what that effective response looks like."

When a virus like COVID-19 enters the human body, the immune system responds instantly, with no time to lose.

That, too, is how the MSK community reacted to COVID-19.

www.mskcc.org/msk-news/fall-2020/msk-experts-draw-expertise-unmask-secrets-covid-19

"The course of disease and recovery is still not fully understood. We had to give patients time to make sure they didn't go through another phase of illness."

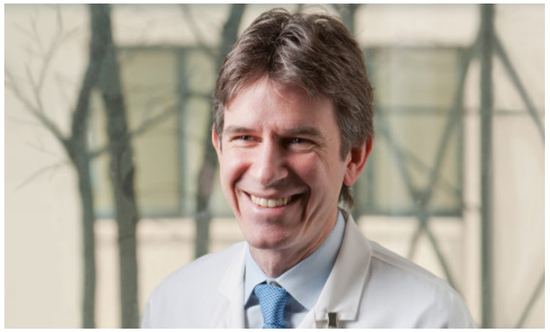
Mini Kamboj
Chief Medical Epidemiologist

Services

Appointments, Promotions and Awards

New Leadership Roles

Sergio Giralt



Miguel Perales

In February 2020, Sergio Giralt was named Deputy Division Head, Division of Hematologic Malignancies, Department of Medicine, Memorial Hospital, and Miguel Perales was named Chief, Adult Bone Marrow Transplant (ABMT) Service, Department of Medicine, Memorial Hospital.

Dr. Giralt received his medical degree from the Central University of Venezuela and completed a residency at Good Samaritan Hospital and a fellowship at MD Anderson Cancer Center. He was appointed at MD Anderson, and then became Deputy Chair in the Department of Stem Cell Transplantation and Cellular Therapies. In May 2010, Dr. Giralt came to Memorial Sloan Kettering to lead the ABMT Service. He was also appointed Professor of Medicine at Weill Cornell Medical College and named to the Melvin Berlin Family Chair in Myeloma Research.

Dr. Giralt is a world-renowned expert who has made important contributions to the field of bone marrow transplantation, and, with his colleagues, pioneered the use of reduced-intensity conditioning regimens for older or more debilitated patients with blood cancers. Currently, Dr. Giralt's research is examining the use of T cell depletion techniques to dramatically reduce the risk of graft-versus-host disease.

In his new role as Deputy Division Head, Dr. Giralt will oversee and coordinate activities of transplant and cellular therapy in the Department of Medicine and foster collaborations between members of the Division and other departments to develop a joint research program for stem cell transplant and cellular therapies.

Dr. Perales received his MD from the Free University of Brussels, after which he was a postdoctoral fellow in the Division of Hematology-Oncology at Tufts-New England Medical Center. Dr. Perales completed his internship and residency in internal medicine at Tufts-New England Medical Center and was a fellow in Hematology/Oncology at MSK. Dr. Perales joined the faculty at MSK in 2001 and has served as the Deputy Chief of the ABMT Service since 2012 as well as the Director of the ABMT Fellowship Program in the Department of Medicine.

Dr. Perales has established a national and international reputation with his track record in preclinical, translational, and clinical studies in stem cell transplantation. Currently, he is responsible for directing studies of immune monitoring in patients undergoing stem cell transplantation at the center. Dr. Perales is also actively involved in hematopoietic stem cell transplantation beyond MSK and serves on several national committees.

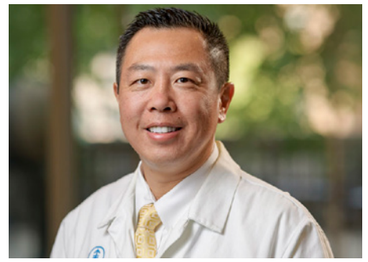
The appointment of Dr. Perales as Chief will continue the ongoing efforts of expanding the development of clinical and research activities and educational programs within the service. He truly has been part of the success of the service and his long-standing experience makes him well poised to lead.

New Leadership Roles (continued)

Juliet Barker, MBBS, Attending Physician in the ABMT Service, was named Associate Vice Chair of Faculty Development. In this role, Dr. Barker will assure, enrich, and advise on the mentorship of junior faculty so that they follow a professional path that is commensurate with their skills, interests, and aspirations. She will meet with faculty and serve as a resource to the PAC chair and junior faculty preparing for promotion.

Esperanza B Papadopoulos, MD, was named Associate Vice Chair of Inpatient Operations in the Division of Hematologic Malignancies (DHM). In this role, Dr. Papadopoulos will help optimize inpatient care for DHM patients, working in partnership with the Vice Chair of Quality Safety and Medical Operations and the Division Head of Hematologic Malignancies.

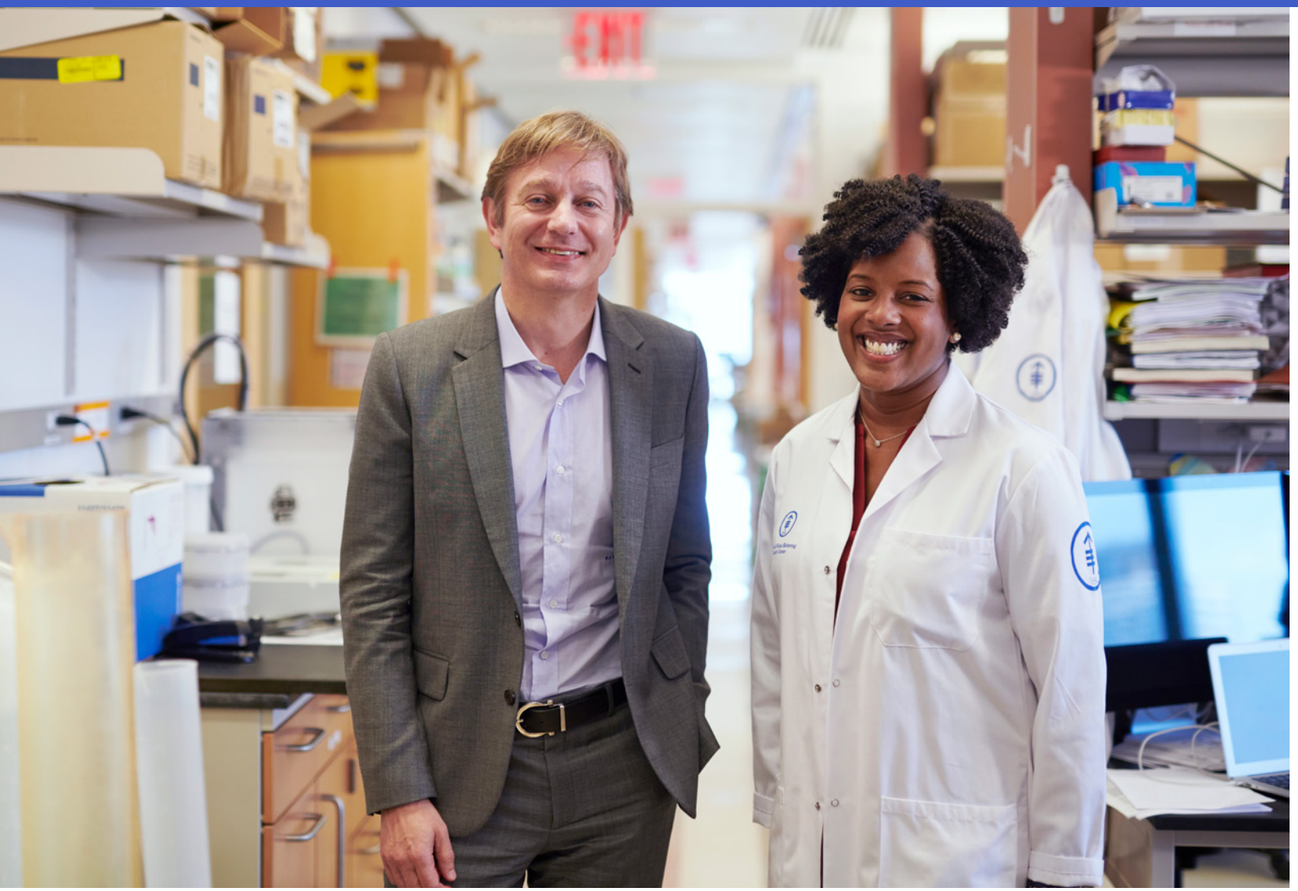
Promotions



Doris Ponce, MD, was promoted to the rank of Associate Member at MSK, Associate Attending Physician in the Adult BMT Service in the Department of Medicine, and Associate Professor of Medicine at Weill Cornell Medical College in January 2020.

Gunjan Shah, MD, was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician in the Adult BMT Service in the Department of Medicine, and Instructor of Medicine at Weill Cornell Medical College in January 2020.

Richard Lin MD, PhD, was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician in the Adult BMT Service in the Department of Medicine, and Assistant Profesor of Medicine at Weill Cornell Medical College in January 2021.



Marcel van den Brink, MD, PhD and Melody Smith, MD, MS

Awards

Marcel van den Brink, MD, PhD, was elected to the Royal Netherlands Academy of Arts and Sciences (Koninklijke Nederlandse Akademie van Wetenschappen, or KNAW) in 2020. Dr. van den Brink was one of 18 new members to be elected to KNAW. Members consist of leading scientists across all disciplines and are chosen for their scientific achievements.

Melody Smith, MD, MS, received a 2020 Internal Diversity Enhancement Award (IDEA) for her project "Investigating Immunophenotype and Metabolism of TCR KO Donor CD19-Targeted Chimeric Antigen Receptor T Cells."

Scott James, MD, PhD, received a K08 award from the National Cancer Institute (NCI) for his project titled "Multi-antigen-specific CAR T cells to treat acute myeloid leukemia."

Katharine Hsu, MD, PhD, received a U01 award from the Fred Hutchinson Cancer Research Center/National Institute of Health (NIH) for her project titled "Hematopoeitic Stem Cell and Cord Blood Transplantation."

David Chung, MD, PhD, received an award from NexImmune for his project titled "A Phase 1/2 Study to Evaluate the Safety and Tolerability of Adoptively Transferred Autologous T cells in Patients with Relapsed Refractory Multiple Myeloma."

Alan Hanash, MD, PhD, received an award from the Parker Institute for Cancer Immunotherapy (PICI) for his project titled "Mining the marrow for anti-tumor immunity after hematopoietic transplantation." He was also elected to the American Society for Clinical Investigation.

Richard O'Reilly, MD, received the Steven A. Greenberg Startup Grant award for his project titled "Phosphopeptides as shared targets for T cell therapy of viral and non-viral lymphomas."

Michel Sadelain, MD, PhD, received an award from the Technology Development Fund for his project titled "Optimizing CAR, TCR and costimulatory combinations for dual-antigen T cell targeting."

Roni Tamari, MD, received an MPN Research Foundation grant award for her project titled "Multicenter Retrospective Analysis to Study the Impact of Molecular Mutations on Transplant Outcomes in Patients with Myelofibrosis" (along with Co-PI, Dr. Raajit Rampal).

The following physicians received the **2020 ASH Scholar Award:**
- Richard Lin, MD, PhD
- Roni Shouval, MD, PhD

The following physicians received the **ABMT Translational Science Research Awards — 2020-2021:**
- Richard Lin, MD, PhD
- Kate Markey, MBBS, PhD
- Jonathan Peled, MD, PhD
- Roni Shouval (SAA), MD, PhD

The following Adult Bone Marrow Transplant Service Faculty Members were recognized on various **2020 Top Doctor Lists:**

Sergio Giralt, MD
Top Doctors New York Metro Area, *New York Magazine*; Top Doctors, *Castle Connolly America's Top Doctors;* Castle Connolly *America's Top Doctors for Cancer*

Ann Jakubowski, MD, PhD
Top Doctors New York Metro Area

Highlighted Clinical Trials and Publications

Highlighted Clinical Trials

A Phase I/II Trial of Ipilimumab after CD34-Selected Allogeneic Stem Cell Transplantation for Patients with Relapsed/Refractory Multiple Myeloma
IRB: 20-329; PI: Gunjan Shah; Co-PI: Sergio Giralt
Allogenic stem cell transplantation, the receipt of stem cells from a matched donor, is used to treat some patients with multiple myeloma that has continued to grow or came back despite other treatments. In this study, researchers want to see if adding the immunotherapy drug ipilimumab after the stem cell transplant can reduce the chance of the cancer from coming back. They believe that ipilimumab may help boost the power of the immune system to fight the cancer.

MCT: Ixazomib Maintenance Following Initial Therapy in Patients with Immunoglobulin Light Chain (AL) Amyloidosis
IRB: 18-069; PI: Heather Landau; Co-PI: Hani Hassoun
A certain class of medications has been shown to be effective in patients with amyloidosis. Ixazomib is a drug that belongs to this class of medications. It has been shown to be effective in patients with amyloidosis whose disease has not responded to or progressed despite other therapies. In this study, researchers want to see if ixazomib can be used as a maintenance treatment to prevent or delay disease relapse in patients with light chain amyloidosis that has responded well to initial therapy.

Highlighted Publications

Shah GL, DeWolf S, Lee YJ, et al. Favorable outcomes of COVID-19 in recipients of hematopoietic cell transplantation. J Clin Invest. 2020;130(12):6656-6667. doi:10.1172/JCI141777

Understanding outcomes and characteristics of the immune system of cellular therapy recipients with SARS-CoV-2 is critical to performing these potentially lifesaving therapies in the COVID-19 era. In this study of recipients of allogeneic (Allo) and autologous (Auto) hematopoietic cell transplant and CD19-directed chimeric antigen receptor T cell (CAR T) therapy, researchers aimed to identify clinical variables associated with COVID-19 severity and assess lymphocyte populations. They report overall favorable clinical outcomes for patients with COVID-19 without active malignancy and provide preliminary insights into the types of white blood cells that are key for the antiviral response and immune reconstitution.

Barker JN, Devlin SM, Naputo KA, et al. High progression-free survival after intermediate intensity double unit cord blood transplantation in adults. Blood Adv. 2020;4(23):6064-6076. doi:10.1182/bloodadvances.2020003371

Cord blood transplantation (CBT) after high-intensity or nonmyeloablative conditioning has limitations. Researchers investigated cyclosporine-A/mycophenolate mofetil–based intermediate-intensity (cyclophosphamide 50 mg/kg, fludarabine 150 mg/m2 , thiotepa 10 mg/kg, total body irradiation 400 cGy) unmanipulated double-unit CBT (dCBT)

Gunjan Shah, MD

with prioritization of unit quality and CD341 cell dose in graft selection. Intermediate intensity dCBT is associated with high progression-free survival. Use of highly HLA mismatched and unmanipulated grafts permits wide application of this therapy, and the low relapse rates support robust graft-versus-leukemia effects even in patients with minimal residual disease.

Sermer D, Batlevi C, Palomba ML, et al. Outcomes in patients with DLBCL treated with commercial CAR T cells compared with alternate therapies. Blood Adv. 2020;4(19):4669-4678. doi:10.1182/bloodadvances.2020002118

In this study of 215 patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL), researchers compared outcomes in patients treated with CAR T cell therapy with a historical population treated with alternate therapies. After adjusting for unfavorable pretreatment disease characteristics, superior overall response rate in the CAR T cohort remained significant; however, differences in progression-free survival (PFS) and overall survival (OS) between cohorts did not. In addition, patients who responded to alternate therapies demonstrated prolonged remissions comparable to those who responded to CAR T therapy. Researchers contend that in select clinical scenarios, alternate therapies may be as efficacious as CAR T therapy; thus, additional study is warranted, ideally with randomized prospective trials.

Landau HJ, Yellapantula V, Diamond BT, et al. Author Correction: Accelerated single cell seeding in relapsed multiple myeloma. Nat Commun. 2021;12(1):591. Published 2021 Jan 20. doi:10.1038/s41467-021-20978-y

This study is the first to investigate by whole genome sequencing the anatomical evolutionary process of multiple myeloma relapse in a systematic fashion. Results show that an evolutionary process promotes multiple myeloma seeding. Using chemotherapy-related mutational signatures as a genomic barcode linked to a known timepoint in each patient's life, researchers demonstrated that relapse can be driven by a single surviving cell that may disseminate throughout the body in a very short time frame. The patterns of relapse were strikingly different from those observed during spontaneous evolution before diagnosis and initial exposure to therapy.

Markey KA, Schluter J, Gomes ALC, et al. The microbe-derived short-chain fatty acids butyrate and propionate are associated with protection from chronic GVHD. Blood. 2020;136(1):130-136. doi:10.1182/blood.2019003369

Researchers examined the potential relationship of the microbiome with chronic GVHD (cGVHD) by analyzing stool and plasma samples collected late after allogeneic hematopoietic stem cell transplantation (allo-HCT) using a case-control study design. They found lower circulating concentrations of the microbe-derived short-chain fatty acids (SCFAs) propionate and butyrate in day 100 plasma samples from patients who developed cGVHD, compared with those who remained free of this complication, in the initial case-control cohort of transplant patients and in a further cross-sectional cohort from an independent transplant center. An additional cross-sectional patient cohort from a third transplant center was analyzed; however, serum (rather than plasma) was available, and the differences in SCFAs observed in the plasma samples were not recapitulated. In sum, findings from the primary case-control cohort and one of two cross-sectional cohorts explored suggest that the gastrointestinal microbiome may exert immunomodulatory effects in allo-HCT patients, at least in part, due to control of systemic concentrations of microbe-derived SCFAs.

Peled JU, Gomes ALC, Devlin SM, et al. Microbiota as Predictor of Mortality in Allogeneic Hematopoietic-Cell Transplantation. N Engl J Med. 2020;382(9):822-834. doi:10.1056/NEJMoa1900623

The microbiota composition of fecal samples obtained from patients who were undergoing allogeneic hematopoietic-cell transplantation (allo-HCT) at four centers was profiled by means of 16S ribosomal RNA gene sequencing. In an observational study, researchers examined associations between microbiota diversity and mortality using Cox proportional-hazards analysis. They observed patterns of microbiota disruption characterized by loss of diversity and domination by single taxa. Higher diversity of intestinal microbiota was associated with a lower risk of death in independent cohorts. Subgroup analyses identified an association between lower intestinal diversity and higher risks of transplantation-related death and death attributable to graft-versus-host disease. Baseline samples obtained before transplantation already showed evidence of microbiome disruption, and lower diversity before transplantation was associated with poor survival. Patterns of microbiota disruption during allo-HCT were similar across transplantation centers and geographic locations; patterns were characterized by loss of diversity and domination by single taxa. Higher diversity of intestinal microbiota at the time of neutrophil engraftment was associated with lower mortality.

Pennisi M, Jain T, Santomasso BD, et al. Comparing CAR T-cell toxicity grading systems: application of the ASTCT grading system and implications for management. Blood Adv. 2020;4(4):676-686. doi:10.1182/bloodadvances.2019000952

Various grading systems are currently used for chimeric antigen receptor (CAR) T cell–related toxicity, cytokine release syndrome (CRS), and immune effector cell–associated neurotoxicity syndrome (ICANS). Researchers compared the recently proposed American Society for Transplantation and Cellular Therapy (ASTCT) grading system to other grading scores in two populations of adults: patients with B-cell acute lymphoblastic leukemia (B-ALL) treated with 1928z CAR T cells, and patients with diffuse large B-cell lymphoma (DLBCL) treated with axicabtagene-ciloleucel (axi-cel) or tisagenlecleucel after FDA approval. Investigation of possible management implications in DLBCL patients showed that different recommendations on tocilizumab and steroids across current guidelines potentially result in either overtreating or delaying treatment. Moreover, because these guidelines are based on single products and different grading systems, they cannot be universally applied. To avoid discrepancies in assessing and managing toxicities of different products, researchers propose that unified grading be used across clinical trials and in practice and that paired management guidelines with product-specific indications be developed.

Montoro J, Ceberio I, Hilden P, et al. Ex Vivo T Cell-Depleted Hematopoietic Stem Cell Transplantation for Adult Patients with Acute Myelogenous Leukemia in First and Second Remission: Long-Term Disease-Free Survival with a Significantly Reduced Risk of Graft-versus-Host Disease. Biol Blood Marrow Transplant. 2020;26(2):323-332. doi:10.1016/j.bbmt.2019.10.003

Large series of patients with acute myelogenous leukemia (AML) after ex vivo T cell-depleted (TCD) allogeneic hematopoietic stem cell transplantation (allo-HSCT) have not been reported previously. Researchers retrospectively analyzed the outcomes of 266 patients with AML who received CD34-selected TCD allo-HSCTs while in first (75%) or second (25%) complete remission (CR1/CR2) at a single institution. The conditioning regimens were all myeloablative, and no additional graft-versus-host disease (GVHD) prophylaxis was given. There were no significant differences in overall survival (OS), disease-free survival (DFS), and relapse rates for patients who underwent transplantation in CR1 and those who did so in CR2. However, patients with high-risk cytogenetics at diagnosis had significantly poorer outcomes. The OS and DFS rates compare favorably with those for unmodified allo-HSCT, but with considerably lower rates of GVHD.

MSK Study Is the First to Link Microbiota to Dynamics of the Human Immune System

Systems biologist Joao Xavier combines experimental and computational approaches to study the microbiota.

In recent years, the microbiota — the community of bacteria and other microorganisms that live on and in the human body — has captured the attention of scientists and the public, in part because it's become easier to study. It has been linked to many aspects of human health.

A multidisciplinary team from Memorial Sloan Kettering has shown for the first time that the gut microbiota directly shapes the makeup of the human immune system. Specifically, their research demonstrated that the concentration of different types of immune cells in the blood changed in relation to the presence of different bacterial strains in the gut. The results of their study, which used more than ten years of data collected from more than 2,000 patients, is being published November 25, 2020, in *Nature*.

"The scientific community had already accepted the idea that the gut microbiota was important for the health of the human immune system, but the data they used to make that assumption came from animal studies," says Sloan Kettering Institute systems biologist Joao Xavier, co-senior author of the paper together with his former postdoc Jonas Schluter, who is now an assistant professor at NYU Langone Health. "At MSK, we have a remarkable opportunity to follow how the composition of the microbiota changes in people being treated for blood cancers," Dr. Xavier adds.

A Unique System for Studying Changes in the Body

The data that were used in the study came from people receiving allogeneic stem cell and bone marrow transplants (BMTs). After strong chemotherapy or radiation therapy is used to destroy cancerous blood cells, the patient's blood-forming system is replaced with stem cells from a donor. For the first few weeks until the donor's blood cells — including the white blood cells that make up the immune system — have established themselves, the patients are extremely vulnerable to infections. To protect them during this time, patients are given antibiotics.

But many of these antibiotics have the unwanted side effect of destroying healthy microbiota that live in the gut, allowing dangerous strains to take over. When the patient's immune system has reconstituted, the antibiotics are discontinued, and the gut microbiota slowly starts to grow back.

"The parallel recoveries of the immune system and the microbiota, both of which are damaged and then restored, gives us a unique opportunity to analyze the associations between these two systems," Dr. Schluter says.

A Years-Long Effort to Find Answers

For more than ten years, members of MSK's BMT Service have regularly collected and analyzed blood and fecal samples from patients throughout the BMT process. The bacterial DNA were processed by the staff at MSK's Lucille Castori Center for Microbes, Inflammation, and Cancer, which played a key role in creating the massive microbiota dataset. "Our study shows that we can learn a lot from stool — biological samples that literally would be flushed down the toilet," Dr. Xavier notes. "The result of collecting them is that we have a unique dataset with thousands of datapoints that we can use to ask questions about the dynamics of this relationship."

This wider effort has been led by Marcel van den Brink, Head of the Division of Hematologic Malignancies, and a team of infectious disease specialists, BMT doctors, and scientists. "For a fair number of patients, we collected daily samples so we could really see what was happening day to day," Dr. van den Brink says. "The changes in the microbiota are rapid and dramatic, and there is almost no other setting in which you would be able to see them."

Previous research using samples collected from this work has looked at how the gut microbiota affects patients' health during the BMT process. A study published in February 2020 reported that having a greater diversity of species in the intestinal microbiota is associated with a lower risk of death after a BMT. It also found that having a lower diversity of microbiota before transplant resulted in a higher incidence of graft-versus-host disease, a potentially fatal complication in which the donor immune cells attack healthy tissue.

New Clues about a Complicated Relationship

The databank that the MSK team created contains details about the types of microbes that live in the patients' guts at various times. The computational team, including Drs. Schluter and Xavier, then used machine learning algorithms to mine electronic health records for meaningful data. The data from the health records included the types of immune cells present in the blood, information about the medications that patients were given, and the side effects patients experienced. "This research could eventually suggest ways to make BMTs safer by more closely regulating the microbiota," Dr. van den Brink says.

Analyzing this much data was a huge undertaking. Dr. Schluter, who at the time was a postdoctoral fellow in Dr. Xavier's lab, developed new statistical techniques for this. "Because experiments with people are often impossible, we are left with what we can observe," Dr. Schluter says. "But because we have so many data collected over a period of time when the immune system of patients as well as the microbiome shift dramatically, we can start to see patterns. This gives us a good start toward understanding the forces that the microbiota exerts on the rebuilding of the immune system."

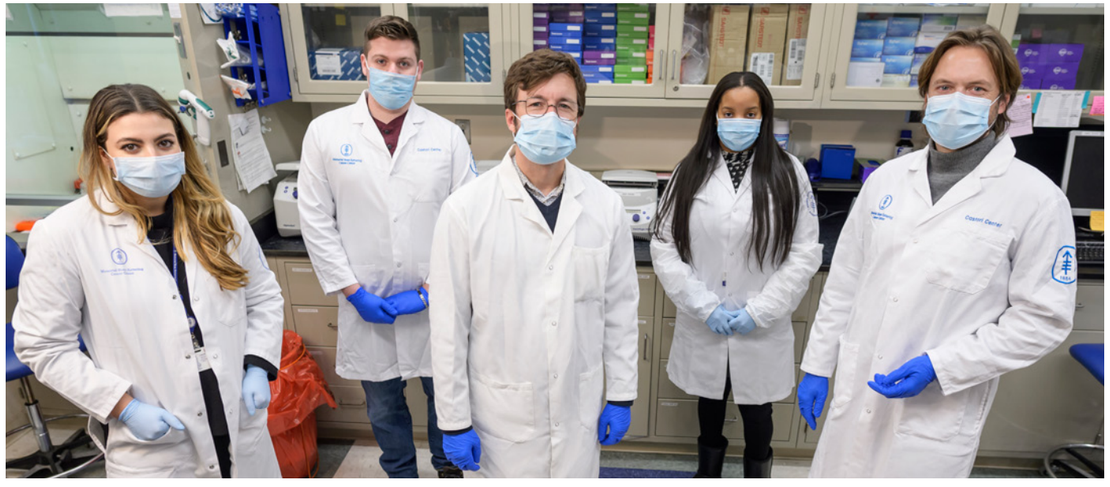
"The purpose of this study was not to say whether certain kinds of microbes are 'good' or 'bad' for the immune system," Dr. Xavier explains, adding that this will be a focus of future research. "It's a complicated relationship. The subtypes of immune cells we would want to increase or decrease vary from day to day, depending on what else is going on in the body. What's important is that now we have a way to study this complex ecosystem."

The researchers say they also plan to apply their data to studying the immune system in patients receiving other cancer treatments.

This research was funded by National Institutes of Health (NIH) grants U01 AI124275 and R01 AI137269. It was also supported by NIH grant P30 CA008748, the Parker Institute for Cancer Immunotherapy at Memorial Sloan Kettering Cancer Center, the Sawiris Foundation, The Society of Memorial Sloan Kettering Cancer Center, an MSK Cancer Systems Immunology Pilot Grant, the Empire Clinical Research Investigator Program, the Burroughs Wellcome Fund Postdoctoral Enrichment Program, a Damon Runyon Physician-Scientist Award, and the Robert Wood Johnson Foundation.

Dr. van den Brink has provided paid consulting or other compensated services for DKMS, Duke-NUS Medical School, Juno Therapeutics, King Faisal Specialist Hospital & Research Centre, Technical University of Denmark, The Meredith A. Cowden Foundation, and Xinqiao Hospital. He has also provided uncompensated services for CRYOSTEM, European Federation for Immunogenetics, European Society for Blood and Marrow Transplantation, the Falk Foundation e.V., Fred Hutchinson Cancer Research Center, the French National Research Agency, Lille University Hospital (Chu De Lille), Magenta, Ospedale Pediatrico Bambino Gesù, the Parker Institute for Cancer Immunotherapy, the Korean Society of Blood and Marrow Transplantation, and the University of Copenhagen. He has intellectual property rights, ownership, and equity interests in Seres Therapeutics.

www.mskcc.org/news/msk-study-first-link-microbiota-dynamics-human-immune-system



Researchers Emily Fontana, Luigi Amoretti, Joao Xavier, Roberta Wright, and Jonas Schluter in the lab.

INTERVIEW

Miguel Perales
Chief, Adult BMT Service

MSK Leads Research Examining COVID-19 in People Receiving BMTs and CAR T Therapy

In March and April of 2020, New York City was the epicenter of the COVID-19 pandemic in the United States. Because of the large number of stem cell and bone marrow transplants (BMTs) performed at Memorial Sloan Kettering, MSK ended up treating among the largest number of transplant patients infected with COVID-19 of any hospital.

At the same time, due to lack of space in the intensive care unit, MSK's BMT team had to put a number of scheduled transplants on hold. Although this situation resulted in extensive challenges for both staff and patients, it also led to a number of important studies that shed light on the relationship between BMTs and COVID-19 infection.

"MSK was one of the first hospitals in the United States to face this situation," says Miguel-Angel Perales, Chief of the Adult Bone Marrow Transplant Service. "We made the decision very early on to collect data on everything that was going on so that we could tell the story of what happened."

Recovery Rates for COVID-19 in Immunocompromised Patients

Although BMTs were delayed for most patients, MSK had a number of patients who had recently received transplants and were recovering when the pandemic reached New York City. There were also patients who were recovering from treatment with CAR T therapies, which have similar risks when it comes to infections.

In December 2020, Dr. Perales — together with a number of colleagues, including hematologic oncologist Gunjan Shah and hematology oncology fellow Susan DeWolf — published a study in the *Journal of Clinical Investigation* that looked at outcomes for 77 patients treated at MSK who became infected with COVID-19 while recovering from a BMT or CAR T treatment between March and May 2020.

Of that group, they found that about half were never sick enough to be admitted and could be monitored as outpatients. Of those who were sick enough to be admitted, the risk of dying was 20%. The patients who were at highest risk were those whose cancer had recurred and who had active disease. "Some of these patients had incurable leukemia," Dr. Perales explains, "and for them the mortality from COVID-19 was high."

But he adds that among those who were in remission, many did quite well, even if they had other risk factors, like being older. "The presence or absence of active disease was the main factor that determined how well these patients did if they became infected," he says.

Long Infectious Periods in the Immunocompromised

Another study from MSK, published in the *New England Journal of Medicine* in December 2020, looked at how long patients with profoundly compromised immune systems due to recent BMT or CAR T treatments were able to shed live virus if they become infected with COVID-19. The researchers found that, despite general guidelines that most people who are infected with SARS- CoV-2 and other respiratory viruses shed virus for 10 to 20 days, those who are immunocompromised can remain infectious for much longer — some up to two months.

"This work is important because it has implications for transmission of the virus to other patients as well as staff," Dr. Perales says. "This paper received a lot of interest in the medical community, especially as it is now recognized that variant strains of the virus are more likely to develop during these prolonged infections in immunocompromised patients. It demonstrates our responsibility to share our findings with the wider public."

MSK Chief Medical Epidemiologist Mini Kamboj and Esther Babady, Director of the Clinical Microbiology Service, were the senior authors of that study, to which Dr. Perales and other members of the BMT Service also contributed.

> "The presence or absence of active disease was the main factor that determined how well these patients did if they became infected."
>
> Miguel Perales
> Chief, Adult BMT Service

Leading the Way for Broader Reseach

Dr. Perales and his colleagues have many additional studies that they're writing or that are now under review. One, which looks at the impact of delaying treatment due to pandemic concerns, was published in March in *Transplantation and Cellular Therapy* by hematology oncology fellow Mariam Nawas and hematologist oncologist Roni Tamari. It found that patients who were scheduled for an allogeneic BMT (using stem cells from a donor) or CAR T therapy should not wait, but for those who were scheduled for an autologous BMT (using their own cells), many fared well when they waited and finally did receive treatment.

Another study found that BMTs and CAR T therapy were safe in people who had been infected with COVID-19 but had recovered from the infection. "We have one of the largest groups of patients who got transplants or cell therapy after having COVID-19," Dr. Perales notes.

Throughout the pandemic, he and his colleagues at MSK have made efforts to share their findings with other clinicians and researchers so that other hospitals can learn from MSK's experiences at the height of the pandemic.

In addition to leading the BMT Service at MSK, Dr. Perales also serves in advisory roles for many BMT-related organizations, including the National Marrow Donor Program and the Center for International Blood and Marrow Transplant Research. He recently was elected Vice President of the American Society of Transplantation and Cellular Therapy. These groups remained active throughout the pandemic and have released a number of guidelines for treating patients with blood cancers during the pandemic.

Bone Marrow Transplant Survivors Unite Online to Celebrate

Medical oncologist Oscar Lahoud (left) spoke via Zoom with former bone marrow transplant patient Dan Roeper (right) as part of MSK's online celebration for transplant "thrivers."

The first online version of MSK's annual bone marrow transplant survivors celebration united "thrivers" and caregivers scattered far and wide with their doctors, nurses, and other medical staff.

"We all live in incredible times." Those were the words of Sergio Giralt, a bone marrow transplant (BMT) expert at Memorial Sloan Kettering. On October 5, he opened MSK's 25th annual celebration for transplant survivors by explaining that the rise of COVID-19 had prompted long discussions among MSK staff about whether the event should be held this year. "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."

This year's BMT Thrivers Celebration, for people welcoming their return to health after a transplant, was the first to be held remotely. A Zoom session enabled more than 200 patients scattered far and wide, along with family, friends, donors, and caregivers, to convene with doctors, nurses, and other staff from the Bone Marrow Transplant Service.

"Bone marrow transplant patients are the world experts at social distancing," says Miguel-Angel Perales, who recently became Chief of the Bone Marrow Transplant Service. "They know what it is like to wear a mask and be careful."

As part of the online program, two people who received transplants were interviewed by their doctors in prerecorded presentations. The patients recounted their difficult and tumultuous journeys while praising the high level of medical care and emotional support provided by their doctors, nurses, and support staff members.

Dan Roeper received a transplant for the treatment of primary central nervous system lymphoma in late 2017. He said medical oncologist Oscar Lahoud gave him much-needed reassurance on their first meeting. "You looked in my eyes and said, 'It's going to be okay. We can do this.' I can't say enough about how great you guys are at being human. You're great scientists, great doctors, but your humanity — the way you treat a patient and you care for the inner person — is unbelievable." Berenice Martinez received a transplant at age 14 after a diagnosis of acute myeloid leukemia. She relapsed several years later and needed a second transplant, making her a "double-thriver" in the words of pediatric oncologist Susan Prockop. Dr. Prockop said Ms. Martinez inspired the entire medical team with her resolve and maturity. Ms. Martinez, now a student at New York University, said that the devastation she felt upon her second diagnosis was eased a bit by knowing she was returning to the same doctors who had guided her through the entire journey since her first year in high school. "I knew a lot of the doctors and nurses there, how they took care of me, and how they would take care of me in the future to make me get better."

> **"Bone marrow transplant patients are the world experts at social distancing. They know what it is like to wear a mask and be careful."**
>
> Miguel Perales
> Chief, Adult BMT Service

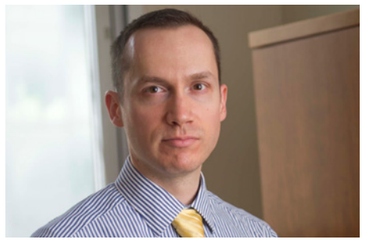
Dr. Giralt noted that the celebration has grown so large over the years as more survivors return after successful treatment that an online component may become permanent. "We can't even have everyone in one room anymore, but a hybrid virtual and in-person event will be great for all of us." At the end of the program, Dr. Giralt asked that everyone be briefly unmuted so that all participants could "scream, shout, and applaud" to encourage the current transplant patients in Memorial Hospital who were watching the event.

The event concluded with the opportunity for virtual attendees to split off into smaller Zoom breakout rooms to connect with fellow thrivers based on similar "thrivership anniversaries." Participants were encouraged to share memories, recount what powered them through treatment, and give advice to caregivers supporting loved ones going through their own BMT process.

www.mskcc.org/news/bone-marrow-transplant-survivors-unite-online-celebrate

Appointments, Promotions, and Awards

Promotions



Simon Mantha, MD, MPH, was promoted to the rank of Clinical Member at MSK, Attending Physician in the Myeloma Service in the Department of Medicine, and Professor of Medicine at Weill Cornell Medical College in January 2020.

Rekha Parameswaran, MD, was promoted to the rank of Clinical Member at MSK, Attending Physician in the Myeloma Service in the Department of Medicine, and Professor of Medicine at Weill Cornell Medical College in February 2020.

Awards

Jodi Mones, MD, received the 2020 Hematology Teaching Award

The following Hematology Service Faculty Members were recognized on various **2020 Top Doctor Lists:**

Rekha Parameswaran, MD
NY Best Doctors list, *New York Magazine*: Top Doctors, Top Doctors New York Metro Area, Exceptional Women In Medicine

Gerald Soff, MD
New York Magazine: Top Doctors, Castle Connolly America's Top Doctors, Top Doctors New York Metro Area

Highlighted Clinical Trials and Publications

Highlighted Clinical Trials

Romiplostim for Prevention of Severe Chemotherapy Induced Thrombocytopenia in Lymphoma Patients - Phase II Study
IRB: 20-492; PI: Gerald Soff; Co-PI: Erel Joffe

The purpose of this study is to see if the study drug, romiplostim, helps low platelet count caused by standard chemotherapy treatment for lymphoma. This study will also look at whether romiplostim can prevent the need for chemotherapy dose delays, chemotherapy dose reductions, and platelet transfusions. In addition, we will determine how safe it is to give romiplostim to people with lymphoma who have low platelet count from chemotherapy.

An Open-Label, Pilot Study of Romiplostim for Conditioning Regimen-Related Thrombocytopenia after High-Dose Therapy and Autologous Hematopoietic Cell Transplantation
IRB: 20-180; PI: Gerald Soff; Co-PI: Sergio Giralt and Michael Scordo

Platelets are blood cells that help the body to form clots to stop bleeding. Chemotherapy and autologous hematopoietic cell transplantation (healthy blood stem cells from a patient's own body used to replace diseased or damaged bone marrow) can lower platelet counts, requiring patients to receive platelet transfusions. Romiplostim is a medication designed to increase platelet production. In this study, researchers are assessing romiplostim to see if it can improve the recovery of platelet counts in patients receiving chemotherapy for an autologous stem cell transplant for a blood cancer and reduce the need for platelet transfusions.

Highlighted Publications

Dunbar A, Bolton KL, Devlin SM, et al. Genomic Profiling Identifies Somatic Mutations Predicting Thromboembolic Risk in Patients with Solid Tumors [published online ahead of print, 2020 Dec 3]. Blood. 2020; blood.2020007488. doi:10.1182/blood.2020007488

The purpose of this study was to assess potential associations of molecular signatures with cancer-associated venous thromboembolism (CAT), including tumor-specific mutations and the presence of clonal hematopoiesis using data from the MSK-IMPACT™ platform. Several tumor-specific mutations were associated with a significantly increased risk of CAT independent of tumor type. One tumor-specific mutation was associated with a decreased risk of CAT. The presence of clonal hematopoiesis was not associated with an increased venous thromboembolism (VTE) rate. Several tumor mutations were associated with an increased risk of VTE in solid tumor patients. This is the first large-scale analysis to elucidate tumor-specific genomic events associated with CAT. Further analysis is needed to validate these findings and identify additional molecular signatures unique to individual tumor types.

Cy Wilkins, MD

Bauersachs R, Khorana AA, Lee AYY, Soff G. Cancer-associated venous thromboembolism: Treatment and prevention with rivaroxaban. Res Pract Thromb Haemost. 2020;4(4):532-549. Published 2020 Apr 4. doi:10.1002/rth2.12327

Cancer-associated venous thromboembolism (VTE) is a frequent, potentially life-threatening event that complicates cancer management. This review summarizes the evidence base for rivaroxaban use in cancer-associated thrombosis (CAT), the patient profile potentially most suited to direct oral anticoagulants (DOAC) use, and ongoing controversies under investigation. Researchers also describe ongoing studies from the CALLISTO (Cancer Associated thrombosis—exploring solutions for patients through Treatment and Prevention with RivarOxaban) program, which comprises several randomized clinical trials and real-world evidence studies.

Nawar T, Morjaria S, Kaltsas A, et al. Granulocyte-colony stimulating factor in COVID-19: Is it stimulating more than just the bone marrow?. Am J Hematol. 2020;95(8):E210-E213. doi:10.1002/ajh.25870

Granulocyte-colony stimulating factor (GCSF) is routinely administered in cancer patients as prophylaxis or treatment of neutropenia, a low number of a type of white blood cell (WBC) called neutrophils. We describe three patients who received GCSF and developed severe disease from COVID-19 within 72 hours. All patients were admitted to the hospital in late March 2020 for symptomatic COVID-19 infection, proven by qualitative RNA PCR assay. All three patients had a severe infection with SARS-CoV-2 and received hydroxychloroquine 400mg twice a day for the first day, followed by 200mg twice a day for four days, for a total five-day course in accordance with hospital criteria that were in place at that time. To our knowledge, this is the first report describing the course of COVID-19 infection in selected cancer patients who received GCSF for neutropenic fever in the United States. All three patients had rising neutrophils 24 hours after GCSF administration. At 72 hours after administration of GCSF, all three patients had even higher levels of neutrophils and suffered respiratory decline.

INTERVIEW

Rekha Parameswaran

Hematologist

Hematology Service Leads the Way in Telemedicine — during COVID-19 Pandemic and Beyond

When the COVID-19 pandemic reached New York City in March 2020 and everyone was urged to stay at home, certain services within Memorial Sloan Kettering were more equipped to pivot to telemedicine than others. One service that adapted quickly was the Hematology Service within the Division of Hematologic Malignancies.

"Everyone at MSK committed to telemedicine right away, but our service in particular was able to switch very quickly," says hematologist Rekha Parameswaran, who helped lead the efforts in this transition for the five-physician hematology team. "The coordinators in our offices were making sure that everyone got the blood work they needed, and were tracking down the results, to ensure that our patients were getting the same care that they had in the past."

MSK's Hematology Service specializes in the treatment of benign hematologic disorders, especially conditions that may result from cancer and its treatment. This includes anemia, excess bleeding, and potentially dangerous blood clots. Because consultation with the service doesn't require a physical exam and is mainly focused on reviewing blood work and determining a patient's symptoms and how they are feeling, MSK's hematologists were confident they would be able to give patients the same high level of care they had always received.

Caring for Patients during a 'Scary Time'

Still, the move to telemedicine was not without challenges. Although many people are comfortable using devices such as smartphones, tablets, and computers for video chats, not everyone is. Some, especially older adults, may not even have access to these devices.

"One of my patients, an elderly woman in the Bronx, only has a landline and a flip phone. My telemedicine visit with her was a phone call," Dr. Parameswaran notes. "We're used to seeing our patients face to face, sitting down with them and holding their hands, so I didn't know how telemedicine would be received. But we found these phone visits were so valuable, and many went on even longer than a regular appointment would have as our patients shared details of what was happening in their lives."

In addition to talking to patients about their symptoms and medications, the hematology team was able to provide stability and a caring voice. They talked to patients about how they were coping emotionally with isolation and ensured that they were getting food delivered and having other daily needs met.

"Our patients knew we were there for them during this scary time and that we were committed to making sure they got quality care," Dr. Parameswaran says.

She adds that MSK's regional sites played an important role in offering hematology care, by allowing patients to get their blood work done closer to home during a time when many people avoided traveling into Manhattan.

Reaching Beyond MSK to Play a National Role

Doctors and patients faced challenges with telemedicine beyond the limitations of technology. Traditionally, reimbursements from Medicare and Medicaid have treated telemedicine, whether by phone or video, differently from in-person visits. These limitations were lifted during the pandemic, but many healthcare provides want to make these changes permanent. This expansion would provide long-term benefits for patients, especially those who have rare diseases or who would otherwise have to travel great distances to meet with specialists in person.

In September, Dr. Parameswaran participated in a virtual "Hill Day" sponsored by the American Society of Hematology (ASH). She and colleagues met with a staffer from the office of New York Senator Kirsten Gillibrand to discuss the value of virtual care and the importance of continuing to offer reimbursement for these appointments, even when they are telephone visits. "I shared the story of my patient in the Bronx," Dr. Parameswaran says. "Audio-only appointments should have permanent coverage so that we can continue to offer care and make sure that no one gets left behind."

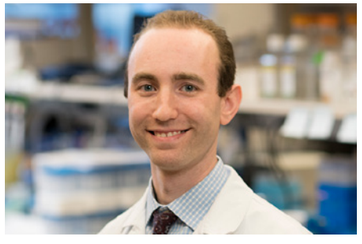
This was not Dr. Parameswaran's first time lobbying as a member of ASH. She had previously participated in ASH's Advocacy Leadership Institute, which provides opportunities for hematologists to learn more about advocacy, health policy, and the legislative process. In 2019, she visited in person with congressional representatives and members of their staffs in Washington, DC.

"At MSK, we're always striving to do better," she concludes. "Through these activities, I've been able to not only make a difference for patients being treated here but also far beyond."

Appointments, Promotions, and Awards

Appointments

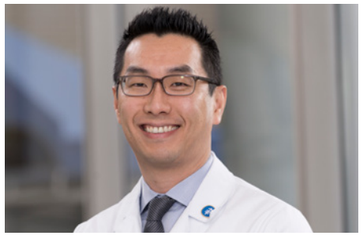
In August 2020, **Lindsey Roeker, MD,** joined the Leukemia Service as an Assistant Attending Physician. Dr. Roeker received her MD from the Mayo Medical School and completed a residency in internal medicine at Brigham and Women's Hospital in Boston, Massachusetts. Dr. Roeker also did her fellowship at MSK. As a clinical investigator, Dr. Roeker will care for patients with chronic lymphocytic leukemia (CLL) and other lymphoproliferative disorders.



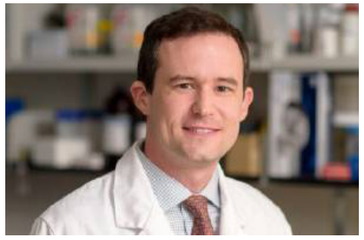
In May 2020, **Scott Millman, MD, PhD**, joined the Leukemia Service as an Instructor. Dr. Millman received his PhD in Molecular Oncology and Immunology at New York University School of Medicine, where he also received his medical degree. He served his residency at Massachusetts General Hospital and completed his fellowship at MSK. As a lab investigator, Dr. Millman focuses on developing innovative therapeutic strategies for patients with acute myeloid leukemia (AML).

In May 2020, **David Knorr, MD, PhD,** joined the Leukemia Service as an Assistant Attending Physician. Dr. Knorr received his undergraduate degree from the University of North Dakota and completed his MD and PhD degrees from the University of Minnesota. He served his residency at NewYork-Presbyterian/ Weill Cornell Medical Center and completed his fellowship at MSK. As a lab investigator, Dr. Knorr focuses on immunotherapy for leukemias and other hematologic malignancies.

Promotions



Sheng F. Cai, MD, PhD, was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician in the Leukemia Service in the Department of Medicine, and Instructor in Medicine at Weill Cornell Medical College in January 2020.



Andrew Dunbar, MD, was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician in the Leukemia Service in the Department of Medicine, and Instructor of Medicine at Weill Cornell Medical College in January 2020.

David A. Scheinberg, MD, PhD

Awards

Anthony Daniyan, MD
- Received an award from the Center for Experimental Therapeutics for his project titled "The Development of a Novel AML-directed CAR T Cell Capable of Bystander Tumor Killing"
- 2020 Internal Diversity Enhancement Award (IDEA) winner

David A. Scheinberg, MD, PhD, received the National Cancer Institute's (NCI) 2020 Outstanding Investigator Award (OIA). In 2020, he also received:
- 1 R01 grant award from the NCI
- 1 R35 grant award from the NCI
- 1 research grant award from Emerson Collective
- 1 Steven A. Greenberg Startup Grant

Michel Sadelain, MD, PhD
- Received the 49th Fondation ARC Léopold Griffuel Award for Translational and Clinical Research, which recognizes internationally renowned researchers whose work has led to a major breakthrough in the study of cancer.

Sheng Cai, MD, PhD
- Received the Edward P. Evans Career Development award for "Identifying therapeutic vulnerabilities in high-risk EVI1-positive myelodysplastic syndromes"

Mark Geyer, MD
- Received an award from the Comedy vs Cancer Grant for his project titled "Iomab-ACT: A Phase I/II Study of Iomab-B Followed by CD19-Targeted CAR T-Cell Therapy for Patients with Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia or Diffuse Large B-Cell Lymphoma"

Jae Park, MD
- Received an award from the Center for Experimental Therapeutics for his project titled "Novel IL-18 Secreting Chimeric Antigen Receptor (CAR) T-Cell Therapy for The Treatment of Acute Lymphoblastic Leukemia"

Omar Abdel-Wahab, MD, received the following awards in 2020:
- Award from the Fred Hutchinson Cancer Research Center for his project "Genetic and molecular basis for SRSF2 mutations in myelodysplasia"
- R01 award from the NCI for his project "Interrogating the minor spliceosome to understand and treat leukemia"
- R01 award from the NCI for his project "Targeting an RNA Binding Protein Network in Acute Myeloid Leukemia"
- Award from the Edward P. Evans Foundation for his project "Elucidating Critical Targets, Transcripts, and Collaborating Events in Spliceosomal-Mutant MDS"
- Award from the Congressionally Directed Medical Research Programs for his project "Identifying Novel Therapeutic Targets and Combination Strategies for Patients with BPDCN"

Virginia Klimek, MD
- Received an award from the New York University School of Medicine/National Institutes of Health for her project

titled “Clinical and Molecular Heterogeneity in the Mylodysplastic Syndromes”

David Knorr, MD, PhD
- Received an award from The Rockefeller University/National Cancer Institute for his project titled “Fc-enhanced CD40 agonist antibodies for immune modulation of the tumor microenvironment”

Ross Levine, MD, received the following awards in 2020:
- Award from AbbVie Inc. for his project titled “SRA-To characterize the therapeutic efficacy and biologic impact of dual therapy with ruxolitinib and ABBV-744 (BET inhibitor), as well as single agent ABBV-744, in a model of MPN/MF”
- Award from the Jackson Laboratory/National Institute on Aging for his project titled “Discovery of Aging-Associated Mechanisms Causing Expansion and Progression of Clonal Hematopoiesis of Indeterminant Potential (CHIP)”
- Award from the Cure Breast Cancer Foundation for his project titled “SRA-Methods of Treating and Prognosing Nonhematopoietic Malignant Tumors”
- 2019-20 Excellence in Mentoring Award winner, announced by the Junior Faculty Council (JFC). Dr. Levine's unwavering commitment to early career physicians and scientists received particular recognition.

Renier Brentjens, MD, PhD
- Received the Steven A. Greenberg Startup Grant award for his project titled “IsoPlexis, IsoLight”

Charles Sawyers, MD
- Received an award from Congressionally Directed Medical Research Programs for his project titled “Defining Transcription Factor Networks Governing Androgen Receptor-Null Prostate Cancer”

Raajit Rampal, MD, PhD, received the following awards in 2020:
- Award from the Constellation Pharmaceuticals for his project titled “SRA-Therapeutic Efficacy of CPI-482 in Myeloproliferative Neoplasms-Myelofibrosis (MPN-MF) and Secondary AML (sAML)”
- MPN Research Foundation grant award for his project titled “Multicenter Retrospective Analysis to Study the Impact of Molecular Mutations on Transplant Outcomes in Patients with Myelofibrosis” (along with Co-PI Dr. Roni Tamari)

The following Leukemia Service Faculty Members were recognized on various **2020 Top Doctor Lists:**

Martin Tallman, MD
New York Magazine: Top Doctors, Castle Connolly America's Top Doctors, Top Doctors New York Metro Area, Castle Connolly America's Top Doctors for Cancer

Renier Brentjens, MD, PhD
Castle Connolly America's Top Doctors, Top Doctors New York Metro Area, Castle Connolly America's Top Doctors for Cancer

Ellin Berman, MD
Top Doctors New York Metro Area, Exceptional Women In Medicine

Highlighted Clinical Trials and Publications

Highlighted Clinical Trials

A Phase I/II Study of Oral LOXO-305 in Patients with Previously Treated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) or Non-Hodgkin Lymphoma (NHL)
IRB: 19-077; PI: Anthony Mato, Co-PI: Lindsey Roeker and Andrew Zelenetz

The purpose of this study is to determine the highest dose of the investigational drug LOXO-305 that can be used safely in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) or non-Hodgkin lymphoma (NHL) that continues to grow despite treatment and to determine its effectiveness in these patients.

A Phase I/II, Open-label, Dose-Escalation and Dose-Expansion Cohort Study of SNDX-5613 in Patients with Relapsed/Refractory Leukemias, Including Those Harboring an MLL/KMT2A Gene Rearrangement or Nucleophosmin 1 (NPM1) Mutation
IRB: 19-448; PI: Eytan Stein; Co-PI: Martin Tallman

The purpose of this study is to find the highest dose of the investigational drug SNDX-5613 that can be given safely in patients with acute leukemia that has come back or continues to grow despite treatment. SNDX-5613 stops a protein called menin from attaching to proteins called “mixed-lineage leukemia 1” (MLL1). Interactions between menin and MLL1 proteins cause leukemia to get worse. The ability of SNDX-5613 to stop these interactions may shrink or stabilize a patient’s cancer.

A Phase I/II Study of CPI-0610, a Small Molecule Inhibitor of BET Proteins: Phase 1 (Dose Escalation of CPI-0610 in Patients with Hematological Malignancies) and Phase 2 (Dose Expansion of CPI- 0610 with and without Ruxolitinib in Patients with Myelofibrosis)
IRB: 19-188; PI: Raajit Rampal; Co-PI: Ellin Berman and Michael Mauro

Myelofibrosis (MF) is a bone marrow disorder that disrupts the normal production of blood cells. The purpose of this study is to assess the safety and effectiveness of the investigational drug CPI-0610 given alone or in combination with ruxolitinib (a drug called a JAK inhibitor) in patients with MF.

Highlighted Publications

Taylor J, Donoghue MT, Ho C, et al. Germ cell tumors and associated hematologic malignancies evolve from a common shared precursor. J Clin Invest. 2020;130(12):6668-6676. doi:10.1172/JCI139682

One in every 17 patients with primary mediastinal nonseminomatous germ cell tumor (GCT) develop an incurable hematologic malignancy. Researchers discovered that GCTs and hematologic malignancies developing in such individuals evolved from a common shared precursor, nearly all of which harbored allelically imbalanced p53 and/or RAS pathway mutations. Hematologic malignancies arising in this setting genetically resembled mediastinal GCTs rather than de novo myeloid neoplasms. Our findings argue that this scenario represents a unique clinical syndrome initiated by an ancestral precursor that gives rise to the parallel evolution of GCTs and blood cancers in these patients.

Stein EM, DiNardo CD, Fathi AT, et al. Ivosidenib or enasidenib combined with intensive chemotherapy in patients with newly diagnosed AML: a phase 1 study [published online ahead of print, 2020 Oct 5]. Blood. 2020;blood.2020007233. doi:10.1182/blood.2020007233

Ivosidenib (AG-120) and enasidenib (AG-221) are targeted, oral inhibitors of the mutant isocitrate dehydrogenase (mIDH) 1 and 2 enzymes, respectively. Given their effectiveness as single agents in mIDH1/2 relapsed or refractory acute myeloid leukemia (AML), this phase I study evaluated the safety and efficacy of ivosidenib or enasidenib combined with intensive chemotherapy in patients with newly diagnosed mIDH1/2 AML. Ivosidenib 500 mg once daily and enasidenib 100 mg once daily were well tolerated in this setting, with safety profiles generally consistent with those of induction and consolidation chemotherapy alone.

Mato AR, Roeker LE, Lamanna N, et al. Outcomes of COVID-19 in patients with CLL: a multicenter international experience. Blood. 2020;136(10):1134-1143. doi:10.1182/blood.2020006965

Given advanced age, comorbidities, and immune dysfunction, chronic lymphocytic leukemia (CLL) patients may be at particularly high risk of infection and poor outcomes related to coronavirus disease 2019 (COVID-19). Robust analysis of outcomes for CLL patients, particularly examining effects of baseline characteristics and CLL-directed therapy, is critical to optimally manage CLL patients through this evolving pandemic. CLL patients diagnosed with symptomatic COVID-19 across 43 international centers were included. CLL-directed treatment with BTKi’s at COVID-19 diagnosis did not impact survival, though the BTKi was held during the COVID-19 course for most patients. These data suggest that the subgroup of CLL patients admitted with COVID-19, regardless of disease phase or treatment status, are at high risk of death.

Why Do Certain Chemotherapies Increase the Likelihood of Blood Cancer?

Caption: Researchers Ahmet Zehir (left) and Elli Papaemmanuil are studying clonal hematopoiesis, an age-related blood condition that increases the risk of blood cancer.

In recent years, improvements in cancer therapy have led to a significant increase in cancer survivorship. Experts estimate that by 2022, the United States will have 18 million cancer survivors, but a subset of those survivors will have long-term health problems to be addressed.

One rare complication of cancer treatment is the development of a secondary blood cancer — therapy-related acute myeloid leukemia or myelodysplastic syndrome. These blood cancers are very aggressive and do not respond well to treatment. Historically, doctors thought that cancer treatments such as chemotherapy and radiation caused an accumulation of mutations in the blood that led to these therapy-related cancers.

In recent years, however, researchers have found that these mutations in the blood can also occur spontaneously with increasing age. This phenomenon is called clonal hematopoiesis (CH), and it's found in 10 to 20% of all people over age 70. The presence of CH increases the risk of developing a blood cancer. Using data from MSK-IMPACT™, Memorial Sloan Kettering's clinical genomic sequencing test, researchers have shown that CH is also frequent in cancer patients.

In a study published in *Nature Genetics* on October 26, 2020, MSK investigators sought to understand the relationship between CH in cancer patients and the risk of later developing a treatment-related blood cancer. The study included data from 24,000 people treated at MSK. The researchers found CH in about one-third of them.

"Because many people treated at MSK have genetic testing done using MSK-IMPACT, we have this amazing resource that allows us to study CH in cancer patients at a scope that nobody else has been able to do," says physician-scientist Kelly Bolton, lead author of the study.

Decoding Genetic Changes Specific to Cancer Treatment

Focusing on a subset of patients on whom they had more detailed data, the investigators observed increased rates of CH in people who had already received treatment. They made specific connections between cancer therapies such as radiation therapy and particular chemotherapies — for example certain platinum drugs or agents called topoisomerase II inhibitors — and the presence of CH.

Unlike the CH changes found in the general population, the team found that CH mutations after cancer treatment occur most frequently in the genes whose protein products protect the genome from damage. One of these genes is TP53, which is frequently referred to as "the guardian of the genome."

The work was supported by the Precision Interception and Prevention (PIP) program at MSK, a multidisciplinary research program focused on identifying people who have the highest risk for developing cancer and improving methods for screening, early detection, and risk assessment.

The authors embarked on a three-year study to understand the relationship between CH and cancer therapy. For this part of the research, more than 500 people were screened for CH when they first came to MSK and then at a later point during their treatment. One finding from the study was that people with pre-existing CH whose blood carried mutations related to DNA damage repair such as TP53, were more likely to have those mutations grow after receiving cancer therapies, when compared to people who did not receive treatment.

"This finding provides a direct link between mutation type, specific therapies, and how these cells progress towards becoming a blood cancer," says Elli Papaemmanuil of MSK's Center for Computational Oncology, one of the two senior authors of the study. "Our hope is that this research will help us to understand the implications of having CH and to begin to develop models that predict who with CH is at higher risk for developing a blood cancer."

For a subset of patients with CH who developed therapy-related blood cancers, the researchers showed that blood cells acquired further mutations with time and progressed to leukemia. "We are now routinely screening our patients for the presence of CH mutations," adds computational biologist Ahmet Zehir, Director of Clinical Bioinformatics and the study's co-senior author. "The ability to introduce real-time CH screening for our patient population has allowed us to establish a clinic dedicated to caring for cancer patients with CH. As we continue to study more patients in the clinic, we expect to learn more about how to use these findings to find ways to detect treatment-related blood cancers early when they may be more treatable."

Applying Findings to Future Treatments

In the future, this research may help to guide therapy by indicating whether some chemotherapy drugs are more appropriate than others in people with CH. People who are at a high risk of developing a treatment-related leukemia also may benefit from a different treatment schedule. "We hope that this research will allow us to ultimately map which CH mutations a person has and use that information to tailor their primary care and also mitigate the long-term risk of developing blood cancer," Dr. Papaemmanuil says.

"We explored this in collaboration with investigators from the National Cancer Institute, Dana-Farber Cancer Institute, Moffit Cancer Center, and MD Anderson, and showed that such risk-adapted treatment decisions could achieve significant reduction of leukemia risk, without affecting outcomes for the primary cancer," Dr. Bolton adds.

> **"We are now routinely screening our patients for the presence of CH mutations."**
>
> **Ahmet Zehir**
> **computational biologist**

The investigators also hope to use the data from this study to develop better methods for detecting CH-related blood cancers when they first begin to form — and potentially to develop new interventions that could prevent CH from ever progressing to cancer. "We're excited about the idea of continuing to grow and expand the CH clinic as part of the integrated vision of PIP," says physician-scientist Ross Levine, who leads MSK's CH clinic and is a member of the Human Oncology and Pathogenesis Program.

"In addition to continuing to follow people who are at the highest risk of developing a secondary cancer, we want to continue to use the clinic as a vehicle for studies like this," he adds. "Our long-term goal is to move toward therapeutic interventions and preventing disease in a way that we've never been able to do before."

The study's lead author, Kelly Bolton, left MSK the end of September 2020 for Washington University in St. Louis.

This research was funded by National Institutes of Health grants K08 CA241318, K12 CA120780, P50 CA172012, UG1 HL069315, and P30 CA008748. It was also supported by the American Society of Hematology, the EvansMDS Foundation, the European Hematology Association, Gabrielle's Angels Foundation, the V Foundation, the Geoffrey Beene Foundation, the UNC Oncology Clinical Translational Research Training Program, Cycle for Survival, the Starr Cancer Consortium, and the Colorectal Cancer Dream Team Translational Research Grant from SU2C.

Dr. Levine is on the supervisory board of Qiagen and is a scientific advisor to Loxo, Imago, C4 Therapeutics, and Isoplexis, which include equity interest. He receives research support from and has consulted for Celgene and Roche and has consulted for Lilly, Janssen, Astellas, Morphosys, and Novartis. He has received honoraria from Roche, Lilly, and Amgen for invited lectures and from Gilead for grant reviews. Dr. Papaemmanuil receives research funding from Celgene and is a co-founder of Isabl Technologies, a software analytics company. Dr. Zehir has received honoraria from Illumina. Dr. Bolton has received research funding from GRAIL.

Novel Tool Enables Study of Rare Acute Myeloid Leukemia Stem Cells

If you think of cells as factories for making proteins, and DNA as the instructions contained within those factories, RNA is the workforce that actually carries out the manufacturing. Understanding how RNA does its job is essential for figuring out what goes wrong in many diseases, including cancer.

To take the analogy one step further, RNA-binding proteins (RBPs) are tools that RNA uses in the production process. There are more than 1,500 RBPs in any given cell, which creates a challenge for scientists who want to study them on an individual basis. But researchers are looking for ways to overcome this hurdle because RBPs are an important target for the development of new drugs.

In a paper published April 24, 2020, in *Nature Communications*, Sloan Kettering Institute cancer biologist Michael Kharas, members of his laboratory, and collaborators in the lab of computational biologist Christina Leslie describe a new tool for studying RBPs. In addition to having broad applications for a range of cell types, the team reports that this tool has already uncovered details about one particular RBP, called Musashi-2. Musashi-2 helps stem cells in the blood become more-specialized cell types. It is known to be overly active in acute myeloid leukemia (AML) cells.

“This is an exciting study because it changes how we study RBPs,” Dr. Kharas says. “It also changes what we know about how they function in specific cells.”

This illustration represents how HyperTRIBE technology works. The chemical adenosine in RNA (represented by the letter A) is changed to the chemical inosine (represented by the letter I). The samurai symbolizes the Musashi-2 protein, and the horse symbolizes the enzyme that makes the switch. Art by Olga Kharchenko

Translating a Lab Technique from Flies to Mammals

The experimental technique used in the study is called HyperTRIBE. It was originally developed to study nerve cells from fruit flies. Dr. Kharas says this is the first published study demonstrating that HyperTRIBE can be used in mammalian cells. The cells they used were blood stem cells from mice and leukemia stem cells from mice and humans.

HyperTRIBE uses a technology that is different from current methods for studying RBPs. Other approaches require millions of cells. The biggest benefit of HyperTRIBE is that it works in rare cells that are available only in very small numbers.

“Our study shows that this technique can be used to study RBPs, not just in fruit fly cells but more broadly,” says Dr. Kharas, a member of SKI’s Molecular Pharmacology Program. “This will have global impact for anyone studying RBPs in rare cell populations, whether those are blood stem cells, neurons, germ cells, or other kinds of stem cells.”

New Clues about a Protein’s Role in Leukemia

In the *Nature Communications* paper, the investigators report that HyperTRIBE has already revealed important findings about Musashi-2 and how it contributes to AML. Dr. Kharas and the other researchers are developing drugs to treat AML that work by blocking Musashi-2, but they still have a lot to learn about how these drugs modify the function of RBPs.

Using this novel tool, Dr. Kharas’s lab learned that Musashi-2 behaves differently in leukemia cells than it does in regular blood stem cells. “We knew that leukemia cells seemed to be more addicted to Musashi-2 for their growth than normal cells,” Dr. Kharas says. “Now we know that’s because Musashi-2 increases its RNA-binding activity and changes how RNA gets translated into proteins in cancer cells compared to normal cells.”

The investigators plan to continue studying why this is the case. Dr. Kharas says it could aid the development of drugs that slow leukemia growth by affecting Musashi-2’s activity while avoiding side effects that could result if Musashi-2 changes the production of healthy cells. “Because HyperTRIBE doesn’t require a large number of cells, we’ll be able to do more experiments to test potential drugs under many different conditions,” he concludes.

Dr. Kharas is a scholar of the Leukemia and Lymphoma Society (LLS). This research was supported by National Institutes of Health grants (R01-DK101989-01A1, 1R01CA193842-01, R01HL135564, R01CA225231-01, 3R01DK101989-03S1, K99 CA229993, and P30 CA008748), the Starr Cancer Consortium, an Alex’s Lemonade Stand Foundation A Award, the New York State Stem Cell Science program (NYSTEM), the Peter and Susan Solomon Family Foundation, the Tri-Institutional Stem Cell Initiative, and an LLS Career Development Award.

Dr. Kharas is a consultant for Accent Therapeutics, and his laboratory receives some financial support from 28-7 Therapeutics.

Postdoctoral fellows Linde Miles (left) and Robert Bowman are learning more about genetic changes that lead to cancer in blood cells.

Single-Cell Study Sheds Light on Leukemia’s Family Tree

When Memorial Sloan Kettering postdoctoral fellows Linde Miles and Robert “Bobby” Bowman began working on a new research project in May 2019, they didn’t know how massive a task it would be.

Their undertaking — the biggest study ever to examine the genetic causes of leukemia at the level of individual cells — was published October 28, 2020, in *Nature*. The findings revealed how a series of mutations in normal blood cells can lead to them eventually becoming cancerous. The study also showed how these mutations accumulated as the disease progresses.

“This single-cell approach gave us new insights into the journey that blood cells take on their path to becoming leukemia,” says physician-scientist Ross Levine, senior author of the paper and a member of the Human Oncology and Pathogenesis Program. “Our hope is that this glimpse into how and why leukemia develops will open up new areas of research in early diagnosis and treatment.”

Learning about Cancer, Cell by Cell

Traditional genomic analysis of cancers — including MSK-IMPACT™, a test that looks for mutations in 468 genes in patients’ tumors — uses what is called bulk sequencing. That means that it surveys the mutations that are present across all the cells in a tumor sample.

By contrast, the approach used in this study deciphered the mutations found in every single cell. The samples were obtained from 146 people who were treated at MSK for acute myeloid leukemia (AML), as well as those with two blood conditions that can lead to AML: clonal hematopoiesis and a blood cancer called myeloproliferative neoplasms. The analysis yielded data on nearly 750,000 unique blood cells.

“Instead of just broadly profiling all leukemias, we wanted to be able to ask pointed biological questions,” Dr. Bowman explains. “Understanding how

these mutations work together will give us insight into their biological function."

One aspect the study focused on is what's called the clonal architecture of the cancer. This is the order in which the mutations occur. Dr. Levine compares it to a family tree, with each branch taking the cells in a different direction — some remain healthy and others become aggressive cancer.

"Trying to figure out the clonal architecture is like looking at a maze," says Dr. Miles, a biochemist who was recently awarded a Marie-Josée Kravis Women in Science Endeavor (WiSE) fellowship. "It required a lot of work to begin to make sense of what we found and begin to detect patterns."

A United Effort

Dr. Miles spent the summer and fall of 2019 sequencing patient samples. She was able to complete five or six samples a day. When she finished, the amount of data that had been generated was overwhelming.

> "[This is] probably the most collaborative project I've ever worked on."
>
> Linde Miles
> postdoctoral fellow

As a computational biologist, Dr. Bowman's role was to figure out which mutations occurred together in the same cells and determine the order in which they appeared. At one point, he decided to consult his younger brother, Michael Bowman, a PhD student in mechanical engineering at the Colorado School of Mines.

Michael helped the MSK team develop the right mathematical formulas with an approach he normally uses to study robot behavior. Eventually he came to visit New York City, and spent much of the time that was supposed to be a vacation pouring over data with his brother, Dr. Miles, and Dr. Levine. Michael Bowman is a co-author on the paper.

Robert Bowman

Linde Miles

"This was very much a team effort, and Ross was involved at every step, too," Dr. Miles says. "It's probably the most collaborative project I've ever worked on."

Building a New Playbook for Cancer Research

Dr. Levine says the goal of this work is to take the new information about the clonal architecture back to the lab and use it to create more accurate disease models that can then be deployed to develop new diagnostic methods and potentially test new drugs.

"The analogy I like to use is that cancer is like the Death Star in *Star Wars*," he says. "You can't take it apart until you know where the critical nodes are — where the cells are most vulnerable to attack."

He also explains that, historically, leukemia research has led to methods that can be used to study many other cancers. "Because we can get leukemia samples with a simple blood draw, they've always been more accessible," he says. "Our hope is that similar single-cell studies in solid tumors and other blood cancers will follow and that our work will provide a playbook on how to approach these studies with other kinds of cancer."

This research was funded by National Institutes of Health and the National Cancer Institute grants P30 CA008748, K99 CA248460, K08 CA241318, K08 CA215317, R37 CA226433, P30 CA056036, R35 CA197594, and R01 CA173636. It was also supported by the Leukemia and Lymphoma Society, the Sohn Foundation, the Damon Runyon Cancer Research Foundation, the Swiss National Science Foundation, the American Society of Hematology, the Edward P. Evans Foundation, the Concern Foundation, the Sidney Kimmel Cancer Center, Cycle for Survival, and the Samuel Waxman Cancer Research Foundation.

Dr. Miles has received travel support and honoraria from Mission Bio.

> "Understanding how these mutations work together will give us insight into their biological function."
>
> Robert Bowman
> postdoctoral fellow

Dr. Levine is on the supervisory board of QIAGEN and is a scientific advisor to Imago, C4 Therapeutics, Mission Bio, and Isoplexis. He was also a scientific advisor to Loxo Oncology until February 2019. He receives research support from and has consulted for Celgene and Roche and has consulted for Lilly, Jubilant, Janssen, Astellas, Morphosys, and Novartis. He has received honoraria from Roche, Lilly, and Amgen for invited lectures and from Celgene and Gilead for grant reviews.

Appointments, Promotions, and Awards

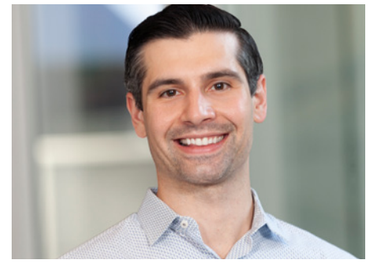
Appointments

In February 2020, **Gilles Salles, MD, PhD,** was appointed to Chief of the Lymphoma Service. Dr. Salles received his MD and PhD from the Université Claude Bernard Lyon and completed a residency in medicine at Lyon University Hospitals in Lyon, France. He also did a postdoctoral fellowship at Harvard Medical School (Dana Farber Cancer Institute) in immunology. Most recently, he was the Chair (since 2011) of the Department of Hematology in Lyon University Hospital and has held (since 1996) the position of Professor of Medicine (Hematology) at the Université Claude Bernard of Lyon.

For more than 20 years, Dr. Salles has been interested in the clinical and biologic diversity of malignant lymphoma. Major focuses of his work include the description and validation of prognostic factors as well as clinical trials in indolent lymphomas. He has well over 600 peer-reviewed publications. An established international leader in the field of lymphoma, Dr. Salles also led several programs and developed expertise in the clinical care of patients with lymphoma, development of novel clinical trials, and held numerous leadership positions. He is well suited to continue to build and enhance a world-class medical Lymphoma Service at MSK, dedicated to patient care, medical research, and teaching; a place where each member of the service is proud that we offer our patients the best care. Additionally, Dr. Salles plans to develop an ambitious translational research program and optimize the career development of our medical residents, fellows, and faculty. Dr. Salles works with medical oncologist Marcel van den Brink to accomplish the strategic vision of the service and the goals to expand the clinical and research activities in lymphoma, maintain the highest standard of care, and expand and enrich the research program at MSK.

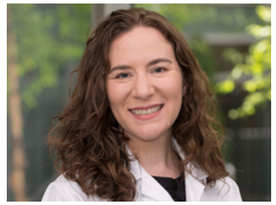
Christina Lee, MD, joined the Lymphoma Service as an Assistant Attending Physician in August 2020. Dr. Lee received her MD from the University of North Carolina and completed a residency in Internal Medicine at New York University. Dr. Lee also did a fellowship in Hematology and Medical Oncology at Weill Cornell Medicine. As a hospitalist, she will care for lymphoma inpatients, teach and supervise house staff, and build a clinical research program focused on lymphoma-associated hemophagocytic lymphohistiocytosis.

Niloufer Khan, MD, MS, joined the Lymphoma Service as an Assistant Attending Physician in August 2020. Dr. Khan received her MD from Case Western Reserve University School of Medicine and completed a residency in Internal Medicine/Pediatrics at the University of Chicago. Dr. Khan subsequently completed a fellowship in Hematology and Medical Oncology at MSK and obtained an MS in Clinical Epidemiology and Health Services Research at Weill Cornell Graduate School of Medical Sciences. As a clinical investigator, Dr. Khan will focus on the care of adolescents and young adults with lymphoma. She will care for patients with Hodgkin lymphoma, cutaneous T-cell lymphomas and peripheral T-cell lymphomas, as well as other non-Hodgkin lymphomas.



William Johnson, DO, joined the Lymphoma Service as an Assistant Attending Physician in August 2020. Dr. Johnson received his DO from the Philadelphia College of Osteopathic Medicine and completed a residency in Internal Medicine at the Lankenau Medical Center in Wynnewood, PA. Dr. Johnson also completed his fellowship in Hematology and Medical Oncology at Thomas Jefferson University in Philadelphia. As a hospitalist, he will care for lymphoma inpatients, teach and supervise house staff, and aid in developing novel treatment approaches for T-cell lymphoma.

Promotions



Alison J. Moskowitz, MD, was promoted to the rank of Associate Member at MSK, Associate Attending Physician in the Lymphoma Service in the Department of Medicine, and Associate Professor of Medicine at Weill Cornell Medical College in April 2020. She serves as the Clinical Director for the Lymphoma Inpatient Unit.

Connie Lee Batlevi, MD, PhD, was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician in the Lymphoma Service in the Department of Medicine, and Assistant Professor of Medicine at Weill Cornell Medical College in August 2020.

Steven M. Horwitz, MD, was promoted to the rank of Member at MSK, Attending Physician in the Lymphoma Service in the Department of Medicine, and Professor of Medicine at Weill Cornell Medical College in September 2020.

Santosha Vardhana, MD, PhD, was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician in the Lymphoma Service in the Department of Medicine, and Assistant Professor of Medicine at Weill Cornell Medical College in January 2021.

Awards

Santosha Vardhana, MD, PhD, received the following awards in 2020:
- K08 award from the National Cancer Institute for his project titled "Investigating altered T-cell metabolism during chronic antigen encounter"
- Award from the Pershing Square Sohn Cancer Research Alliance with Co-PI Omar Abdel-Wahab for their project titled "Leveraging cancer-driven immune dysregulation to understand and enhance anti-COVID-19 immunity."
- Award from Immunai for his project titled "SRA-Identifying peripheral blood biomarkers of response to anti-cancer therapy in bladder cancer using single-cell RNA sequencing"
- Steven A. Greenberg Startup Grant award for his project titled "Tumor and immune cell evolution during lymphoma immunotherapy"

Connie Batlevi, MD, PhD
- Received the Steven A. Greenberg Startup Grant award for her project titled "Optimizing Data Entry for the Lymphoma Outcomes Database"

Erel Joffe, MD, MSc, received the following awards in 2020:
- Award from the Paraxel International Corporation for his project titled "SRA-An observational retrospective cohort study of systemic therapies for relapsed or refractory diffuse large B cell lymphoma (R/R DLBCL), to compare outcomes to those from Tafasitamab + Lenalidomide in the L-MIND study"
- The Steven A. Greenberg Startup Grant award for his project titled "Distinguishing Refractory from Responsive TP53-Mutated Diffuse Large B Cell Lymphoma and Evaluating TP53 Clonal Evolution—an Integrative DNA-RNA Sequencing Study"

Andrew Intlekofer, MD, PhD, received the following awards in 2020:
- R01 award from the National Cancer Institute for his project titled "Metabolic control of normal and malignant hematopoiesis"
- Awards from Starr Cancer Consortium for two projects: "Microbiome-derived Hydrogen Sulfide as a Trigger for CIMP Colorectal Cancer" and "Metabolic Coupling of Hypoxia to Intratumoral Heterogeneity"
- Received the Steven A. Greenberg Startup Grant award for his project titled "Metabolic and epigenetic regulation of T cell differentiation and lymphomagenesis"

Christina Lee, MD
- Received an award from the Lymphoma Research Foundation for her project titled "Dual CDK4/6 and immune checkpoint inhibitor therapy in indolent non-Hodgkin lymphoma"

Gottfried von Keudell, MD, PhD
- Received the Steven A. Greenberg Startup Grant award for his project titled "Assessment of Circulating Tumor DNA (ctDNA) Derived from Cell-Free DNA in Patients with Marginal Zone Lymphoma"

The following Lymphoma Service Faculty Members were recognized on various **2020 Top Doctor Lists:**

David Straus, MD
Castle Connolly America's Top Doctors, Top Doctors New York Metro Area, Castle Connolly America's Top Doctors for Cancer

Andrew D. Zelenetz, MD, PhD
New York Magazine: Top Doctors, Castle Connolly America's Top Doctors, Top Doctors New York Metro Area, Castle Connolly America's Top Doctors for Cancer

Audrey M. Hamilton, MD
Top Doctors New York Metro Area, Exceptional Women in Medicine

Philip C. Caron, MD, PhD
Westchester Magazine: Top Doctors, Top Doctors New York Metro Area

Steven M. Horwitz, MD
Castle Connolly America's Top Doctors, Top Doctors New York Metro Area, Castle Connolly America's Top Doctors for Cancer

Highlighted Clinical Trials and Publications

Highlighted Clinical Trials

Phase II Study of Zanubrutinib, Obinutuzumab, and Venetoclax in Previously Untreated Patients With Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL) and Mantle Cell Lymphoma (MCL)
IRB: 18-427; PI: Andrew Zelenetz; Co-PI: Anita Kumar and Anthony Mato

The purpose of this study is to assess the safety and effectiveness of combination therapy with zanubrutinib, obinutuzumab, and venetoclax in patients newly diagnosed with chronic lymphocytic leukemia (CLL) or small lymphocytic leukemia (SLL). Obinutuzumab targets a protein called CD20, which is found on the surface of B cells (the white blood cells that are affected by CLL and SLL). Obinutuzumab destroys B cells by direct killing as well as making them more visible to the immune system, which then attacks and destroys B cells. Venetoclax blocks a protein called Bcl-2 in cancer cells. Bcl-2 helps cancer cells survive and resist the effects of cancer treatments. By blocking Bcl-2, venetoclax may kill cancer cells and/or make them more vulnerable to the effects of other cancer treatments. Zanubrutinib blocks a protein in B cells called Bruton tyrosine kinase (BTK). BTK helps CLL/SLL cells live and grow. By blocking BTK, zanubrutinib may slow or stop the activity of CLL/SLL cells.

Phase II Study of Second-Line Pembrolizumab Plus GVD for Relapsed or Refractory Hodgkin Lymphoma
IRB: 18-160; PI: Alison Moskowitz; Co-PI: Heiko Schoder and Gunjan Shah

This is a study to assess the safety and effectiveness of combining pembrolizumab immunotherapy with standard chemotherapy drugs and autologous stem cell transplantation (ASCT) in patients with Hodgkin lymphoma that has come back or continued to grow despite one regimen of prior therapy. Pembrolizumab blocks PD-1, a protein cancer cells use to evade detection by the immune system, thereby enabling the immune system to find and kill cancer cells. In this study, patients will receive pembrolizumab with three chemotherapy drugs: gemcitabine, vinorelbine, and liposomal doxorubicin. Depending on how well they respond to this treatment, they may also have ASCT. During ASCT, a patient's own blood-forming stem cells are collected, and he or she is then treated with high doses of chemotherapy. Afterward, the collected stem cells are re-infused back into the patient to re-establish the blood-forming system.

A Phase I Multiple Ascending Dose Study of DS-3201B in Subjects with Lymphomas
IRB: 19-297; PI: Steven Horwitz; Co-PI: Alison Moskowitz

The purpose of this study is to assess the safety and effectiveness of the investigational drug DS-3201b in people with T-cell leukemia-lymphoma (ATL) or peripheral T-cell lymphoma (PTCL) that came back or continues to grow despite prior treatment. DS-3201b may work by blocking the activity of two proteins called EZH1 and EZH2, which are involved in cancer growth.

Hematologic oncologist Anita Kumar and a patient

Phase II Study of N-acetylcysteine in Severe or Critically Ill Patients with Refractory COVID-19 Infection (COVID)
IRB: 20-168; PI: Santosha Vardhana; Co-PI: Jedd Wolchok

The FDA has approved N-acetylcysteine to treat the liver side effects resulting from an overdose of the anti-inflammatory medication Tylenol® (acetaminophen). N-acetylcysteine is also used to loosen the thick mucus in the lungs of people with cystic fibrosis or chronic obstructive pulmonary disease (COPD). This study is the first to test N-acetylcysteine in people with severe COVID-19 infections. By helping your immune system fight the virus, the researchers believe that the infection will get better, which could allow the patient to be moved out of the critical care unit or go off a ventilator, or prevent them from moving into a critical care unit or going on a ventilator.

A Phase I, Multicenter, Open-label Study of JCAR017, CD19-targeted Chimeric Antigen Receptor (CAR) T cells, for Relapsed and Refractory (R/R) B-cell Non-Hodgkin Lymphoma (NHL)
IRB: 15-295; PI: Lia Palomba; Co-PI: Jae Park and Craig Sauter

This is an open-label, multicenter Phase I study to determine the safety, pharmacokinetics (PK), and antitumor activity of JCAR017 in adult patients with relapsed or refractory diffuse large B cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL), follicular lymphoma Grade 3B, and mantle cell lymphoma (MCL). This study will evaluate and refine the dose and schedule of JCAR017 to optimize safety and antitumor activity. A dose-confirmation group or groups will further evaluate the safety and efficacy of JCAR017 at the recommended regimen(s).

Highlighted Publications

Straus DJ, Długosz-Danecka M, Alekseev S, et al. Brentuximab vedotin with chemotherapy for stage III/IV classical Hodgkin lymphoma: 3-year update of the ECHELON-1 study. Blood. 2020;135(10):735-742. doi:10.1182/blood.2019003127

The Phase III ECHELON-1 study demonstrated that brentuximab vedotin (A) with doxorubicin, vinblastine, and dacarbazine (AVD; A+AVD) exhibited superior modified progression-free survival (PFS) compared to doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) for frontline treatment of patients with stage III/IV classical Hodgkin lymphoma (cHL). Upon continued follow-up, 78% of patients with peripheral neuropathy on A+AVD had either complete resolution or improvement compared with 83% on ABVD. These data highlight that A+AVD provides a durable efficacy benefit compared with ABVD for frontline stage III/IV cHL, consistent across key subgroups regardless of patient status at PET2, without need for treatment intensification or bleomycin exposure.

Ghione P, Faruque P, Mehta-Shah N, et al. T follicular helper phenotype predicts response to histone deacetylase inhibitors in relapsed/refractory peripheral T-cell lymphoma. Blood Adv. 2020;4(19):4640-4647. doi:10.1182/bloodadvances.2020002396

Histone deacetylase inhibitors (HDACi) are active agents for peripheral T-cell lymphoma (PTCL). Anecdotally, angioimmunoblastic T-cell lymphoma (AITL) appears to respond better than PTCL–not otherwise specified (NOS) to HDACi. The new World Health Organization classification shows that a subgroup of PTCL carries similarities in phenotype and gene expression profiling to AITL, comparable to T follicular helper (TFH) cells. The disease might behave similarly to AITL when treated with HDACi. The results show differential efficacy that can help inform subtype-specific therapy and guide interpretation of HDACi trials.

Batlevi CL, Sha F, Alperovich A, et al. Follicular lymphoma in the modern era: survival, treatment outcomes, and identification of high-risk subgroups. Blood Cancer J. 2020;10(7):74. Published 2020 Jul 17. doi:10.1038/s41408-020-00340-z

Patients with follicular lymphoma (FL) frequently require multiple treatments during their disease course; however, survival based on lines of treatment remains poorly described. The Follicular Lymphoma International Prognostic Index (FLIPI) score was developed to predict survival at diagnosis, yet it remains unknown whether increase in FLIPI score following an initial observation period is associated with less-favorable outcomes. To address these knowledge gaps, these researchers retrospectively studied 1,088 patients with FL grade 1-3A managed between 1998 and 2009 at our institution. This study also highlights the utility of changes in FLIPI score at diagnosis and after observation in identifying patients likely to have worse outcomes.

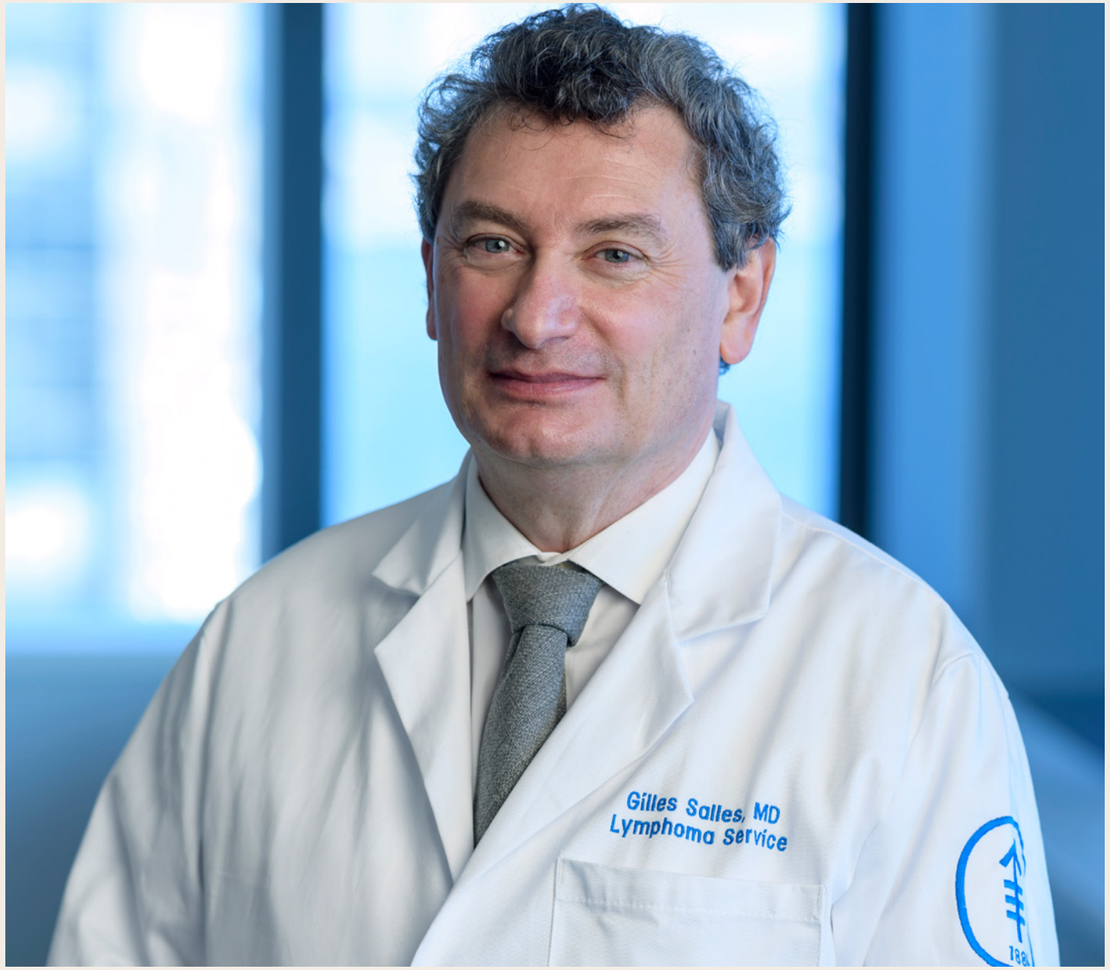
Noy A, de Vos S, Coleman M, et al. Durable ibrutinib responses in relapsed/refractory marginal zone lymphoma: long-term follow-up and biomarker analysis. Blood Adv. 2020;4(22):5773-5784. doi:10.1182/bloodadvances.2020003121

Advanced marginal zone lymphoma (MZL) is an incurable B-cell malignancy dependent on B-cell receptor signaling. The phase II PCYC-1121 study demonstrated the safety and efficacy of single-agent ibrutinib 560 mg/d in 63 patients with relapsed/refractory MZL treated with prior rituximab (RTX) or rituximab-based chemoimmunotherapy (RTX-CIT). Patients with prior RTX treatment had better outcomes than those with prior RTX-CIT. With up to 45 months of ibrutinib treatment, the safety profile remained consistent with prior reports. Final analysis of PCYC-1121 demonstrated long-term safety and efficacy of ibrutinib in patients with relapsed/refractory MZL, regardless of prior treatment or MZL subtype.

Vardhana SA, Hwee MA, Berisa M, et al. Impaired mitochondrial oxidative phosphorylation limits the self-renewal of T cells exposed to persistent antigen. Nat Immunol. 2020;21(9):1022-1033. doi:10.1038/s41590-020-0725-2

Most tumor-infiltrating T cells exhibit a terminally exhausted phenotype, marked by a loss of self-renewal capacity. How repetitive antigenic stimulation impairs T cell self-renewal remains poorly defined. These researchers show that persistent antigenic stimulation impaired ADP-coupled oxidative phosphorylation. These data reveal that loss of ATP production through oxidative phosphorylation limits T cell proliferation and effector function during chronic antigenic stimulation. Furthermore, treatments that maintain redox balance promote T cell self-renewal and enhance anti-tumor immunity.

Alison J. Moskowitz, MD, Clinical Director, Lymphoma Inpatient Unit



INTERVIEW

Gilles Salles
Chief, Lymphoma Service

Taking on New Challenges: 8 Questions

Gilles Salles recently joined Memorial Sloan Kettering as Chief of the Lymphoma Service within the Division of Hematologic Malignancies. Dr. Salles came to MSK after a long career at Claude Bernard Université in Lyon, France.

In an interview conducted in early December 2020, just before the annual American Society of Hematology (ASH) meeting, where he presented updates from several studies he's conducted, Dr. Salles spoke about his decision to join MSK, his research, and his plans for the Lymphoma Service.

Why did you decide to come to MSK?
MSK is a fantastic place in terms of clinical care, clinical research, and basic research. There are not many places in the world that have strengths in all three of these areas. There are so many opportunities here to bring talented scientists together with clinicians who can help them deliver their discoveries to patients.

I've been successful in my career, and I've been able to bring many improvements in lymphoma care to patients. I asked myself, "Should I just continue here in France and then retire in six or eight years, or should I take on a new challenge?" I decided that this kind of opportunity, to be able to interact more with basic scientists and to build upon translational research projects, doesn't happen very often. That's why I took the leap.

What was your relationship with MSK before you came here?
I already knew many members of the Lymphoma Service as well as people in other groups at MSK. I've been involved in collaborations with them over the years and have met them at conferences. They are a large part of the reason I decided to join MSK — it's exciting to work with such talented people.

What was it like moving to a new continent in the middle of a pandemic?
It was strange. I moved to New York over the summer and started working at MSK in mid-August. I haven't been in the same room with most of my new colleagues yet. We've all been meeting on Zoom.

I studied in the United States for my postdoc about 30 years ago in Boston. And I've been to New York and other parts of the United States many times since then, both for work and for vacations with my family. This is not the New York I was wishing to rediscover, but I'm hopeful that the pandemic will end soon.

What's different about MSK's Lymphoma Service?
We have the SPORE in Lymphoma [Specialized Programs of Research Excellence, a project funded by the National Cancer Institute to help move basic science findings into the clinic]. That was started by my predecessor, Anas Younes, and is now being led by Andrew Zelenetz, a leading physician in the field of B cell malignancies.

MSK's Lymphoma Service is quite large, with more than 20 faculty. Because there are so many of us, we can specialize not just in lymphoma but in particular types of lymphoma.

What types of lymphoma do you specialize in treating?
I was very fortunate 20 years ago to be part of the early development of the first monoclonal antibody drug for diffuse large B cell lymphoma (DLBCL), called rituximab. I'm continuing to work on developing new antibody drugs for DLBCL.

I also treat follicular lymphoma. This disease is unusual because some patients who are diagnosed with it don't require treatment right away, only active surveillance. But it also doesn't have a cure. Thanks to new treatments, we've been able to extend survival for this disease considerably, from an average of eight to ten years to an average of 15 to 20 years. But I think that with the addition of new treatments, especially different kinds of immunotherapy, we will soon be able to offer a cure for some patients.

What are some of the research collaborations you're planning?
There are many projects I plan to pursue with people here at MSK.

I'm very excited to work with physician-scientist Santosh Vardhana, who recently started his own lab in the Human Oncology and Pathogenesis Program. He has so much knowledge about T cell biology, and we want to apply this to some of the clinical trials we are developing.

I've already had the opportunity to work on projects with hematopathologist Ahmet Dogan. To understand lymphoma, we have to really know what's happening in the tumor, and pathology is the cornerstone of that.

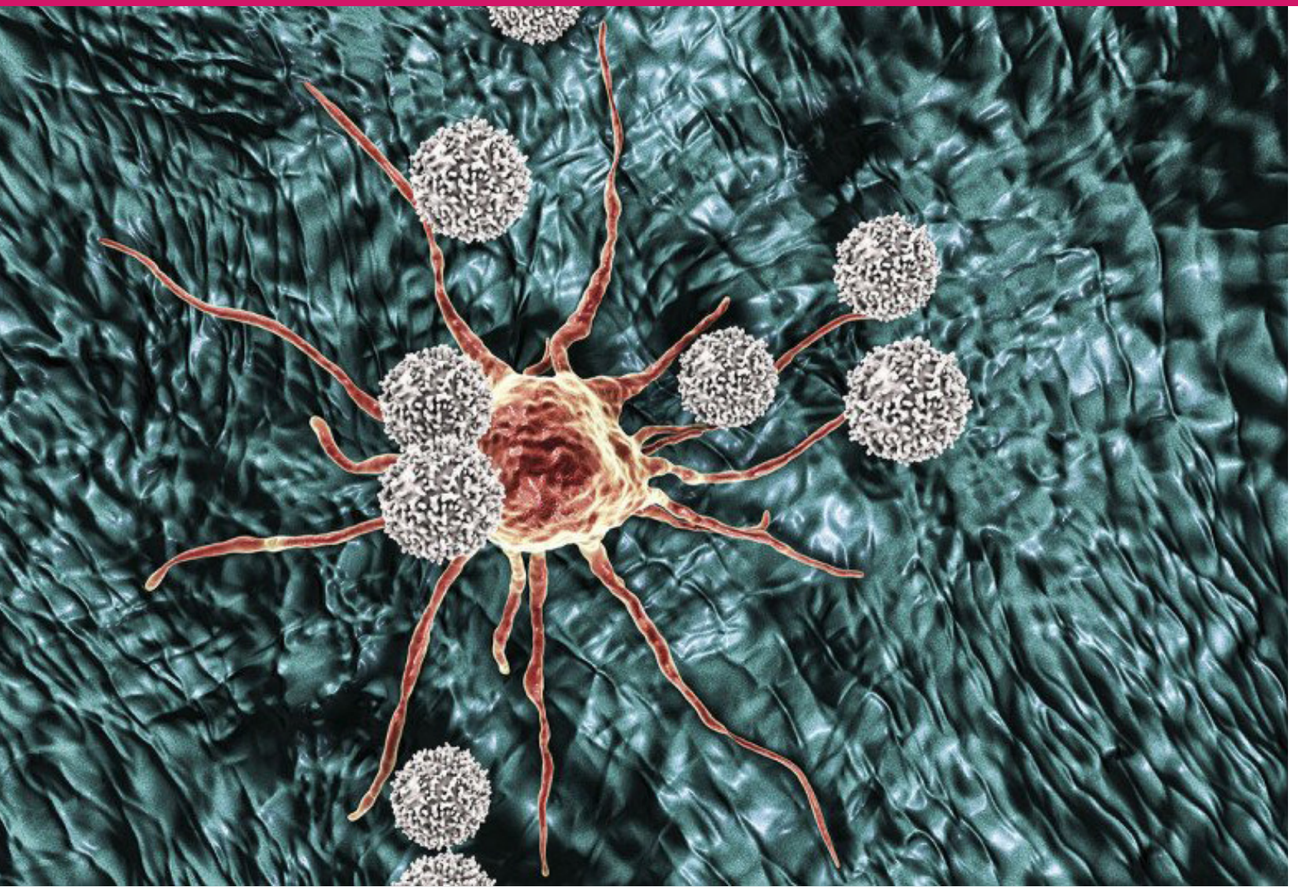
Before I came here, I had met Sloan Kettering Institute cancer biologist Hans-Guido Wendel a few times, and I knew his work. I've joined his very innovative project looking at abnormal RNA translation in lymphoma to help bring his findings to the clinic.

In the past, I've participated in studies that looked at the ways a person's genes influence how they respond to treatments for lymphoma. Through this work, I've been involved in some consortia with geneticist Vijai Joseph, who studies hereditary cancer. Now that we're in the same place, we can find time to work more on this project.

What made you interested in pursuing science and medicine as a career — particularly cancer?
I got interested in medicine because I wanted to help people. Medicine is a profession where you bring something to others — health, one of the most precious things we have. I'm also a curious person, so that made science a natural fit.

When I finished medical school, and I had to choose where to focus, the field of oncology was attractive, in part because it was challenging. At that time, there weren't many options for people with cancer, other than chemotherapy. We in the field were starting to learn more about the biology and immunology of the disease, and it felt like there were many opportunities to improve treatment for cancer patients.

What are you most looking forward to doing in New York once the pandemic is over?
My wife and I are both excited about getting into the jazz music scene. We sometimes hear musicians when we're walking through Central Park, and it's so good to hear live music.



Immune T cells (white) often home in on cancer cells but then fail to finish the job of killing them.

Study Shows How Immune Cells Lose Their Power to Fight Tumors

Perhaps the biggest challenge facing cancer immunotherapy is figuring out why it doesn't work for everyone. Currently only 20% to 40% of people respond to these treatments, which harness the power of immune cells (T cells) to attack tumors. A major hurdle appears to be something called T cell exhaustion.

T cells seek and destroy cells that have molecular markers on their surface, which the immune system recognizes as a foreign signal. These markers are called antigens. But when T cells sense the same antigen signal for extended periods they become "exhausted" and lay down their arms. This prevents the immune system from attacking for too long and harming the body's own tissue.

"The T cells turn on the brakes to tamp down their own activity," says physician-scientist Santosha Vardhana, at the time a researcher in the Craig Thompson laboratory at the Sloan Kettering Institute.

This phenomenon explains why T cells often flock to tumors and invade them, only to then lose their power. Cancer immunotherapies called checkpoint inhibitors work when they manage to release the brakes on T cells and prod them back into action. But for most people, the immune cells stay dormant. Understanding exactly how T cell exhaustion develops could be critical for making immunotherapy treatments work for more people.

A new study led by Drs. Vardhana and Thompson has found that T cell exhaustion starts with the cells' metabolism — the chemical processes that enable cells to produce energy from nutrients. These changes in metabolism send T cells down the path to exhaustion.

"We've shown that if you really want to rewire a T cell so it can be better at killing tumors, you have to change its metabolism," Dr. Vardhana says.

The finding is published in *Nature Immunology*.

> **"We've shown that if you really want to rewire a T cell so it can be better at killing tumors, you have to change its metabolism."**
>
> **Santosha Vardhana**
> **physician-scientist**

The Source of the Problem

The idea that metabolism might play a critical role arose after studies showed that a successful response to immunotherapy depends on whether the T cells maintain their ability to divide and make new cells (proliferate). Nearly 20 years ago, Dr. Thompson and colleagues showed that T cells require a shift in their metabolic behavior to proliferate.

Dr. Vardhana and his collaborators therefore wondered whether loss of the ability to proliferate in T cells from patients who do not respond to immunotherapy might result from a defect in the cells' metabolic fitness. But it was hard to tell if this was the case because researchers had largely been looking at T cells taken out of tumors. By then, the T cells were both exhausted and metabolically inactive, and it was hard to determine cause and effect.

"It was like reading the last chapter of a book and trying to figure out what the main conflict was," Dr. Vardhana explains.

To understand this, the research team built a model system that allowed them to tease apart the process of T cell exhaustion. In a dish, they continuously exposed T cells to foreign signals from tumor antigens and watched the reaction over time. They found that continuous exposure to tumor antigens overtaxed a part of the T cell called the mitochondrion — otherwise known as the "powerhouse" of the cell — which is responsible for converting nutrients into energy.

Unable to shoulder the load imposed by persistent exposure to tumors, the mitochondria within T cells begin to leak molecules called free radicals, which block essential cellular processes — including the ability to proliferate — and damage different parts of the cell, including the mitochondria themselves.

"Over time, T cells in tumors get trapped in a vicious cycle," Dr. Vardhana says. "Damaged mitochondria leak even more free radicals, which further damage the mitochondria." Of note, Dr. Vardhana and colleagues saw signs of free radical damage early on, suggesting that this metabolic abnormality is a cause, rather than a consequence, of T cell exhaustion.

The researchers subsequently tried to block the damage. They dosed T cells with antioxidants, which soak up free radicals. This seemed to work, allowing T cells to proliferate and kill tumor cells indefinitely.

"What was even more surprising was that in addition to recovering T cell function, antioxidants seemed to essentially move the T cell 'backwards in time' on the exhaustion trajectory — from a more exhausted cell to a less exhausted cell," Dr. Vardhana says. "We are still trying to understand how a T cell senses a change in metabolism and reacts by changing its entire cell state."

Ultimately, Dr. Vardhana and colleagues feel that this discovery could be an important step toward making cancer immunotherapies work better. "Knowing what lies at the heart of T cell exhaustion gives us a strategy for making all these immunotherapies work for more people," Dr. Vardhana says.

Santosha Vardhana

Dr. Vardhana is a Senior Fellow with the Parker Institute of Cancer Immunotherapy and is supported by a Burroughs Wellcome Fund Career Award for Medical Scientists. This work was additionally supported by the Memorial Sloan Kettering Cancer Center Support Grant P30 CA008748 and R25 Training Grant AI140472-01A1.

Dr. Vardhana has received honoraria from Agios Pharmaceuticals and Rheos Pharmaceuticals, is an advisor for Immunai, and has consulted for ADC Therapeutics. Dr. Thompson is a founder of Agios Pharmaceuticals and a member of its scientific advisory board. He is also a former member of the Board of Directors and stockholder of Merck and Charles River Laboratories.

Appointments, Promotions, and Awards

Appointments

Carlyn Rose Tan, MD, joined the Myeloma Service as an Assistant Attending Physician in March 2020. Dr. Tan received her MD from Albert Einstein College of Medicine and completed a residency in Internal Medicine at Cedars-Sinai Medical Center. Dr. Tan completed her hematology/oncology fellowship at Fox Chase Cancer Center, Temple University Hospital. Subsequently, she was appointed as an Assistant Professor at Temple University Hospital. As a clinical investigator at MSK, Dr. Tan focuses on the development of innovative therapeutic approaches for the management of multiple myeloma and the exploration of biomarkers to predict and track responses to these therapies.

Promotions

Malin Hultcrantz, MD, PhD, was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician in the Myeloma Service in the Department of Medicine, and Assistant Professor of Medicine at Weill Cornell Medical College in April 2020.

Hani Hassoun, MD, was promoted to the rank of Member at MSK, Attending Physician in the Myeloma Service in the Department of Medicine, and Professor of Medicine at Weill Cornell Medical College in August 2020.

Awards

Urvi Shah, MD, was selected by the American Society of Hematology to participate in the 2020 ASH Clinical Research Training Institute.

Sydney Lu, MD, PhD, received the following awards in 2020:

- K08 award from the National Cancer Institute for his project titled “Dissecting the Roles and Requirements for RBM39 in Acute Myeloid Leukemia and Normal Hematopoiesis”
- Award from the Parker Institute for Cancer Immunotherapy for project titled “Enhancing the anti-tumor immune response through therapeutic modulation of RNA splicing”
- Awarded a Parker Institute for Cancer Immunotherapy, Bridge Scholar Fellowship (2020-2023)

The following Myeloma Service Faculty Members were recognized on various **2020 Top Doctor Lists:**

Hani Hassoun, MD
Top Doctors New York Metro Area

Alexander Lesokhin, MD

Highlighted Clinical Trials and Publications

Highlighted Clinical Trials

A Study of Health-Related Quality of Life in People with Multiple Myeloma Receiving Daratumumab or Lenalidomide IRB: 20-198; PI: Urvi Shah; Co-PI: Sham Mailankody

The purpose of this study is to compare maintenance therapy approaches in people with newly diagnosed multiple myeloma (MM) that have responded well to a first round of treatment. The researchers will compare giving the usual maintenance therapy (lenalidomide) with giving daratumumab as maintenance therapy, and they will look at which drug gives participants a better health-related quality of life during treatment.

C1071001: A Phase I, Open Label Study to Evaluate the Safety, Pharmacokinetic, Pharmacodynamic and Clinical Activity of PF-06863135, A B-Cell Maturation Antigen (BCMA)- CD3 Bispecific Antibody, As A Single Agent and In Combination With Immunomodulatory Agents In Patients With Relapsed/Refractory Advanced Multiple Myeloma (MM) PI: Alexander Lesokhin; Co-PI: Sham Mailankody

This study is a Phase I, open label, multicenter study of the drug PF-06863135 in adult patients with advanced multiple myeloma who have relapsed from or are refractory to standard therapy. This two-part study will assess the safety and tolerability of increasing dose levels of the drug in part 1 and establish the recommended Phase II dose in part 2.

Highlighted Publications

Jain T, Knezevic A, Pennisi M, et al. Hematopoietic recovery in patients receiving chimeric antigen receptor T-cell therapy for hematologic malignancies. Blood Adv. 2020;4(15):3776-3787. doi:10.1182/bloodadvances.2020002509

In an analysis of 83 patients with blood cancers treated with CAR T cell therapy, this paper describes patterns of recovery and evaluates potentially associated factors. The results showed several factors that were statistically, significantly associated with a lower likelihood of complete count recovery at one-month post infusion. These results should be studied further in larger prospective studies.

Hultcrantz M, Richter J, Rosenbaum C, et al. COVID-19 infections and outcomes in patients with multiple myeloma in New York City: a cohort study from five academic centers. Preprint. medRxiv. 2020;2020.06.09.20126516. Published 2020 Jun 11. doi:10.1101/2020.06.09.20126516

Patients with multiple myeloma are immunocompromised, raising the question whether they are at higher risk of severe COVID-19 disease. In this large case series on COVID-19 in patients with multiple myeloma, the researchers report 29% mortality rates among hospitalized patients and identify race/ethnicity as the most significant risk factor for severe outcome.

MSK Spearheads the Development of CAR T Therapy for Multiple Myeloma

Over the past few years, chimeric antigen receptor (CAR) T therapy has been an important addition to the arsenal of treatments for certain types of leukemia and lymphoma. As of early 2021, four CAR T therapies have received approval from the FDA. Investigators at Memorial Sloan Kettering have led the development of this treatment approach from the earliest stages, beginning with years of preclinical research in the laboratory of physician-scientist Michel Sadelain.

In addition to therapies for leukemia and lymphoma, MSK researchers have also been at the forefront of developing CAR T treatments for multiple myeloma, including initiating several first-in-human clinical trials. Some of the very first patients to get these therapies have been treated by doctors in MSK's Division of Hematologic Malignancies.

Sham Mailankody, MBBS, Medical Oncologist

"Since 2017, we have treated more than 60 patients with multiple myeloma on all phases of clinical trials examining this approach," says MSK medical oncologist Sham Mailankody, who specializes in treating plasma cell disorders such as multiple myeloma. "We start with research that is developed here in the basic science labs, and we help those discoveries make their way into trials. We have the advantage of having our own Cell Therapy and Cell Engineering Facility, where we manufacture CAR T cells that can be used to treat patients."

Studying an Off-the-Shelf Treatment

Dr. Mailankody has played leading roles in two clinical trials. Early findings from the first, a phase I, first-in-human, multicenter trial of a drug called ALLO-715, were presented at the American Society of Hematology (ASH) meeting in December 2020.
This drug is made by the company Allogene Therapeutics.

ALLO-715 is an off-the-shelf, allogeneic (made from donor cells) CAR T therapy for people with multiple myeloma. The T cells are engineered to recognize and target BCMA, a protein that's found on the surface of multiple myeloma cells. "Autologous CAR T treatments, which use patients' own T cells, are effective, but they take several weeks to manufacture," Dr. Mailankody explains. "This can present challenges for patients who are so sick they can't wait." He adds that collecting enough healthy T cells to create an engineered treatment can be difficult when patients have already received several rounds of chemotherapy that diminish their immune cells.

"For these reasons, we think making CAR T cells from T cells donated by healthy volunteers may be a good approach," he says, explaining that the cells are engineered to have additional constructs that don't require them to be matched precisely to the patients' immune systems.

Early results from the trial demonstrated that, for a population of patients who had already received several other treatments, 60% of patients who were treated at higher doses responded to the drug. In addition, the side effects observed were mostly manageable with available treatments. "These findings are exciting, but going forward we need to look at the safety and efficacy in more patients, including studying how this treatment compares to an autologous CAR T therapy," Dr. Mailankody says. Those trials are now ongoing at MSK and elsewhere.

Focus on a New Target

The second trial, for which the investigators have not yet presented or published results, is looking at a target other than BCMA and originated at MSK. This protein is called GPRC5D. Preclinical research that identified GPRC5D as a valuable target was published in 2019 in *Science Translational Medicine* by Renier Brentjens.

Research in mice showed that CAR T cells engineered to seek out GPRC5D were effective in targeting multiple myeloma cells that were able to evade cells that sought out BCMA. The first-in-human, dose-escalation trial, which is now ongoing, is being done completely in-house at MSK. The CAR T cells are being manufactured by the Cell Engineering and Cell Therapy Facility, led by Isabelle Rivière, and the trial is being administered by Cellular Therapeutics Service, which is led by Renier Brentjens.

"We started enrolling patients a few months ago," Dr. Mailankody says. "It's too soon to say much about efficacy, but we feel it's important to highlight MSK's ability to bring these kinds of therapies into the clinic — from the initial discoveries made in the lab to manufacturing and, finally, to treating patients in the clinic."

INTERVIEW

Urvi Shah
Hematologic Oncologist

Hematologic Oncologist Urvi Shah Writes Article Sharing Experiences with Cancer and COVID-19

Memorial Sloan Kettering hematologic oncologist Urvi Shah is a double survivor, having faced what she calls "the two C words: cancer and COVID-19." Dr. Shah's COVID-19 symptoms were relatively mild, but the weeks she spent recovering brought back emotions from four years earlier: In the spring of 2016, while she was training as a fellow in oncology, she was diagnosed with Hodgkin lymphoma.

In May 2020, Dr. Shah penned an article for *JAMA Oncology* about her experiences with both diseases. "Given my cancer history, I could not help but wonder if my immune system had returned to its baseline and if I would be able to weather this infection without serious complications," she wrote. "Would the prior chemotherapy affect my current outcomes?"

In this Q&A, Dr. Shah describes how she coped during two incredibly challenging times in her life.

When were you diagnosed with COVID-19?
On March 22, 2020, I developed a fever and cough. I didn't have a runny nose or other symptoms of a cold, so I thought it might be COVID-19. I filled out a form on MSK's website and was seen the next morning. By the end of the day, I learned that I had tested positive.

What was your experience with COVID-19 like?
Thankfully, it wasn't bad. It was a week of fevers, and I took Tylenol and checked my oxygen regularly. My oxygen levels didn't drop, and I never felt short of breath. The cough lasted a few weeks after that. I completely lost my sense of smell for about a month. It gradually returned but remained altered for nine months. Some specific foods I previously enjoyed, such as onions, tasted and smelled awful, so I had to avoid them.

At the time I was sick, my colleagues were overwhelmed with treating people in the hospital, so I didn't ask them to cover my patients. I was able to keep appointments with everyone using telemedicine, except for one afternoon when I was really fatigued.

Having COVID-19 brought back many of the feelings I had during my cancer experience, and I decided to write about them.

What were some of those feelings?
With both diseases, there is a fear of the unknown. You don't know how you'll do and must remain patient. They make you face your mortality, even if you're young. At the time I was diagnosed with COVID-19, we didn't know much about the course of disease in anyone, especially cancer survivors.

On a physical level, I experienced a change in my sense of smell and taste with both cancer and COVID-19. With cancer, it was altered due to chemotherapy, and with COVID-19, it's a symptom of the virus, but the sensation is similar.

Another thing is the sense of isolation. While I was going through cancer treatment, I socially distanced myself. I didn't want a lot of people to know what I was dealing with at that time. But even though I had less human contact with COVID-19 than I did with cancer, I actually didn't feel as alone. I think that's because I was more open to talking about it. And everyone around the world is dealing with this simultaneously.

How did you learn you had cancer?
I was in the first year of my fellowship in hematology and oncology at Montefiore Medical Center in the Bronx. It was a Friday, and I was taking the subway home to my apartment on the Upper East Side when I noticed a neck swelling. The physician in me knew it could be cancer, but I decided to wait until Monday because I didn't want to go to urgent care. That was a very long weekend.

When I got to work on Monday, I showed the swelling to the attending physician I was rounding with on the inpatient unit, and he ordered a CT scan right away. The scan showed that many of the lymph nodes in my neck and chest were enlarged. That led to a biopsy and to eventually getting diagnosed with Hodgkin lymphoma.

Because I was a doctor, I was able to get my diagnosis quickly, in about ten days. But it made me appreciate how hard those first weeks are for my patients. I try to help them as much as I can through that critical time. The anxiety of not knowing what it is is much harder than knowing and being able to manage it. I always make a very clear plan for my patients so they know what to expect at every step.

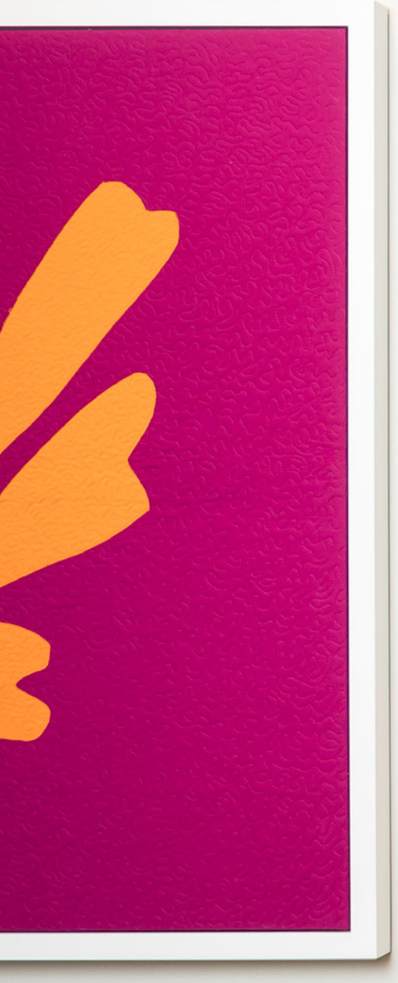
Where did you get your treatment for Hodgkin lymphoma?
I decided pretty quickly that I wanted to be treated at MSK. I lived nearby, and MSK is obviously the place to go for cancer. Also, I didn't want to be treated where I worked.

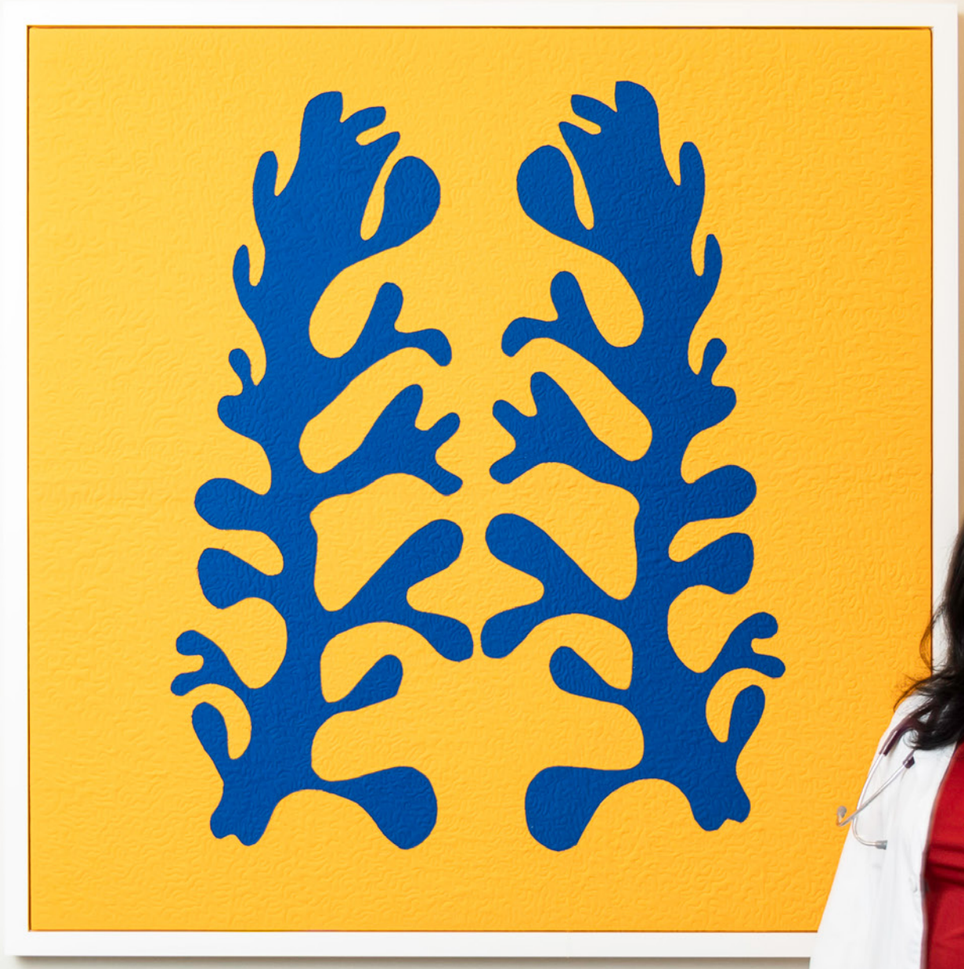
My oncologist was Craig Moskowitz. He left MSK about the time I started working here, in 2018. I now have my follow-up visits with Anita Kumar.

Do you tell your patients about your own cancer history?
I didn't in the beginning. But in the past few years, I've become more open to talking about my experiences. When I share my story with a patient, I worry that the conversation will end up being about me. But I realize that sometimes it's very helpful for patients to know that I truly understand what they're facing. That's why I decided to share my COVID-19 experience as well — because some of my patients were going through it.

I chose to go into oncology because during my residency I saw that the bonds oncologists have with their patients are different from other specialties. It's a very special relationship because they come to you in a major crisis situation. I realize now that for some patients, sharing my own experience is another way I can help them realize they are not alone and that I understand them.

How are you feeling now?
I've been in remission from the cancer since September 2016. I recovered from COVID-19 in a few weeks, but my sense of smell and taste only returned to normal many months later. Since my COVID-19 antibodies were only present for a short period after the infection, I got the Pfizer-BioNTech COVID-19 shot in December 2020 at MSK. I am participating in a research study to understand the immune response to the vaccine in cancer patients and survivors.






Gunjan L. Shah, MD, MS
Bone Marrow Transplant
1884

Administrative Spotlight

Throughout 2020, the administrative teams in the Department of Medicine stepped up to adapt to remote work and provide the best care for patients, even under difficult, evolving circumstances. The Care Coordinator teams in at the David H. Koch Center for Cancer Care at Memorial Sloan Kettering were on site during the height of the pandemic, covering in clinic and managing the limited-visitor policy and COVID-19 testing clinic. Clinical Research Coordinators and Clinical Research Specialists also pitched in to help with clinic coverage across different roles. Office Coordinators did an incredible job adapting to remote work and ensuring a seamless transition to telemedicine for our patients. It has truly required teamwork and dedication to get through this year, and we are grateful for the administrative staffs' dedication throughout 2020.

We would like to highlight the following people for their dedication and performance:

Office Coordinators

Ruth Seixas
Senior Office Coordinator
Leukemia Service
Ruth has done an incredible job at overseeing the scheduling and coordination for all bone marrow under sedation (BMAUS) procedures, including inpatient and outpatient procedures, while keeping her office well organized and taken care of.

Oliver Sarzynski
Office Coordinator
Leukemia Service
Oliver played a big role in the roll out of telemedicine at the start of the pandemic. He worked with several services across the institution, assisting with troubleshooting technology issues and ensuring that patients were successfully connected.

Raman Kaur
Administrative Assistant
Leukemia Service
Raman was a huge help to the Leukemia Service throughout 2020. In addition to ensuring that the administrative needs of Dr. Tallman and the Leukemia Service were met, she frequently flexed into the office coordinator role, helping her colleagues whenever needed. Raman also assisted with obtaining telemedicine licensures across the service.

Victoria Steward
Senior Office Coordinator
Hematology Service
Victoria did an incredible job managing a high volume of consultation requests with limited availability within the service. She ensured that each request was managed and escalated appropriately, in a timely manner.

Taylor Noto
Senior Office Coordinator
ABMT Service
Taylor played a major role in keeping patient care in the ABMT Service running smoothly this year by managing the Human Leukocyte Antigen (HLA) office and ensuring that workflows surrounding donor kits were not interrupted when staff were shifted into the remote setting.

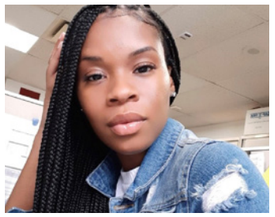
Hanna Bordacs
Office Coordinator
Lymphoma Service
Hanna has done a phenomenal job supporting multiple offices within the Lymphoma Service in 2020. Her answer to every request, favor, and challenge is always 'Yes, how can I help?'

Kayla Zambrana
Office Coordinator
Lymphoma Service
Throughout 2020, Kayla has consistently gone out of her way to help her team, both admin and clinical alike. She was loved by patients, quick to offer aid, and always asked what more she could do.

Catherine Sweeney
Office Coordinator
Myeloma Service
Catherine was a constant and reassuring support for her peers and clinical team in 2020. Her dedication to MSK's patients and mission was applauded by patients, through submission of caring hearts, and her Myeloma team.

Danielle Connolly
Office Coordinator
Myeloma Service
Throughout 2020, Danielle received numerous caring hearts from patients, showing her dedication not just to MSK but also to Dr. Shah's practice and the patients she treats. In addition, Danielle shared her experience in her role to aid in MSK's efforts to enhance diversity and inclusion.

Kelly Bevacqua and Lisandra Rosales
Administrative Assistants, ABMT Service
Both Kelly and Lisandra have played integral roles in the service this year by ensuring ongoing, smooth administrative operations in both Dr. Perales' and Dr. Giralt's offices and keeping meetings and communication streamlined for the service in the remote setting.



Sandy Lewis and Natasha Taylor
Care Advisors, ABMT Service
Sandy and Natasha have worked collaboratively throughout this year to manage the changing volumes of incoming ABMT consult requests and have continued to provide our patients with timely and clear information for their first visits, despite the new restrictions and workflows in place due to COVID-19.

Clinical Research Staff

Beth Hoover
Clinical Research Manager
ABMT Service
Beth was instrumental in getting the convalescent plasma protocol (IRB #20-144) open to accrual to provide a treatment option for COVID-19 positive patients.

Elizabeth Cathcart
Clinical Research Coordinator
Elizabeth has been and continues to be instrumental in managing the n-acetylcysteine protocol (IRB #20-168) that provides a treatment option for COVID-19 positive patients.

Laura Barton and Kelcey Skinner
Clinical Research Associates, ABMT Service
Laura and Kelsey managed the convalescent plasma trial (IRB #20-144), which accrued 70 patients in four months, with the first 62 alone in one month of the trial opening.

Cristina Soto Izquierdo and Lisa Flynn (right)
Clinical Research Associate; Research Program Manager
ABMT Service
Cristina and Lisa were instrumental in managing the tocilizumab study (IRB #20-185) as a treatment for COVID-19 positive patients, especially during last year's spring peak.

INTERVIEW

Chelsea Brooklyn
Manager,
BMT & Supportive Care

Bone Marrow Transplant Program Pioneers the Development of New Treatments

Memorial Sloan Kettering is a leader in offering the latest treatments for blood cancer. This includes chimeric antigen receptor (CAR) T cell therapies as well as the most cutting-edge approaches to stem cell and bone marrow transplantation (BMT).

One of the people who plays a vital role in making sure these groundbreaking treatments continue to move forward is Chelsea Brooklyn, the Administrative

Manager for the Bone Marrow Transplant Program at MSK. Ms. Brooklyn helps to coordinate all of the different groups that are responsible for the administration of these therapies, including doctors, nurses and advanced practice providers, pharmacists, and others.

"These treatments, including CAR T, are complex," Ms. Brooklyn says. "There are many different things that go into us being able to offer them to our patients. One of the most important is having good communication to make sure that everyone understands the specifics of every therapy that we offer."

A Mission to Offer the Best, Cutting-Edge Treatments

When a new CAR T product receives approval from the FDA, there are several things that need to happen before MSK can offer the treatment to patients. "One of the most important parts is our risk management program," Ms. Brooklyn explains. Because these products are so complicated and have so many side effects, everyone who's responsible for prescribing or administering a CAR T therapy needs to go through risk evaluation and mitigation training.

"MSK is very lucky because we've been doing CAR T treatments for more than ten years in the research setting," she adds. "There's a lot of knowledge here about how to treat these patients."

> "One of the most important things is having good communication to make sure that everyone understands the specifics of every therapy that we offer."
>
> Chelsea Brooklyn

Despite the excitement when a new treatment is approved, being able to offer clinical trials of new therapies or of new ways to give existing therapies, rather than standard treatment, is the focus at MSK. "It's part of our mission, ensuring that our patients are always getting the best treatment option for their disease," Ms. Brooklyn says. "That could be a new, investigational treatment. It also could mean we are giving a commercial product, but doing it as part of a trial — such as changing the dose of steroids or comparing CAR T to another treatment, like a BMT or standard-of-care chemotherapy."

Expanding the Role of Cell Therapy

Within the next year, treatment options for patients are expected to expand with the FDA's anticipated approval of new CAR T treatments. "Something I'm most excited about are CAR T indications for multiple myeloma patients who have failed every other treatment," Ms. Brooklyn says. We are anticipating a large rollout when this goes live."

Also on the horizon is a different kind of cell therapy: tumor-infiltrating lymphocytes (TILs), which are being developed for metastatic solid tumors, especially melanoma. With this treatment, the patient's cells are collected in the operating room when they undergo surgery to remove all or part of their primary tumor. The cells are treated and later infused back into the bloodstream so where they can travel through the body and seek out metastatic disease.

Several other important efforts have been a focus of MSK's BMT team over the past few years. These include revamping the way that HLA testing is done so that stem cell recipients and donors can be matched more efficiently. They also include streamlining and revamping the new visit process so that patients can see physicians in the fastest time frame possible. The team has also expanded the BMT initiative within the MSK Alliance with Hartford HealthCare Cancer Institute. This program helps patients being treated at Hartford to receive their transplants at MSK.

Recognizing Dedication to Patient Care

In 2020, Ms. Brooklyn received the Spirit of Transplant Award from MSK. This award was created ten years ago, in recognition of the one-year anniversary of MSK's Adult Bone Marrow Transplant Service. The award recognizes MSK employees and teams who have had an important impact on the lives of patients undergoing BMTs.

"Chelsea has been invaluable as our administrative program manager, and her organizational skills and talents have allowed us to better integrate with our pediatric colleagues and other services in the institution," said Sergio Giralt, Deputy Head of the Division of Hematologic Oncology, at the time the recipients were announced. "In addition, she has been instrumental in onboarding the different CAR T products in a seamless manner."

"I always try to put my heart and soul into the transplant team," Ms. Brooklyn concludes. "I do everything I can to make sure we're doing the very best we can for our patients."

Advanced Practice Providers

The Division of Hematologic Malignancies' advanced practice providers (APPs) display a high level of commitment and professionalism every day. In 2020, the APP staff demonstrated exceptional dedication to their patients and colleagues during a particularly challenging year. We are incredibly grateful for their efforts and proud of their collective accomplishments, including those APPs that were redeployed to other units.

APP Highlighted Contributions

- During the height of the COVID-19 pandemic, the inpatient liquid team, made up of the Leukemia, Lymphoma, and Myeloma Services, worked cohesively with other multidisciplinary colleagues to staff three dedicated COVID-19 heme teams — no easy feat. Their dedication, grit, and overall commitment to providing excellent patient care never faltered despite being faced with this enormous challenge.
- In August 2020, MSK launched the inpatient bone marrow procedure team, which is an APP-run procedure team. In collaboration with nursing, medicine, and anesthesia colleagues, the Leukemia Service APPs have been trained to perform bone marrow biopsies. With the launch of this team, the APPs have been able to increase the availability of bone marrow procedure slots to inpatients. This includes procedures performed with anesthesia at the bedside.

APP Honors:

- **Naomi Cazeau** (outpatient BMT nurse practitioner) was appointed Associate Editor for the *Clinical Journal of Oncology Nursing's* Supportive Care Department in 2020.
- **Angela Chan, DNP, AGPCNP-BC,** defended her doctoral dissertation and was awarded her Doctorate in Nursing Practice from Hunter College School of Nursing. Her dissertation title is "Enhancement of a Standardized Handoff Tool with Automated Key Elements in Oncology Patients to Improve Patient, Provider, and Organizational Outcomes."
- **Kevin O'Hara** (outpatient BMT physician assistant) was elected to the PA Council at MSK.

Nursing

Even before COVID-19, the World Health Organization designated 2020 the "Year of the Nurse and Midwife," marking the 200th anniversary of Florence Nightingale's birth. It's part of a global recognition that nurses and midwives are first responders and are often the sole providers on the front line of care in their communities. In hindsight, this designation was prophetic as nurses across the globe, including at MSK, have responded to COVID-19 and are heroes on the front lines providing hands-on-care to those afflicted with the disease.

Nurses at MSK have risen to the occasion with the same selflessness, determination, compassion, and excellence that they provide every day to our cancer patients. They did not hesitate to embrace new clinical demands and operational changes. They quickly adopted new technology and maintained focus during a rapidly and continuously evolving landscape. They continue to support one another and the entire MSK community in caring for patients and their families during this unprecedented period. Their unparalleled dedication and resilience will always be remembered.

Nursing Highlighted Contributions

- **Jessica Magaldi** was redeployed to the COVID-19 unit.
- **Kelly Gleason** was redeployed to the COVID-19 vaccine clinic.
- **Philip Rivera** was redeployed to the inpatient unit to support patients with COVID-19.
- **Erica Dunn** was redeployed to support the COVID-19 vaccine clinic at 67th Street Haupt Pavilion for employee and patient vaccinations. She played an integral role to the vaccine clinic relocation to the David H. Koch Center for Cancer Care at Memorial Sloan Kettering Cancer Center in mid-February 2021.
- **Erica Dunn, Carina McLoughlin, Elizabeth Ga**, and **Joanne Taylor** worked diligently on the Clinical Nurse Coordinator (CNC) taskforce to help clarify the role of the CNC.
- **Rachel Baruch** and **Philip Rivera** worked to streamline germ cell tumor transplants.
- **Erica Dunn** and **Elizabeth Ga** created an electronic document to guide CAR T cell collections.

M-7 Nursing Team

In a collaboration between Nursing and Lab Medicine, we opened the first apheresis unit outside of MSK's main campus at the David H. Koch Center for Cancer Care at MSK. Pictured here from the left: Peter Li, Cheryl Gilroy, Krystal Brad, Christopher Padilla, and Kayon Nash

Our Patient Care Technician group was exceptional and integral to device integration at the David H. Koch Center for Cancer Care at MSK. Patient care technicians **Brian Deverteuil, Joanie Ramirez,** and **Milagros Pacheco** were redeployed to inpatient units to assist with the COVID-19 pandemic.

The Cell Infusion Unit will support cell infusions throughout the institution, including transplants and CAR T cell therapy. These infusion nurses have a unique competency to care for patients receiving any cell therapies.

Nursing Promotions

- **Kerry-Ann Newell** from the new Cell Infusion Unit was promoted to Clinical Nurse III.
- **Meghan Salcedo** was promoted to Clinical Trials Nurse IV.
- **Kelly Werner**, **Linh Nguyen**, and **Julie Kinoshita** were promoted to Clinical Trials Nurse III.
- **Carina McLoughlin** was promoted to Clinical Nurse III.

Nursing Certifications

The following individuals became Oncology Certified Nurses in 2020:

- **Jacqueline Malanban** (Clinical Nurse II — Cell Infusion Unit)
- **Julie Kinoshita** (Clinical Nurse III — Leukemia)
- **Claudia Simone** (Clinical Trials Nurse II — Inpatient)

The following individuals became blood and marrow transplant certified nurses in 2020:

- **Julie Harris** (Clinical Nurse II — BMT Outpatient)
- **Linh Nguyen** (Clinical Nurse III — BMT)
- **Natasia Rodriguez** (Clinical Trials Nurse II — BMT)

Nursing Honors

- **Meghan Salcedo** received the 2020 Samuel and May Rudin Award for Excellence in Clinical Trials Nursing. Meghan is a clinical trials nurse III in the Outpatient Myeloma Service.
- **Meredith Caprio** (Clinical Nurse IV — Cell Infusion Unit) worked on a multidisciplinary project and submitted an abstract that was accepted to TCT meeting: How Clinical Inquiry Directed a Multidisciplinary Evidence-Based Practice Change. This project will change the way MSK administers stem cells.
- **Lilly Reilly** (Clinical Nurse IV) received the 2020 Clinical Nursing Excellence Award for American Society for Transplantation and Cellular Therapy. This award is presented to a nurse who has made a significant impact in the field of BMT nursing or achieved a professional milestone.
- In recognition of outstanding service in the Bone Marrow Transplant Service, the **M-7 Nursing Team** received the Spirit of Transplant Award. The M7 Nursing Team stood out this year with their ability to rapidly become a COVID-19 Unit and the dedication in which they took care of these challenging patients. During the peak of the pandemic, 54 registered nurses, 16 patient care technicians, and six unit assistants worked onsite to care for COVID-19-positive patients.

DHM Advanced Practice Providers and Nursing Highlighted Presentations:

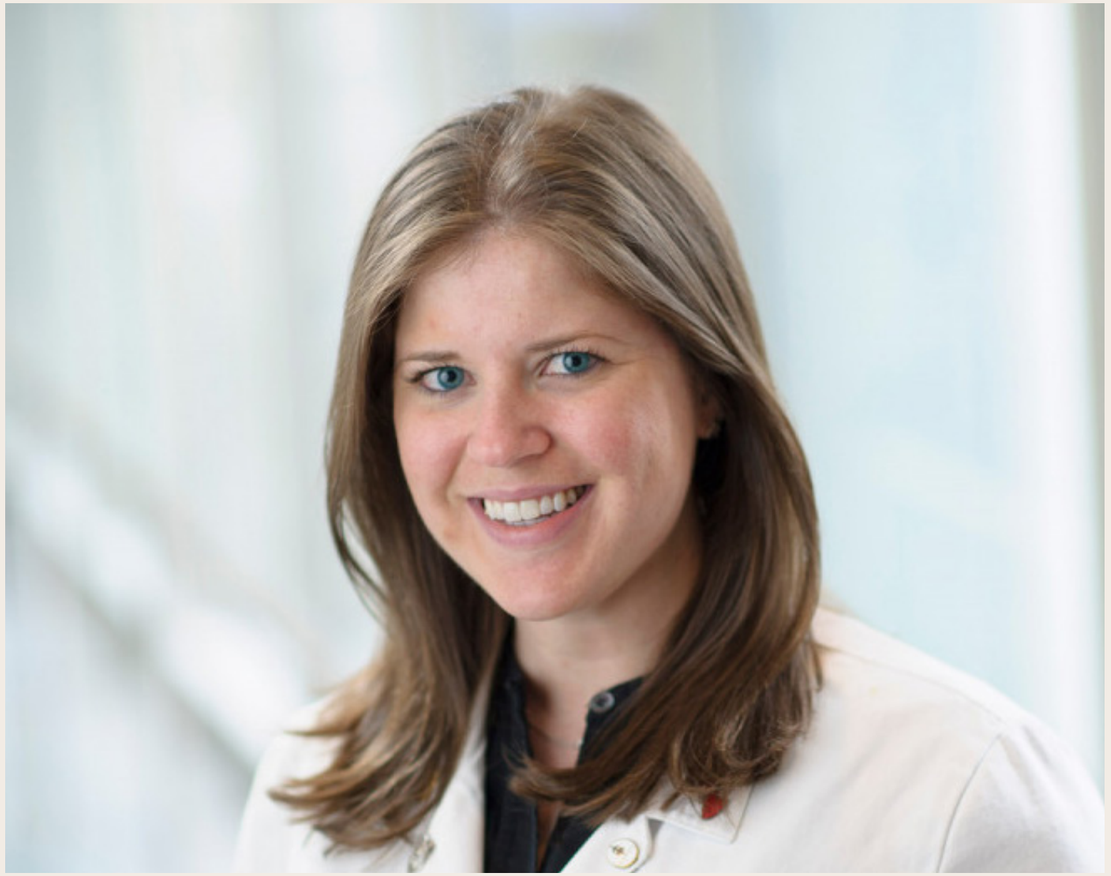
- **Kathleen Cavalier** and **Naomi Cazeau** (outpatient BMT NPs) presented abstract at the Transplantation & Cellular Therapy annual conference in 2020, titled: "Outpatient BEAM using daily etoposide and cytarabine with autologous hematopoietic stem cell transplantation for lymphoma is feasible and decreased inpatient length of stay."
- **Melanie Douglas** (Inpatient Lymphoma) presented "Lymphoma: Common Chemotherapy Regimens and Side Effects" during this year's Physician Assistant week, held in November 2020.
- **Marci Andrejko** (outpatient BMT NP) presented at the National Comprehensive Cancer Network Virtual Nursing Forum: Advancing Oncology Nursing in Hematologic Malignancies, which was held on October 8, 2020. The presentation was titled: "Optimizing Outpatient Care in Hematopoietic Stem Cell Transplant Patients."
- **Helen Hancock** (Clinical Trials Nurse Practitioner) presented "My Role in Clinical Trials in T Cell Lymphoma and Relapsed/Refractory Hodgkin's Lymphoma" at "Gathering Together Around Cancer." She works alongside physicians Alison Moskowitz and Steven Horwitz in the management of patients on predominantly phase I and II clinical trials that are exploring novel targeted therapies and on immunotherapy-based trials for T cell lymphoma and Hodgkin lymphoma.
- **Kevin O'Hara** (outpatient BMT PA) presented a talk titled "Overview of immunotherapy toxicity in oncology: A focus on CAR-T and checkpoint inhibitors" at the American Academy of Physician Assistant Annual Conference in 2020.
- **Amy Pierre**, provided expert insights for advanced practitioners into the most talked-about abstracts on hematologic malignancies from the American Society of Clinical Oncology virtual meeting.
- **Natasia Rodriguez1**, Jasme Lee2, Lisa Flynn1, Fiona Murray1, Sean Devlin PhD2, Cristina Soto1, Christina Cho1,3, Parastoo Dahi1,3, Sergio Giralt1,3, Miguel Angel Perales1,3, Craig Sauter MD1,3, Doris M. Ponce, MD1,3. "Secondary Graft-versus-Host Disease (GVHD) Prophylaxis with Oral Proteasome Inhibitor Ixazomib Is Associated with Low Incidence of Recurrent, Late Acute and Chronic GVHD and Facilitated Calcineurin Inhibitor Taper Within the First Year Post Allogeneic Stem Cell Transplantation " – American Society of Hematology Annual Meeting, December 2020.

DHM Advanced Practice Providers and Nursing Highlighted Publications:

- **Douglas M.** Polatuzumab Vedotin for the Treatment of Relapsed/Refractory Diffuse Large B Cell Lymphoma in Transplant-Ineligible Patients. J Adv Pract Oncol. 2020;11(5):521-528. doi:10.6004/jadpro.2020.11.5.8
- **Cazeau N.** Social Isolation: Managing Psychological Distress in Hospitalized Patients During the COVID-19 Pandemic. Clin J Oncol Nurs. 2020 Oct 1;24(5):472-474. doi: 10.1188/20.CJON.472-474. PMID: 32945803.

Our first and novel "Cell Infusion Unit." Starting at the bottom of the screen: Kirsten Louie, Meredith Caprio, Cheryl Gilroy, Elymra Mordkovich, Andrea Arvidson, Mollie Dlugasch, Faye Inumerables, Sweta Patel, and Jacqueline Malabanan (front).

- Gaulin C, **Chan A,** Derkach A, et al. Hypofibrinogenemia and disseminated intravascular coagulation rarely complicate treatment-naïve acute lymphoblastic leukemia. Leuk Lymphoma. 2020;61(10):2497-2501. doi:10.1080/10428194.2020.1765236
- **Kevin Michael OHara,** and coauthor Eric C Nemec II PharmD published a book chapter titled Antimicrobial Pharmacotherapy in the latest textbook for APP titled Advanced Pharmacology for Prescribers. This text instructs the new APP on pharmacology using practical clinical cases.
- Lin RJ, **Cohen AG,** Stabler SM, et al. Characteristics and Impact of Post-Transplant Interdisciplinary Palliative Care Consultation in Older Allogeneic Hematopoietic Cell Transplant Recipients. J Palliat Med. 2020;23(12):1653-1657. doi:10.1089/jpm.2019.0611
- **Pierre A,** Williams TH. African American Patients With Multiple Myeloma: Optimizing Care to Decrease Racial Disparities. Clin J Oncol Nurs. 2020;24(4):439-443. doi:10.1188/20.CJON.439-443
- Maus MV ..., **Claudia Diamonte** et al. Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immune effector cell-related adverse events. J Immunother Cancer. 2020;8(2):e001511. doi:10.1136/jitc-2020-001511
- Mato AR ..., **Colleen Dorsey** et al. Phase 2 Study of the Safety and Efficacy of Umbralisib in Patients with CLL Who Are Intolerant to BTK or PI3Kδ Inhibitor Therapy [published online ahead of print, 2020 Dec 1]. Blood. 2020;blood.2020007376. doi:10.1182/blood.2020007376
- **Salcedo M,** Lendvai N, Mastey D, et al. Phase I Study of Selinexor, Ixazomib, and Low-dose Dexamethasone in Patients With Relapsed or Refractory Multiple Myeloma. Clin Lymphoma Myeloma Leuk. 2020;20(3):198-200. doi:10.1016/j.clml.2019.12.013
- **Kleber J,** Cohen B. Reducing Waste and Increasing Sustainability in Health Care Settings. Am J Nurs. 2020;120(4):45-48. doi:10.1097/01.NAJ.0000660032.02514.ec
- Baldwin-Medsker A, Holland J, **Rodriguez ES.** Access to Care: Using eHealth to Limit Location-Based Barriers for Patients With Cancer. Clin J Oncol Nurs. 2020;24(3):16-23. doi:10.1188/20.CJON.S1.16-23
- Nawas, M. T., Landau, H. J., Sauter, C. S., **Featherstone, C. A., Kenny, S. A., Rodriguez, E. S.,** Johnson, L. G., Giralt, S. A., & Scordo, M. (2020). Pilot Study of Telehealth Evaluations in Patients Undergoing Hematopoietic Cell Transplantation. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation, 26(6), e135–e137. https://doi.org/10.1016/j.bbmt.2020.02.004



INTERVIEW

Susan McCall
Advanced Practice Provider Manager

Advance Practice Providers Build Strong Relationships with Patients

Susan McCall started college as an engineering major, but switched to nursing because she felt a pull to work in a profession where she could help people. She's been a nurse at Memorial Sloan Kettering for her entire career, starting as a Registered Nurse providing chemotherapy, and later becoming a nurse practitioner. In 2019, she was promoted to Advanced Practice Provider (APP) Manager, overseeing other nurse practitioners and physician assistants who work in the inpatient setting caring for patients being treated for leukemia, lymphoma, and multiple myeloma.

"I love patient care, but it's the team who I work with that gets me out of bed every morning," Ms. McCall says. "Every day it's such a privilege to work with such a talented group of professionals and to see the contributions that all of them make. The connections that I've built with the other APPs and my multidisciplinary colleagues are relationships that I value very much."

Ms. McCall works closely with the three other APP managers in the Division of Hematologic Malignancies — Cathy Featherstone, who leads inpatient APPs working within the Bone Marrow Transplant (BMT) Service; Nicole LeStrange, who manages APPs on the BMT outpatient side; and Tara Duggan, who manages APPs working for the Leukemia, Lymphoma, and Multiple Myeloma Services in the outpatient setting. "All of them are extremely talented at what they do," Ms. McCall says. "Cathy and Nicole mentored me when I was starting out as a nurse practitioner, and now I'm mentoring others."

Supporting Patients Throughout Their Treatment Journeys

Before she became an APP manager, Ms. McCall worked on the Lymphoma Service for almost a decade, in partnership with medical oncologists Anita Kumar, Craig Moskowitz, and Alison Moskowitz. One of the diseases she specialized in treating was mantle cell lymphoma (MCL), a rare subtype of non-Hodgkin lymphoma.

"Lymphoma is a very heterogeneous disease, with over 70 subtypes," she notes. "The lymphoma specialists at MSK are great because they not only specialize in lymphoma, but subspecialize in some of these rare types."

> **"At MSK, we take pride in doing everything we can to take care of our patients."**
>
> Susan McCall

As a nurse practitioner, Ms. McCall became familiar with the range of treatments for MCL and other types of lymphoma, including working in the area of clinical trials. "It was a privilege to be a part of that and to see all the progress that was being made," she notes. "For the drugs that eventually were approved by the FDA, it was so rewarding for both the medical team and the patients. It's a huge leap of faith for patients to volunteer for trials, and I felt honored to be part of their journeys."

MCL is a type of lymphoma that is not considered curable, but a number of treatments, including cell therapies like CAR T as well as targeted therapies, have changed the outlook for this disease. They allow some patients to stay in remission for many years. "I always made sure that my patients understood not only the immediate plans for their care but also that we had other tools in our toolbox that we could use to take care of them if those treatments stopped working," she says. "Taking care of these patients as a nurse practitioner had a strong psychosocial component. I always wanted them to know that I was there for them and build these strong relationships, which can last for many years."

Pamela Drulinski, MD, and Susan McCall

Rising to the Challenges of COVID-19

The COVID-19 pandemic has been a challenging time for Ms. McCall and her colleagues. During the first few months of the pandemic, in the spring of 2020 when some treatments were put on hold, many APPs, including those who were only in their first few years of practice, had to adapt and learn how to care for patients who were hospitalized with both blood cancer and COVID-19.

"I was so impressed with all of the APPs," she says. "Early in the pandemic, the teams were faced with several challenges, but we all worked together to identify opportunities of how to manage COVID-19 in this group of patients."

In addition to providing patient care during the pandemic, many APPs within the Division of Hematologic Malignancies have undertaken research projects to determine the best way to manage COVID-19 infections in patients being treated for blood cancers. Some of these projects have led to approaches that have benefited patients being treated at MSK and beyond.

"At MSK, we take pride in doing everything we can to take care of our patients," Ms. McCall says. "As a manager, it was my priority to support the team to the best of my ability because we were all in it together. It requires a lot of grit and perseverance to get through these experiences, whether that's helping patients to cope with COVID-19 or to understand the complexities of cancer treatment."

Pharmacy Clinical Trials and Publications

The clinical pharmacy specialists serve on multidisciplinary teams as experts in the therapeutic use of medications. They also act as liaisons between the Pharmacy Department and physicians, nurses, and other disciplines. Additionally, they are actively involved in clinical research and guideline development and contribute to national organizations essential to their fields. The Hematology/Oncology pharmacists include eight clinical pharmacists on the BMT Service, six clinical pharmacists on the Leukemia Service, five clinical pharmacists on the Lymphoma Service, and two clinical pharmacists on the Multiple Myeloma Service.

Selected Publications

Yerram P, Thackray J, Modelevsky LR, Land JD, Reiss SN, Spatz KH, Levoir AC, Pak TK, Dao PH, Buege MJ, Derespiris LM, Lau C, Orozco JS, Boparai M, Koranteng LA, Reichert KE, Yan SQ, Daukshus NP, Mathew S, Buie LW, Tizon RF, Freeswick S, Liu D, Harnicar S. Outpatient clinical pharmacy practice in the face of COVID-19 at a cancer center in New York City. J Oncol Pharm Pract. 2021 Jan 17;1078155220987625. doi:10.1177/1078155220987625

Daley RJ, Rajeeve S, **Kabel CC,** Pappacena JJ, **Stump SE,** Lavery JA, Tallman MS, Geyer MB, Park JH. Tolerability and toxicity of pegaspargase in adults 40 years and older with acute lymphoblastic leukemia. Leuk Lymphoma. 2021 Jan;62(1):176-184. doi:10.1080/10428194.2020.1824068

Stump SE, Trepte M, Shaw JR, et al. Evaluation of mobilization efficacy with an extended interval following plerixafor administration. J Oncol Pharm Pract. 2020 Oct;26(7):1590-1597. doi:10.1177/1078155219900909

Xiao W, Miles LA, Bowman RL, Durani V, Tian HS, DelGaudio NL, Mishra T, Zhu M, Zhang Y, **Stump SE,** Tallman MS, Levine RL, Cai SF. A JAK2/IDH1-mutant MPN clone unmasked by ivosidenib in an AML patient without antecedent MPN. Blood Adv. 2020 Dec 8;4(23):6034-6038. doi:10.1182/bloodadvances.2020003326

Dixon BN, **Daley RJ**, Buie L, et al. Correlation of IL-6 secretion and hyponatremia with the use of CD19+ chimeric antigen receptor T-cells. Clin Nephrol 2020; 93(1): 42-46. doi:10.5414/CN109872

Buege MJ, Kumar A, **Dixon BN, Tang LA, Pak T, Orozco J, Peterson TJ, Maples KT.** Management of mantle cell lymphoma in the era of novel oral agents. Ann Pharmacother. 2020 Sep;54(9):879-898. doi:10.1177/1060028020909117

LeVoir A, Lee M, Fitzgibbon D, Hsu M, Posner K. Chronic Opioid Therapy in Cancer Survivors at a Specialty Oncology Pain Clinic: Opioid Dosing, Efficacy, and Safety During Five Years of Pain Management. J Pain Symptom Manage. 2020 Nov 10;S0885-3924(20)30866-6. doi:10.1016/j.jpainsymman.2020.11.002

Lin A, Flynn J, **DeRespiris L, Figgins B, Griffin M, Lau C, Proli A,** et al. Letermovir for Prevention of Cytomegalovirus Reactivation in Haploidentical and Mismatched Adult Donor Allogeneic Hematopoietic Cell Transplantation with Post-Transplantation Cyclophosphamide for Graft-versus-Host Disease Prophylaxis. Biol Blood Marrow Transplant. 2020;S1083-8791(20)30663-7. doi:10.1016/j.bbmt.2020.10.009

Peterson TJ, Orozco J, Buege M. Selinexor: A First-in-Class Nuclear Export Inhibitor for Management of Multiply Relapsed Multiple Myeloma. Ann Pharmacother. 2020;54(6):577-582. doi:10.1177/1060028019892643

Poster Presentations

Geyer MB, **King AC,** Park JH. Trials in Progress: Phase II Study of Blinatumomab and Concurrent Oral Tyrosine Kinase Inhibitor Therapy as Consolidation and Maintenance Therapy for Patients with Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia Following Chemotherapy-Sparing Induction. American Society of Hematology Meeting (ASH); December 2020; Virtual.

Buege MJ, Dao PH, Drill E, **Levoir AC, Pak T, Peterson TJ,** Straus DJ. IVAC +/- R for Relapsed or Refractory B-Cell Non-Hodgkin Lymphomas: Real-World Experience in the Modern Era. Poster presented at: American Society of Hematology Annual Meeting (ASH); December 2020; Virtual.

Sawalha Y, Goyal S, Switchenko JM, Romancik JT, Kamdar M, Greenwell IB, Hess BT, Isaac K, Portell CA, Mejia Garcia AV, Goldsmith SR, Grover NS, Riedell PA, Karmali R, Burkart M, **Buege MJ,** Akhtar OS, Torka P, Kumar A, Hill BT, Kahl BS, Cohen JB. Outcomes of Patients with Relapsed Mantle Cell Lymphoma Treated with Venetoclax: A Multicenter Retrospective Analysis. Poster presented at: American Society of Hematology Annual Meeting (ASH); December 2020; Virtual

Lin A, Dahi P, Flynn J, Uruburo C, McGreary I, Schofield R, **Bhatt V, DeRespiris L, Figgins B, Griffin M, Lau C, Proli A,** et al. Effect of Melphalan Exposure in Patients with Lymphoma Undergoing Autologous Hematopoietic Stem Cell Transplant (AHCT). Biol Blood Marrow Transplant 2020; 26: S230-231. doi.org/10.1016/j.bbmt.2019.12.472.

Peterson KT, Lin A, Ruiz JD, Zheng J, et al. Comparison of Conditioning Regimens for Allogeneic Hematopoietic Cell Transplantation in Non-Hodgkin Lymphoma. Biol Blood Marrow Transplant 2020; 26: S161-162. doi.org/10.1016/j.bbmt.2019.12.716.

Lau C, Shah GL, Politikos I, Maoly M, Naptuo K, Skinner K, Devlin SM, **Bhatt V,** et al. Letermovir Cytomegalovirus (CMV) Prophylaxis in Adult Seropositive Cord Blood Transplant (CBT) Recipients Is Highly Efficacious and Likely Cost-Effective. Late-Breaking Abstract, TCT Meeting 2020. Orlando, Florida.

Michael Buege, PharmD, BCOP

National Presentations

- As part of A Comprehensive Guide to the Complexities of Non-Hodgkin Lymphoma, **Michael Buege, PharmD, BCOP (Lymphoma Service)** presented, “Module 4: Therapeutic Breakthroughs in the Treatment of Relapsed/Refractory Mantle Cell Lymphoma” for Pharmacy Times CE. December 2020.

- **Lauren DeRespiris, PharmD, BCOP (BMT Service)** presented “Updates in Cellular Therapy” at the Annual Transplantation and Cellular Therapy Meetings of ASTCT and CIBMTR in Orlando, Florida, in February 2020.

- **Sarah Stump, PharmD, BCOP (Leukemia Service)** presented “Novel Therapies in Acute Myeloid Leukemia (AML)” at the Advanced Practice Providers Oncology Summit in March 2020.

- **Amber King, PharmD, BCOP (Leukemia Service)** presented “Clinical Management of CLL Patients Receiving a BCL-2 Inhibitor” at the Association of Physician Assistants in Oncology (APAO) Clinical Meeting in August 2020.

- **Charlene Kabel, PharmD, BCOP (Leukemia Service)** presented:
  - “Advances in Front-Line Treatment of CLL: Is Chemoimmunotherapy Obsolete?” at the Hematology/Oncology Pharmacy Association in October 2020.
  - “MPNs: Diagnosis, Treatment, and Side Effect Management” at the Leukemia and Lymphoma Society Professional Education Webcast in January 2020.
  - “CLL Challenges and New Options for Care in the Outpatient Setting” at the Advanced Practice Providers Oncology Summit in 2020.

- **Tim Peterson, PharmD, BCOP (Multiple Myeloma Service)** presented:
  - ACCP BCOP Recertification Course: Multiple Myeloma and Gynecologic Malignancies in March 2020.
  - “The Role for Biosimilars in Oncology” at the Pharmacy Times Peer Exchange in February 2020.

- **Terry Pak, PharmD, BCOP (Lymphoma Service)** presented “Diffuse Large B-Cell Lymphoma Treatment Update” at the Hematology/Oncology Pharmacy Association in March 2020.

National Committee Representation

- **Ryan J. Daley, PharmD, BCOP (Leukemia Service)** holds a Pharmacy Committee Appointment on the Alliance f or Clinical Trials in Oncology.

- **Sarah Stump, PharmD, BCOP (Leukemia Service)** is a member of the Practice Outcomes and Professional Benchmarking Committee in the Hematology/Oncology Pharmacy Association.

- **Andréa LeVoir, PharmD, BCOP (Lymphoma Service)**
  - Hematology Oncology Pharmacy Association, Needs Assessment Committee (2019-2020)
  - Hematology Oncology Pharmacy Association, Hematology/Oncology Pharmacy Association Breakout Session Committee (2020-2021)

- **Tim Peterson, PharmD, BCOP (Multiple Myeloma Service)** is an Abstract Review Committee Member for the Hematology/Oncology Pharmacy Association.

- **Michael Buege, PharmD, BCOP (Lymphoma Service)** is a Grant Review Committee Member for the Hematology/Oncology Pharmacy Association.

- **Andrew Lin, PharmD, BCOP (BMT Service)**
  - Chair-elect – American Society for Transplantation and Cellular Therapy Pharmacy Special Interest Group, Research Working Group
  - Grant Review Committee Member, Hematology/Oncology Pharmacy Association

Kathleen Atlas, MD

Nocturnists

From 7:00 PM to 7:00 AM, the nocturnists hospitalist staff provides coverage for the entire medical service at Memorial Sloan Kettering Cancer Center. They handle 40% of admissions in the Department of Medicine.

Kathleen Atlas, MD, Deputy Service Chief (for nights) of the Hospital Medicine Service, and nocturnist Jamie Riches, DO, say that working at night, sacrificing sleep, and caring for critically ill patients is often grueling. But being in the presence of such strong individuals inspires them to make patients as comfortable as possible and to keep each interaction close to their hearts.

On April 10, 2020, Dr. Atlas was promoted to Deputy Service Chief (for nights) on the Hospital Medicine Service. Since 2013, she had served as the Lead Nocturnist and Clinical Director for Nights and has been instrumental in building the MSK Nocturnist program into a thriving group of outstanding MDs and APPs. In her new role as Deputy Service Chief, Dr. Atlas will continue to have accountability for overnight operations of the Hospital Medicine Service, including participation in recruitment and training of new faculty members; and she will continue to foster collaborations and interactions with multidisciplinary night team members.

The Division of Hematologic Malignancies sponsors a seminar series. Nocturnists do not have access to many of the lectures and educational opportunities available during the day, due to their schedules. The seminars are held in the evenings, so nocturnists are better able to attend.

Nocturnists
Kathleen Atlas, MD
Jamie Riches, DO
Stacy Lee Anderson, MD
Elizabeth Maina, MD
Ross Ehmke, MD
Chika Okoli, MD
Evan Stewart, MD
Rezana Mara, MD
Ariel Peleg, MD
Amare Assefa, MD
Darren Pan, MD
Haaris Beg, MD
Samuel Freedman, MD
Raphael Rabinowitz, MD
Nina Kogekar, MD
Jaspreet Banga, MD
Karolina Jaluba, MD
Matthew Kerwin, MD
Margot Hedlin, MD
Karen Ma, MD
Isha Singh, MD
Joie Singh, MD
Andrew Yaeh, MD
Brian Yum, MD

APPs
Shelley Brunkan, PA
Akosua Darkwah, NP
Anna Foskin, NP
Minru Hwang, NP
Yvette Murillo, NP
Sejal Singh, PA
Kadiatou Sow, PA
Ana Villacis-Velez, NP

MSK Fellows Rise to the Challenges of COVID-19 Pandemic

The COVID-19 pandemic has upended lives everywhere around the world. In March 2020, Memorial Sloan Kettering's hematologic oncology fellows were in the middle of their academic year when they had to very quickly change the way they were caring for cancer patients. At the same time, many of them volunteered to take on additional roles, taking care of people with COVID-19 at several New York City-area hospitals.

"Our fellows really rose to the challenge," says hematologist Jodi Mones, who is an Associate Program Director of MSK's Medical Oncology/Hematology Fellowship Training Program. "They showed incredible leadership skills, comradery, and collegiality."

Fellowship training is one of the last steps that new doctors take toward becoming independent physicians. It's also the time when they hone their skills in the area in which they've chosen to specialize. At MSK, many fellows also take part in laboratory work, developing further expertise in a particular area of cancer research.

Jodi Mones, MD, is an Associate Program Director of MSK's Medical Oncology/Hematology Fellowship Training Program

Going Where the Need Was Greatest

"When everything was starting in February and March, it felt like there was a storm approaching," says Ben Diamond, who was acting as chief fellow at that time. "We knew that cases would be rising, and we worked tirelessly to come up with plans to cover any staff who may be out due to illness as well as the influx of patients who would be entering the hospital with COVID-19."

Although MSK treated many patients with COVID-19, as well as its own cancer patients and those who were transferred from other hospitals, Memorial Hospital was not overwhelmed to the degree that many other hospitals in the New York City area were. Additionally, because some cancer treatments were postponed or put on hold, the fellows quickly realized that they could best serve patients by volunteering to work at other area hospitals.

"I had trained at Columbia University Medical Center for my residency, and they reached out and said that they were looking for people to lend a hand," says fellow Susan DeWolf. "It was a tragic time in the city, and everyone felt like they wanted to do everything they could to help. It felt like, if you had the skills, you should put them to good use."

Dr. DeWolf ended up working seven full-day shifts over a two-week period, helping to run a pop-up intensive care unit (ICU) in the emergency room. Other fellows from MSK also volunteered at Columbia as well as Weill Cornell Medical Center and Montefiore Medical Center. "I had ICU training as part of my medical residency experience," she notes. "It was like jumping back into my old scrubs and feeling that old muscle memory. I also felt really well supported by the residents and the faculty there."

Fellow Max Stahl spent one week at Weill Cornell. "The people we were taking care were very sick," he remembers. "We were scared for our patients as well as for ourselves and our own families."

Back in the Clinic with Changes in Place

As the fellows who had gone to work at other hospitals returned to MSK, they found a changed landscape. In many areas of care, including hematologic malignancies, appointments were almost completely virtual, offered by telemedicine. This presented further challenges, although Dr. Mones says that because the fellows tended to have more comfort working in the virtual space than some of their older colleagues, they were able to make important contributions to easing the transition throughout the division.

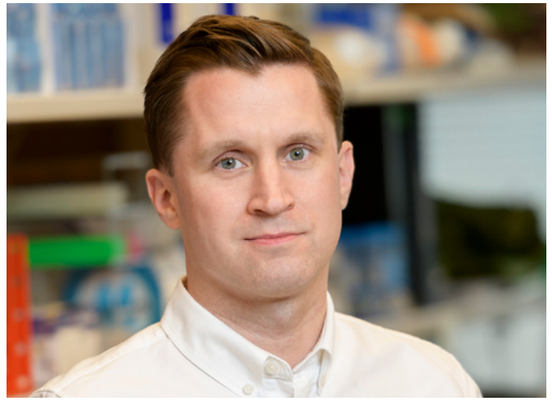
"The fellows were able to take a lead in telemedicine," Dr. Diamond says. "There were growing pains in the beginning, but we were able to get back to patient care. And now we're doing a combination of virtual and in-person visits."

"I was surprised at how quickly MSK went back to clinical operations for cancer patients," Dr. Stahl says. "It was good for our training that the clinical part of our education recovered so quickly, even if we weren't able to resume lab research quite that soon."

"Our fellows overcame their fears and became role models among their peers and more broadly," Dr. Mones concludes. "I'm in awe of how incredible they were."

Medical Oncology/ Hematology Fellowship

Jodi Mones



Andrew Intlekofer

Memorial Sloan Kettering's Medical Oncology/Hematology Fellowship Training Program in the Department of Medicine has a tradition of developing the careers of leading physician-scientists by providing rigorous training in the diagnosis and treatment of neoplastic disorders as well as in the conduct of clinical and/or laboratory investigation. The training program has two main objectives: to provide comprehensive training in the evaluation and care of patients with cancer, leading to board eligibility in the subspecialties of Medical Oncology or both Medical Oncology and Hematology; and to develop highly qualified and productive investigators in clinical and/or laboratory-based cancer research.

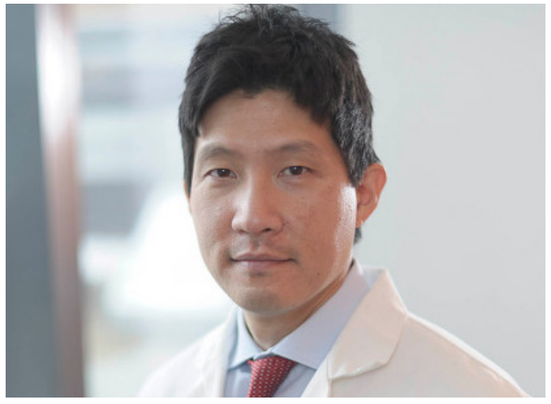
The three-year program, the largest of its kind in the country, attracted over 500 applicants this past year for just 11 coveted spots. In addition to being outstanding physicians, fellows must have a specific interest in clinical research or laboratory investigation and demonstrate scientific curiosity and motivation.

Fellows in the first year of the program concentrate on patient care, treating both inpatients and outpatients while rotating through a range of cancer subspecialties. In years two and three, fellows initiate and conduct clinical trials or work as postdoctoral researchers in a mentor's laboratory. Our fellows continue to perform world-leading research, which has led to many grant awards, impactful scientific publications, and has allowed our fellows to become leaders in our field.

From the Division of Hematologic Malignancies, Drs. Omar Abdel-Wahab (Leukemia Service), Jodi Mones (Hematology Service) and Andrew Intlekofer (Leukemia Service) are Associate Directors of the Hematology/Oncology Fellowship program. Drs. Mones and Intlekofer were appointed as Co-Directors in 2020.

To learn more, visit www.mskcc.org/education/fellowships/fellowship/medical-oncology-hematology

Adult Bone Marrow Transplantation and Parker Institute for Cancer Immunotherapy Fellowships



David Chung, Program Director, Adult BMT Fellowship Program

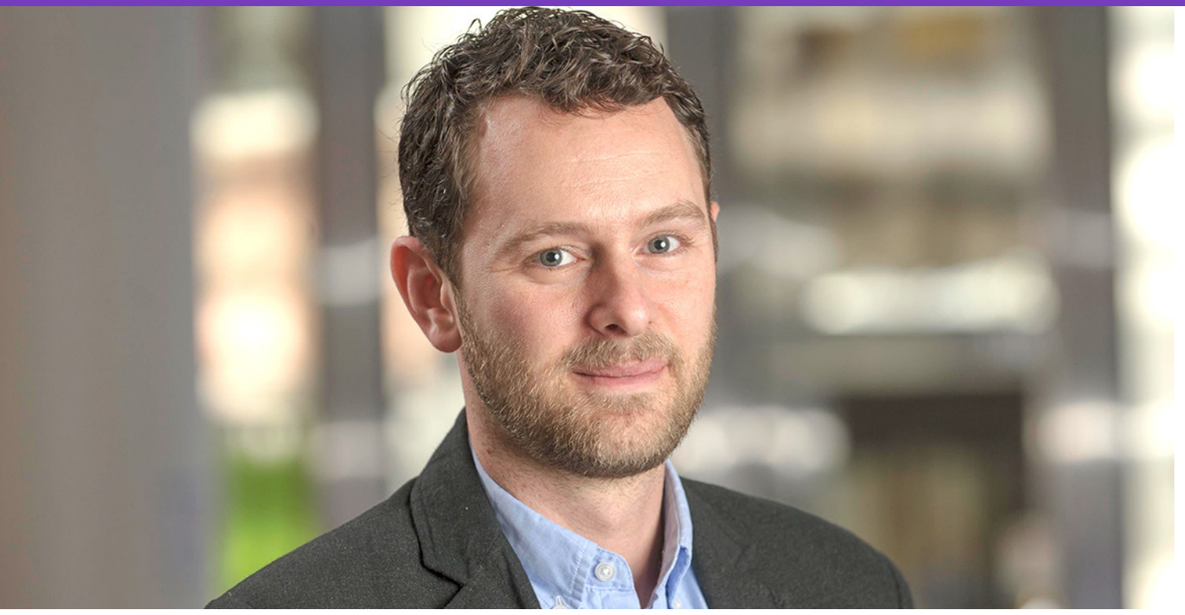
Melody Smith, Associate Director, Adult BMT Fellowship Program

The Adult Bone Marrow Transplantation Fellowship Program at Memorial Sloan Kettering was launched in 2007 as an independent, one-year program designed to prepare physicians for academic careers in stem cell transplantation and cellular therapy, including experience with clinical research. The program is led by Dr. David Chung (Program Director) and Dr. Melody Smith (Associate Director).

The fellowship provides training in inpatient and outpatient settings, with a specific focus on the different subspecialties within hematopoietic stem cell transplantation and cellular therapy as well as exposure to the different disciplines that relate to this field. These include radiation oncology and clinical laboratory rotations. Fellows have opportunities to participate in ongoing research projects or to initiate an independent project. This process is helped by the assigning of a mentor throughout the fellowship, who ensures that the objectives of the fellow are met for the training year. The program also includes a wide variety of conferences which complement the clinical aspects. These are based on a disease management concept and group physicians from different specialties who treat the disease in question. In addition to these patient-based conferences, a weekly research meeting is held.

Since 2007, the program has trained 29 fellows. Twenty-two of the graduates are now full-time faculty on BMT services in academic centers in the US and abroad. One graduate is working as VP of Clinical Development at CRISPR Therapeutics. As of September 2020, research activities of the fellows had resulted in 51 publications.

PICI@MSK continues to provide support for a one-year fellowship in cancer immunotherapy in collaboration with the Adult Bone Marrow Transplantation Service, Immunotherapeutics Clinical Core, and Cellular Therapeutics Center. The fellowship is designed to train Heme/Onc physicians in cancer immunotherapy, providing training in in/outpatient settings with a focus on cell therapy, gene engineering, cancer vaccines, checkpoint inhibitors. Dr. Nishi Shah was selected as the third fellow of the program in July 2020.



Alan Hanash, Recipient of the PICI Career Development Award 2020

Parker Institute for Cancer Immunotherapy

MSK is one of six founding centers of the Parker Institute for Cancer Immunotherapy (PICI). The goal of the center is to build a strong Immuno-oncology community at MSK by supporting basic, translational, and clinical research in the field of cancer immunotherapy, and foster national collaborations with PICI central and other PICI sites.

The Parker Institute at MSK (PICI@MSK) runs two internal competition programs to fund innovative, high-risk ideas related to cancer immunotherapy. In 2020, grant awardees continued to publish their funded research in high-profile peer-reviewed journals.

Dr. Jonathan Peled and Dr. Marcel van den Brink's publications in the *New England Journal of Medicine and Nature*

- **Microbiota as Predictor of Mortality in Allogeneic Hematopoietic-Cell Transplantation.**
  Peled JU, Gomes ALC, Devlin SM, Littmann ER, Taur Y, Sung AD, Weber D, Hashimoto D, Slingerland AE, Slingerland JB, Maloy M, Clurman AG, Stein-Thoeringer CK, Markey KA, Docampo MD, Burgos da Silva M, Khan N, Gessner A, Messina JA, Romero K, Lew MV, Bush A, Bohannon L, Brereton DG, Fontana E, Amoretti LA, Wright RJ, Armijo GK, Shono Y, Sanchez-Escamilla M, Castillo Flores N, Alarcon Tomas A, Lin RJ, Yáñez San Segundo L, Shah GL, Cho C, Scordo M, Politikos I, Hayasaka K, Hasegawa Y, Gyurkocza B, Ponce DM, Barker JN, Perales MA, Giralt SA, Jenq RR, Teshima T, Chao NJ, Holler E, Xavier JB, Pamer EG, van den Brink MRM.

  N Engl J Med. 2020 Feb 27;382(9):822-834. doi: 10.1056/NEJMoa1900623. PMID: 32101664; PMCID: PMC7534690.

- **The Gut Microbiota is Associated with Immune Cell Dynamics in Humans.**
  Schluter J, Peled JU, Taylor BP, Markey KA, Smith M, Taur Y, Niehus R, Staffas A, Dai A, Fontana E, Amoretti LA, Wright RJ, Morjaria S, Fenelus M, Pessin MS, Chao NJ, Lew M, Bohannon L, Bush A, Sung AD, Hohl TM, Perales MA, van den Brink MRM, Xavier JB.

  Nature. 2020 Dec;588(7837):303-307. doi: 10.1038/s41586-020-2971-8. Epub 2020 Nov 25. PMID: 33239790; PMCID: PMC7725892.

The center funded three career development awards ($125,000/year for two years) in 2020. This grant mechanism is intended to provide funds to future research leaders in the field of cancer immunotherapy to fund bold/innovative ideas. Dr. Alan Hanash, Attending Physician on the Adult Bone Marrow Transplant Service, was one of the recipients of this award.

In 2020, PICI@MSK pivoted to provide support for two critical COVID-19 clinical trials initiated by MSK investigators. The first trial, Phase II Study of N-acetylcysteine in Critically Ill Patients COVID-19 Infection (NCT04374461), opened to accrual in May 2020. This trial is led by Santosha Vardhana and Jedd Wolchok. The second trial, Recombinant Human Interleukin-7 (CYT107) to Improve Clinical Outcomes in Lymphopenic Patients with COVID-19 Infection (NCT0442620), is led by Stephen Pastores and Dr. van den Brink and recently opened accrual.

The MSK Center for Hematologic Malignancies

Established in 2016, the MSK Center for Hematologic Malignancies (CHM) serves patients with blood cancer, including leukemia, lymphoma, and myeloma. The center accomplishes this by promoting, supporting, and integrating clinical and laboratory expertise across hematological malignancies at MSK. In April 2020, Omar Abdel-Wahab, MD, was appointed Director of the CHM, succeeding Ross Levine, MD, who served as the inaugural Director.

With the aim of promoting cutting-edge and translational research on primary human specimens from patients with hematologic malignancies, the Hematology/Oncology Tissue Bank (HOTB) integrated with CHM in 2020. Furthermore, the CHM launched the "CHM Team Science Award," its first grant funding program for collaborative and multi-investigator projects. The CHM most recently supported a 2020 NIH Leukemia SPORE application led by Drs. Tallman and Abdel-Wahab.

In addition to these accomplishments, a few of the scientific advances emanating from the CHM's effort in 2020 include:

Understanding leukemia and preleukemia at a single cell level:

- Taylor J, Mi X, North K, et al. Single-cell genomics reveals the genetic and molecular bases for escape from mutational epistasis in myeloid neoplasms. Blood 2020
- Miles LA, Bowman RL, et al. Single-cell mutation analysis of clonal evolution in myeloid malignancies. Nature. 2020.

Determining the risks of leukemia following chemotherapy for solid tumors:

- Bolton KL. Cancer therapy shapes the fitness landscape of clonal hematopoiesis. Nature Genetics 2020

Improving ability to determine outcome in patients with myelodysplastic syndromes (MDS):

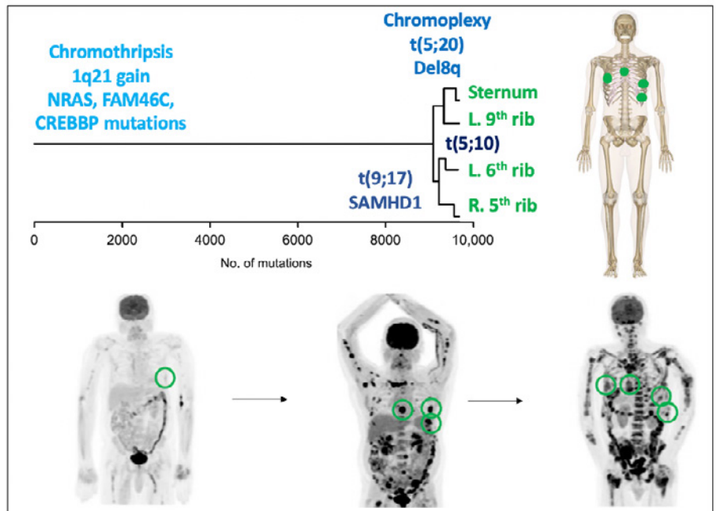
- Bernard E, et al. Implications of TP53 allelic state for genome stability, clinical presentation and outcomes in myelodysplastic syndromes. Nature Medicine 2020

Understanding the genetic basis for rare hematopoietic malignancies:

- Taylor J, Donoghue MT, et al. Germ cell tumors and associated hematologic malignancies evolve from a common shared precursor. Journal of Clinical Investigation 2020.
- Durham BH, Lopez Rodrigo E, Picarsic J, et al. Activating mutations in CSF1R and additional receptor tyrosine kinases in histiocytic neoplasms. Nature Medicine 2019

Understanding the genetics of multiple myeloma:

- Rustad EH, et al. Revealing the impact of structural variants in multiple myeloma. Blood Cancer Discov. 2020
- Landau HJ, et al F. Accelerated single cell seeding in relapsed multiple myeloma. Nat Commun. 2020 Jul 17;11(1):3617. doi: 10.1038/s41467-020-17459-z. PMID: 32680998; PMCID: PMC7368016. **See below image.**



Whole genome sequencing analysis of relapsed multiple myeloma from different anatomic sites by Drs. Landau and her team in collaboration with the CHM. Multiple myeloma is characterized by a seeding of different sites in the body which may vary in their response to therapy. This was one of the first studies to try and understand myeloma cells from different parts of the body from myeloma patients throughout their course of therapy.

Hematologic Oncology Tissue Bank

Founded by the Geoffrey Beene Grant, the Division of Hematologic Malignancies, and the Sloan Kettering Institute in 2010, the Hematologic Oncology Tissue Bank (HOTB) supports many different research projects for Memorial Hospital and Sloan Kettering Institute investigators. The HOTB is now housed within the Center for Hematologic Malignancies.

Organized as an MSK core, the HOTB is a centralized, comprehensive resource for banking human biological specimens to support research using primary human cells and tissue. This facility provides appropriate cell and tissue-based specimens from patients with hematologic and lymphoid malignancies for investigator-initiated experimentation in vitro. These biospecimens are distinct from those handled by the Precision Pathology Biobank Center because they are not fixed but instead cryopreserved in a manner that allows recovery of viable cells. Comparable materials are also available from healthy volunteers, although these are more limited in quantity and scope.

The biobank has become an invaluable resource for biospecimens linked to annotated clinical data. Its value is further enhanced by samples collected both before and after treatment from patients with lymphoid and hematologic malignancies.

- In 2020, the HOTB banked 15,676 samples.
- Currently, the HOTB inventory holds over 383,000 aliquots of the samples collected since 2010.
- The HOTB processes correlative samples for 45 clinical trials (studies with active collections in 2020).
- A workflow has been established to collect, process, and store samples collected under the institution-wide IRB #06-107 for investigators' use under their own biospecimen research protocols:
  - 11 projects and associated budgets have been established since April 2019.
  - Projects are ongoing to collect from COVID-19-positive patients in the Hematologic Malignancies Services, as well as any inpatient service or service involved with cell-based therapies.
  - COVID-19 Vaccine Project is collecting pre- and post-vaccine specimens from healthy controls and patients with lymphoid and hematologic malignancies.

The samples from the HOTB have facilitated research in exploring genetic mutations of cancer diagnoses, testing multiple mass spectrometry-based assays, xenograft profiling of hematologic malignancies, and many more areas. Samples

James Young

may be requested by any MSK investigator with an IRB-approved Biospecimen Research Protocol, including investigators in Memorial Hospital, the Sloan Kettering Institute, and the Human Oncology and Pathogenesis Program.

HOTB Director:
James Young

Research Assistant:
Annie Slingerland

Research Technicians:
Haivy Luu
Hunter Green
Phoebe Clark

Clinical Research Specialists:
Sawsan Boutemine (Lymphoma)
Saddia Momotaj (Leukemia)
LeeAnn Marcello (Adult BMT)
Edith Serrano (Multiple Myeloma)

Research Project Manager:
Jasmine Nicodemus

Division of Hematologic Malignancies Experts at the 2020 Virtual ASH Annual Meeting and Exposition

Martin S. Tallman, MD, named American Society of Hematology President

Every year, the American Society of Hematology (ASH) annual meeting hosts 20,000 to 30,000 physicians and scientists from all over the world to discuss the latest findings in hematology, ranging from basic to clinical research. In 2020, due to the global COVID-19 pandemic, the 62nd annual meeting was virtual. Rather than lowering attendance, however, this setting led to an even larger turnout than usual.

Because Memorial Sloan Kettering has one of the largest programs in the country specialized in the study and the clinical care of blood cancers, and because of our focus on improving patient care and outcomes through our research, MSK always presents many important studies at the ASH meeting.

Despite COVID-19, our team had a full presence at ASH 2020: We were part of 29 abstracts, 12 talks, and 55 posters. This volume of research demonstrates our commitment to basic and clinical research and clinical care as well as to collaboration with other leading institutions. What follows are highlights focusing particularly on clinical abstracts:

- Anthony Mato of the Leukemia Service presented several talks and posters. Among them, was a presentation on a novel triple regimen that used drugs in three different categories, a study that showed efficacy and safety for both chronic lymphocytic leukemia (CLL), and large cell lymphoma. He also presented findings on a novel type of BTK inhibitor and showed the safety and efficacy of this drug for CLL.
- Fellow Zachary Epstein-Peterson presented a novel approach of sequential immunochemotherapy in a combination with lenalidomide, which showed efficacy on mantle cell lymphoma.
- Boglarka Gyurkocza of the Adult Bone Marrow Transplant Service presented a new regimen that uses radioimmunotherapy to makes it possible to offer allogeneic hematopoietic cell transplantation to patients with active disease. This treatment is often the only potentially curative therapy for people with acute myeloid leukemia.
- Steven Horwitz of the Lymphoma Service presented on a first-in-human study of TTI-621 (NCT02663518) and

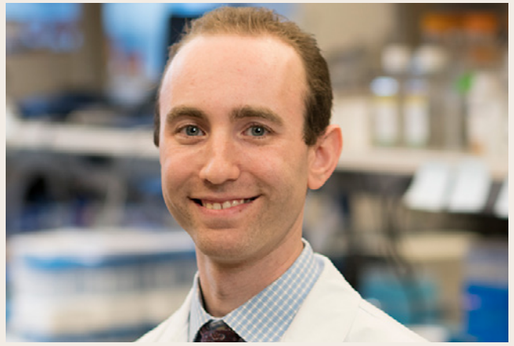
demonstrated that the intervention was well-tolerated and presented single-agent activity in multiple hematologic malignancies.
- Neha Korde of the Myeloma Service presented on a prospective novel trial using mobile wearables in patients who are newly diagnosed with multiple myeloma. The study showed that activity bioprofiles improve with therapy, regardless of depth of response.

MSK has been a leader in the field of CAR T therapy, which over the past few years has been found to be beneficial for treating blood cancer. This therapy works by taking lymphocytes from a patient and engineering them to be better at killing cancer cells. Many presentations from the Division of Hematologic Malignancies focused on this topic, including the following:
- Nayan Jain, a graduate student in Michel Sadelain' s lab, discussed how TET2 might play a critical role in proliferative and effector functions in CAR T cells.
- Martin Klatt, a research fellow from David Scheinberg's lab, discussed how he could specifically engineer CAR T cells that are broadly cancer reactive and display high activity against hematologic malignancies.
- Lia Palomba of the Lymphoma Service presented data on a new type of CAR T therapy, liso-cel, which showed promising efficacy and lower toxicity in patients with refractory and relapse mantle cell lymphoma.
- Sham Mailankody of the Myeloma Service presented a first-in-human study of the Anti-BCMA ALLO-715 and the Anti-CD52 ALLO-647 in relapsed/refractory multiple myeloma.

In addition to presenting our research, several MSK researchers and physicians were recognized with awards and honors.
- **Richard Lin** (Adult Bone Marrow Transplant Service), **Roni Shouval** (Adult Bone Marrow Transplant Service), and **Scott Millman** (Leukemia Service) won the ASH Scholar Award. One of ASH's most prestigious research award programs, the ASH Scholar Awards financially support fellows and junior faculty dedicated to careers in hematology research as they transition from training programs to careers as independent investigators.
- **Susan DeWolf** (Adult Bone Marrow Transplant Service), **Meghan Thompson** (Fellow), and **Maximilian Stahl** (Fellow) won the Abstract Achievement Award 2020.
- **Rekha Parameswaran** (Hematology Service) was elected to the ASH Subcommittee on Stewardship and Systems-Based Hematology.

Richard Lin

Roni Shouval



Scott Millman

ASH elected Martin S. Tallman, Chief of MSK's Leukemia Service, as president for a year-long term. As ASH President, Dr. Tallman will work with other members of ASH to provide ongoing advice and counsel to ASH leadership.

A world-renowned hematologist, Dr. Tallman's research interests include clinical investigation in acute myeloid leukemia, acute lymphocytic leukemia, acute promyelocytic leukemia, and hairy cell leukemia.

"The most important issue facing hematology today is the remarkably rapid pace of progress in the discovery, dissemination, and integration of new knowledge," says Dr.Tallman. "As ASH president, I look forward to facilitating connection and conversation among ASH members of all backgrounds and experience levels to improve care for those living with blood disorders."

Dr. Tallman has been a member of ASH for 21 years, and during that time he has served in various leadership roles representing the group, most recently serving as an ASH Councillor and as ASH Vice President. He completed a three-year term as the Executive Editor of Hematology, ASH's education program book, and he helped establish the ASH Meeting on Hematologic Malignancies as a founding co-chair in 2015 and continued to serve as co-chair the following year. He has also participated in several of ASH's training and educational career development programs.

Clinicians at the Monmouth regional site conducting COVID testing in the parking lot to ensure safety of patients and employees inside the center.

COVID-19 and the Regional Network

MSK's regional locations have been crucial for patient care during the COVID-19 pandemic. Given the overwhelming preference of patients to receive the care they needed closer to home, MSK's investment in the regional care network has been critical to our ability to give ongoing care. Despite the pandemic, none of the regional sites across New York and New Jersey were closed.

Clinical teams across all sites worked diligently to manage testing, post-test follow-up, and care, not only for patients but for MSK employees.

In 2020, DHM faculty in the regional care network collectively completed about 16,000 outpatient visits, more than 10,000 radiation oncology visits, and more than 13,000 physical and occupational therapy visits.

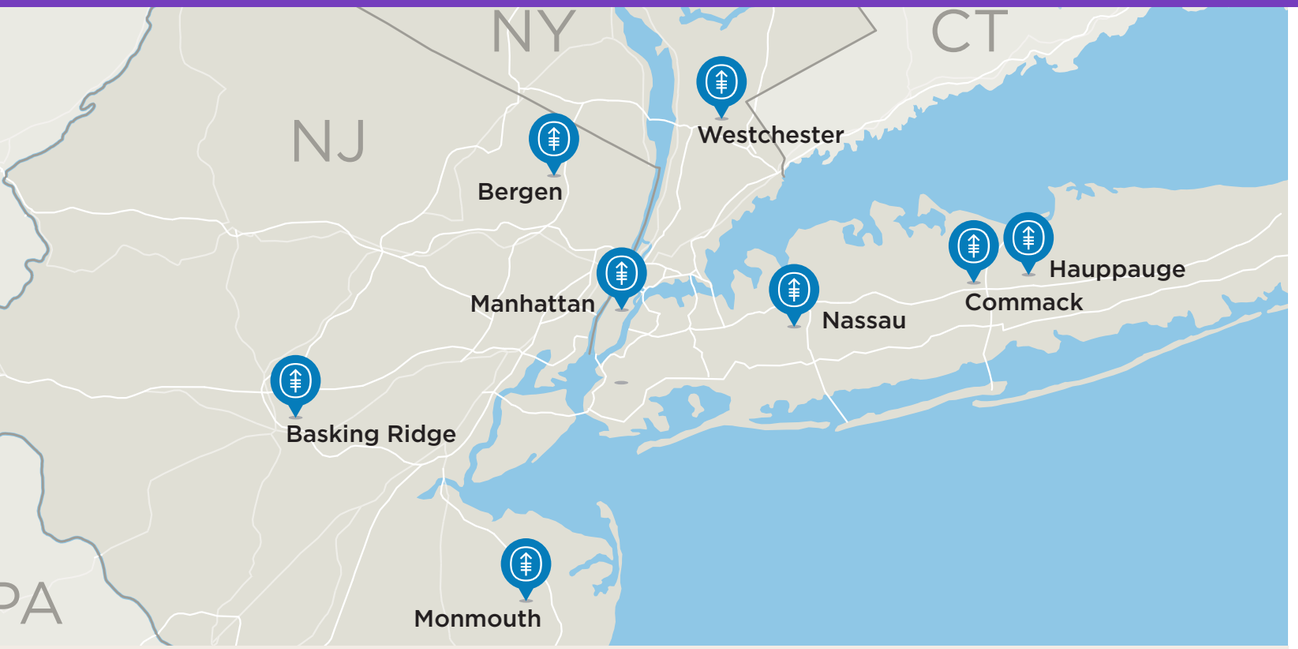
MSK Nassau Wins 2020 Healthcare Design Award

MSK Nassau, located along Hempstead Turnpike in Uniondale, NY, opened in April 2019. The 114,000-square-foot facility replaced the Rockville Centre location on the campus of Mercy Medical Center. In 2020, MSK Nassau received a **2020 Healthcare Design Award** from the American Institute of Architects (AIA) Academy of Architecture for Health. The AIA recognized MSK Nassau for its hospitality-like interiors and calming environment. In particular, the award recognizes cutting-edge designs that help solve aesthetic, civic, urban, and social problems while also being functional and sustainable.

MSK Nassau is part of a growing network of new construction and renovations aimed to better accommodate its patients and research programs and cater to those living outside New York City. It offers comprehensive oncology services, including access to clinical trials, surgical and radiation consultations, and a number of specialized services, such as pain management, survivorship services, and nutrition counseling.

As pictured here, lounge spaces outside private infusion rooms offer patients an opportunity for rest or socialization.

Patients arrive through a hotel-like drop-off area and garden. The garden surrounds the building and toggles between formality and simplicity, eventually giving way to clinical spaces.



Faculty from the Division of Hematologic Malignancies Currently Practicing in the Regional Network

MSK Basking Ridge

Audrey Hamilton
Lymphoma Service

Neha Korde
Myeloma Service

Anita Kumar
Lymphoma Service

MSK Bergen

Anthony Mato
Leukemia Service

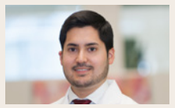
Connie Batlevi
Lymphoma Service

Matthew Matasar
Lymphoma Service

MSK Commack

Michael Mauro
Leukemia Service

Oscar Lahoud
ABMT service



Ildefonso Rodriguez-Rivera
Lymphoma Service

Lindsay Roeker
Leukemia Service

Urvi Shah
Myeloma Service

Niloufer Khan
Lymphoma Service

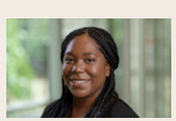
MSK Monmouth

Mark Geyer
Leukemia Service

Aaron Goldberg
Leukemia Service

Carlyn Tan
Myeloma Service

MSK Nassau



Colette Owens
Lymphoma Service

Lorenzo Falchi
Lymphoma Service

Erel Joffe
Lymphoma Service

MSK Westchester

Oscar Lahoud
ABMT service

Philip Caron
Lymphoma Service

Hani Hassoun
Myeloma Service

Gottfried von Keudell
Lymphoma Service

Andrew Zelenetz
Lymphoma Service

Partnerships

Boglarka Gyurkocza, MD

With the growth of the Regional Care Network and our expanding geographic footprint outside of New York City, clinical partnerships are becoming increasingly critical to ensuring that our patients can receive comprehensive care near their homes. Our innovative collaborations with Hackensack Meridian Health, as well as the relationships we're building through own MSK Cancer Alliance, are helping us improve the quality of cancer care for people across the United States and all over the world.

Memorial Sloan Kettering – Hackensack Meridian Health Partnership Announces Funding for Inaugural Immunology Research Collaboration Projects

As part of the Memorial Sloan Kettering – Hackensack Meridian Health Partnership, the two organizations have formed an Immunology Research Collaboration. Through this joint initiative, researchers can apply for funding to support innovative investigations to explore the power of the immune system and ways it may be harnessed to fight cancer.

The three researchers with projects selected in 2020 for funding support over one to two years are:

- **Johannes Zakrzewski, MD,** Associate Member in the Hackensack Meridian Health Center for Discovery and Innovation, is leading the project "Targeting Auto and Neoantigens with In Vivo-Generated Antigen-Specific T Cells."
- **Rena Feinman, PhD**, Associate Member in the Hackensack Meridian Health Center for Discovery and Innovation, is leading a project called "Impact of the Gut Microbiome on Immunotherapeutic Response in Multiple Myeloma."
- **Boglarka Gyurkocza, MD**, a Memorial Sloan Kettering medical oncologist in the Adult Bone Marrow Transplantation Service, is leading the project "Targeting the Gut Microbiome to Improve Outcomes after Allogeneic Hematopoietic Cell Transplantation."

Dr. Gyurkocza's project will explore in an ongoing clinical trial whether certain antibiotics preserve specific anaerobic intestinal microbiota in patients who have received stem cell transplants, and how preserving this gut flora affects the risk of patients developing graft-versus-host disease (GVHD), a serious complication of stem cell transplant. The trial is currently open at MSK and will also open at the John Theurer Cancer Center. Dr. Gyurkocza and colleagues will also examine how the loss of anaerobic gut flora may impact the risk of relapse and progression in multiple myeloma mouse models.

"Immunotherapy has become an essential pillar of cancer treatment, but much remains to be discovered about the immune system and new ways to take advantage of its power to treat cancer effectively," said Paul Sabbatini, MD, Deputy Physician-in-Chief for Clinical Research at Memorial Sloan Kettering. "The Immunology Research Collaboration between Memorial Sloan Kettering and Hackensack Meridian Health gives researchers an opportunity to delve deeply into unexplored facets of the immune system, both in the lab and clinic, and speed discoveries that will ultimately contribute to reducing the burden of cancer on our patients, their families, and the world. We are enthusiastic about the potential of these three research projects and look forward to their results."

"While immunotherapy is revolutionizing cancer treatment, it benefits are not always sustainable over the long term," noted Andre Goy, MD, MS, Chairman and Executive Director of John Theurer Cancer Center and Physician-in-Chief of the Hackensack Meridian Health Oncology Care Transformation Service. "The work of these investigators will expand our knowledge of the immune system and glean new insights that may lead to novel immunotherapeutics that are more powerful and more durable than those we are using today. These projects capture the collaborative spirit of this initiative and could have a significant impact on patient outcomes."

The center funded three career development awards ($125,000/year for two years) in 2020. This grant mechanism is intended to provide funds to future research leaders in the field of cancer immunotherapy to fund bold/innovative ideas. Dr. Alan Hanash, Attending Physician on the Adult Bone Marrow Transplant Service, was one of the recipients of this award.

A Year in Review: Engaged, Embraced, and Empowered at 74th Street

Beautiful areas are designed for employees where they can take a break or eat a meal as well as engage with one another and share ideas.

The David H. Koch Center for Cancer Care at Memorial Sloan Kettering Cancer Center, which opened for patient care in January 2020, is the culmination of years of discussion, planning, and innovation.

According to Senior Director of Ambulatory Care Jennifer Tota, a primary goal of the new center was to free up space at the hospital by moving various services from 1275 York Avenue to 74th Street.

The new facility brought all the outpatient care within the Division of Hematologic Malignancies under one roof for the first time, creating a new kind of clinical environment for patients and their caregivers as well as for staff. It offers many cutting-edge technologies designed to improve the care of people with cancer while at the same time advancing research and innovation.

"When faced with a cancer diagnosis, patients lose a sense of control over their lives," says medical oncologist Paul Hamlin, Medical Director of the David H. Koch Center for Cancer Care at MSK. "One of the goals in the design of this center was to give people back some of that control." To support this effort, schedules and wait times are continually updated and communicated to patients in an effective way.

The center may be a testament to the transformational power of technology, but the staff are committed to using that technology to bring patients and clinicians closer together.

"We want people to feel like they're getting a big hug when they enter this building," says Elizabeth Rodriguez, Director of Nursing. "We can all be our best selves when we feel supported and seen." At the new center, staff are working to marry warm, human interactions with the latest advances in technology. Toward that end, a few technologies and practices will be in use, including providing care coordinators with tablets. Free from their desks, they can now give patients a warm welcome and thoughtful send-off wherever they may be.

Wait times have significantly reduced, with patients now waiting 15 minutes or less to receive infusions and most patients are seen in less than 30 minutes. In the new facility, "We worked to create welcoming spaces that patients would want to navigate to," says Ms. Tota. Staff brainstorming sessions led to the development of three themes for the "neighborhoods" that have taken the place of traditional waiting areas: Restoration, Recreation, and Activation. Patients can choose to rest and relax in one neighborhood, take an art or yoga class in another, or wander the building. Giving patients more choices aligns with the goal of the center to create an atmosphere where patients and staff feel engaged, embraced, and empowered.

The needs of staff have been given equal consideration. "We want this to be a healing environment for staff as well as patients," says Dr. Hamlin. "'Healing' means different things for different people. For our staff, it might mean simply taking a moment to catch their breath and refocus. We've worked to give them the space to do that."

In fact, the facility has been recognized by several industry leaders for its innovative and resilient design, some of the many features that put the 750,000-square-foot facility in a class of its own.

Awards:

- In May 2020, the David H. Koch Center for Cancer Care at MSK was recognized by the NYCxDESIGN Award, presented by Interior Design and ICFF. These awards honor outstanding products and projects in categories that span major areas of design, from architecture to interiors, from products to accessories.
- The David H. Koch Center for Cancer Care at MSK received the prestigious Award of Merit, the highest honor, in the 2020 Healthcare Design Annual Design Showcase.

Media Features:

- The June issue of *Health Facilities Magazine* from the American Society for Healthcare Engineering featured the MSK facility on its cover and highlighted the innovative and unique storm resiliency features which have made the center a role model for other institutions relative to flood proofing, resilient design, energy efficiency, and continuity of service for our patients and staff.
- MSK's Executive Director of Design + Construction, Suzen Heeley, was featured alongside design partners, as part of Interior Design's "Town Hall" series on Design TV. The roundtable discussion highlighted how the David H. Koch Center for Cancer Care at MSK can serve as "a role model for how we think about the future of health and wellness."

The more than 1,200 pieces of art throughout the center are an integral part of the effort to create an environment that is uplifting and restorative — and they were selected by staff.

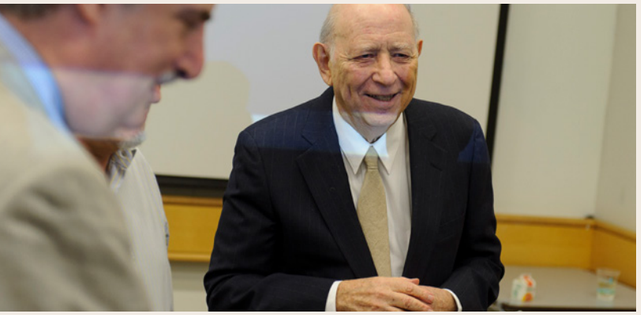
From left to right: Elizabeth Rodriguez, Jen Tota, and Paul Hamlin

Incongruously, a global pandemic was descending upon us the same month the new center opened. With mandatory stay-at-home orders imposed by the state and COVID-19 cases rapidly rising shortly after the building became fully operational, MSK pivoted into emergency response mode. The people at the David H. Koch Center for Cancer Care at MSK pivoted, too. The building emerged as one of the main hubs for COVID-19 testing and the care of COVID-19-positive outpatients.

Since January 2020 and even throughout the global pandemic, the David H. Koch Center for Cancer Care at MSK had:

- **154,305 clinic visits**
- **49,043 infusion visits**
- **5,462 radiation treatment visits**
- **4,405 interventional radiology procedures**
- **97 outpatient transplants**

As a team, Ms. Tota, Dr. Hamlin, and Dr. Rodriguez summed up their vision of the David H. Koch Center for Cancer Care at MSK, a vision that acknowledges what came before even as it looks to the future: "What makes the center unique is what makes MSK unique: extraordinary clinical expertise, extraordinary individuals, and cutting-edge technology and design that bring to life unparalleled cancer care and patient experiences. Every aspect of MSK has a specific hallmark that has moved MSK further in its mission. The David H. Koch Center for Cancer Care at MSK represents the coalescing of these many hallmarks supported by an atmosphere of continuous improvement. It will lead MSK into the next 135 years."



Dr. Mortimer Lacher at the annual Lacher lecture and fellowship conference May 2014 (top), June 2012 (bottom left), and June 2015 (bottom right).

The 11th Annual Mortimer J. Lacher Lecture & Fellows Conference

The 11th Annual Mortimer J. Lacher Lecture and Fellows Conference was hosted by the Division of Hematologic Malignancies on June 16, 2020. The virtual event honored Dr. Lacher, who unfortunately passed away shortly after. He was a longtime member of MSK's Lymphoma Service and the Sloan Kettering Institute, who joined the Lymphoma Service at Memorial Hospital in 1960 and served as a member of the Sloan Kettering Institute from 1960 until 1990.

Dr. Lacher was the co-founder and President of the Lymphoma Foundation and served as a consultant in MSK's Department of Medicine.

Every year since 1983, Dr. Lacher and the Lymphoma Foundation directed and donated funding to help sustain research and, most importantly, the postdoctoral fellowship research program at MSKCC. The Lymphoma Foundation has supported 158 fellows in hematology/oncology and radiation therapy with a focus on hematological malignancies. This program has been extremely successful and 36 of our faculty members are former Lacher Fellows.

The 2020 Lacher Fellows are listed below along with their abstracts:

Benjamin Diamond
Mentor: Ola Landgren
Toward the Use of Chemotherapy-related and Clock-Like Mutational Signatures to Characterize the Genomic Landscape of Relapsed Multiple Myeloma and Secondary Malignancies

Zachary Epstein-Peterson
Mentor: Andrew Intlekofer
Oncogenic mechanisms and therapeutic targeting of mutant isocitrate dehydrogenase 2 in angioimmunoblastic T-cell lymphoma

Brian Ball
Mentor: Eytan Stein
A phase I trial of BTX-A51 in patients with relapsed or refractory AML or high-risk MDS

Lindsey Roeker
Mentor: Anthony Mato
Outcomes of COVID-19 in Patients with CLL: A Multicenter, International Experience

Adam Widman
Mentor: Dan Landau, Omar Abdel-Wahab
Use of deep-learning empowered whole genome sequencing for ultra-sensitive liquid biopsy in melanoma and non-small cell lung cancer

Niloufer Khan
Mentor: Steven Horwitz
Optimizing dosing of brentuximab vedotin for cutaneous T-cell lymphomas

Leslie Modlin
Mentor: Joachim Yahalom
MSK Experience of Radiation Therapy in Burkitt Lymphoma

From top left to bottom right: Marcel van den Brink, Adam Widman, Zachary Epstein, Lindsey Roeker, Benjamin Diamond, Leslie Modlin, Niloufer Khan

In memory and recognition of Dr. Lacher's many contributions and academic accomplishments, the Division of Hematologic Malignancies will continue the Mortimer J. Lacher Fellowship Program as well as the annual Lacher lecture and fellow conference.

We will be forever grateful for his extraordinary devotion, exceptional wisdom, remarkable talent, and generosity.

Ten-Year Anniversary for the Susan and Peter Solomon Genomics Program

This year marked a decade of progress for the Susan and Peter Solomon Divisional Genomics Program. Thanks to the Solomon family's generosity, the next generation of genomics researchers have had the opportunity to establish preliminary data to develop novel hypotheses, advance their careers, and improve the lives of patients.

Solomon Program Mission

Since 2010, Susan and Peter Solomon have supported genomics efforts in the Division of Hematologic Malignancies. Co-directed by Marcel van den Brink, Ross Levine, Elli Papaemmanuil, and Omar Abdel-Wahab, the Susan and Peter Solomon Divisional Genomics Program has brought together investigators from many different departments and disciplines within the center and established a methodology to analyze samples from patients with acute myeloid leukemia (AML) in different and unique ways.

The program has continued to support innovative discovery science and translation to the clinic, including genomic profiling of leukemia patients at MSK. This has been used as the basis for mechanism-based clinical trials and has directly led to two clinical trials (IDH2 and IDH1 inhibition) and one FDA-approved AML therapy (enasidenib for IDH2-mutant disease).

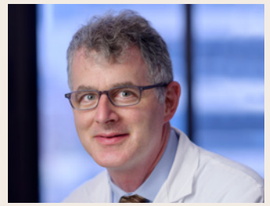
Peter and Susan Soloman

The program funds proposals that address omics-based research, including genomics, epigenetics, proteomics, microbial genomics, and single-cell studies. Since 2010, the Susan and Peter Solomon Divisional Genomics Program has supported 22 unique research projects, totaling over $1.7 million in funding.

Congratulations to this year's awardees!

2020 Awards

Kristian Helin
DNA methylation and hydroxymethylation landscapes in patients with acute myeloid leukemia



Tobias Hohl
Genomic analysis of intestinal fungi and trans-kingdom microbial interactions in hematopoietic cell transplantation

Kseniya Petrova-Drus
Identifying the frequency and clinical impact of clonal hematopoiesis in patients with histiocytic neoplasms

Raajit Rampal
Evaluation of the role of inflammatory pathways in progression of myeloproliferative neoplasm to acute myeloid leukemia

Past Cycle for Survival participants

Memorial Sloan Kettering's Cycle for Survival is a high-energy, indoor team cycling event that allows participants to fight rare cancers in a tangible way.

Cycle for Survival is determined to beat rare cancers by powering groundbreaking research to help patients who often have few or no treatment options. Although the final rides in New York City and Greenwich, Connecticut scheduled for the spring of 2020 were cancelled due to COVID-19, each person in the Cycle for Survival community made an important impact with every dollar raised.

Cycle for Survival had a big fundraising year in 2020. Thanks to the support of our founding partner, Equinox, $40 million was raised in 2020 alone — contributing to a total of $260 million since the event's inception in 2007. This success was only possible because of our dedicated community of riders, supporters, patients, researchers, and doctors. A total of 37,000 people across 17 cities participated in events in 2020, of which over 2,300 were MSK employees. Every dollar empowers researchers to pursue revolutionary ideas that lead to lifesaving breakthroughs. We are proud to support the advancement of several comprehensive initiatives at MSK, which span across many critical areas of research. MSK is on the front line of the battle against rare cancers.

Members from the Division of Hematologic Malignancies participated in the following teams:

1. **The CanCer HaCkers**
2. **DoMinators**
3. **Straight Outta Chemo**
4. **The Mobilizers**
5. **Team HOPP Kreb's Cycle**
6. **MSK BMT Cyclepaths**
7. **BMT Cancer Crushers**
8. **BMT CC's**
9. **Leukemia 2020**

Philanthropic Donors Over $50,000

The Division of Hematologic Malignancies is supported in part by the generous donations of our benefactors.

We wish to thank those who have contributed to the many successes of the division.

Below is a list of patrons who donated $50,000 or more in 2020.

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Thank you notes for nursing staff

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For additional information or to make a gift, call **866-815-9501** or visit **giving.mskcc.org**.

DONATING BLOOD
Blood donations can be designated for a particular patient or MSK's general blood inventory.

For more information or to make an appointment, call **212-639-8177** or **212-639-7648**.

DONATING TO FRED'S TEAM

For information on donating to Fred's Team, visit **www.fredsteam.org**.

DONATING TO CYCLE FOR SURVIVAL
For information on donating to Cycle for Survival, visit **www.cycleforsurvival.org**.

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