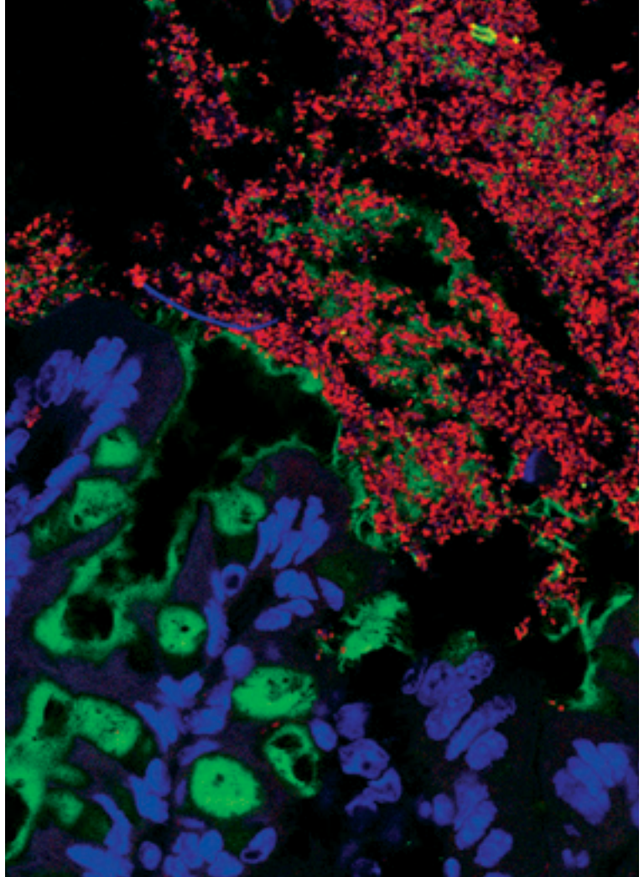
HEMATOLOGIC ONCOLOGY

2016 ANNUAL REPORT

Memorial Sloan Kettering Cancer Center

CONTENTS



A dramatic thinning of the mucus layer of mice treated with imipenem-cilastatin (green). Dissemination of bacteria past the colonic epithelial barrier is also observed. Immunostaining for MUC2 (green) of the colon sections with general bacterial 16S rRNA gene FISH probe EUB338 (red) counterstained with Hoechst (blue) is shown

PHOTO: YUSUKE SHONO

ON THE COVER: TOP, LEFT TO RIGHT: Andrew Lin, Melody Smith, Ginevra Castagna, **BOTTOM:** Donna Mastey, Ola Landgren, Ashley Poliak

LETTER FROM THE DIVISION HEAD

The Division of Hematologic Oncology in the Department of Medicine at Memorial Sloan Kettering Cancer Center is dedicated to treating patients with a variety of blood cancers as well as some benign hematologic diseases.

The 67 faculty members that constitute our 5 services: **Adult Bone Marrow Transplantation**, **Hematology**, **Leukemia**, **Lymphoma** and **Myeloma** are committed to excellence in clinical care, research, and education.

Our 2016 Annual Report will highlight our faculty and their commitment to our mission to provide the best possible clinical care, our research both in the laboratory and in the clinic, and the education of our future leaders in hematological oncology.

Sincerely,

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

DIVISION OF HEMATOLOGIC ONCOLOGY FACULTY

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David Chung


Parastoo Dahi


Sergio Giralt
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Miguel Perales


Doris Ponce


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Brian Shaffer


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Melody Smith


Roni Tamari

LEUKEMIA


Omar Abdel-Wahab


Ellin Berman


Renier Brentjens

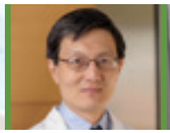

Sheng Cai*

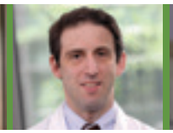

Stephen Chung


Bayard Clarkson

LYMPHOMA


David Scheinberg


Alan Shih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Martin Tallman
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Aaron Viny

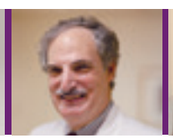

Connie Batlevi*


Craig Moskowitz
CLINICAL DIRECTOR


Ariela Noy


Lia Palomba

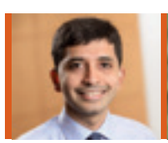

Carol Portlock


David Straus


Elina Tsyvkin


Anas Younes
CHIEF ATTENDING

REGIONAL NETWORK


Sham Mailankody†


Eric Smith*


Philip C. Caron†


Pamela R. Drullinsky†


Audrey M. Hamilton†


Colette Owens*†

*Joined faculty in 2016 † Physicians who also practice in the Regional Network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Katharine Hsu

Ann Jakubowski

Guenther Koehne

Heather Landau

Esperanza Papadopoulos

Jonthan Peled*

Marcel van den Brink
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Peter Maslak

Michael Mauro

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Alison Moskowitz

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hAndrew Zelenetz†

Hani Hassoun†

Neha Korde†

Ola Landgren
CHIEF ATTENDING

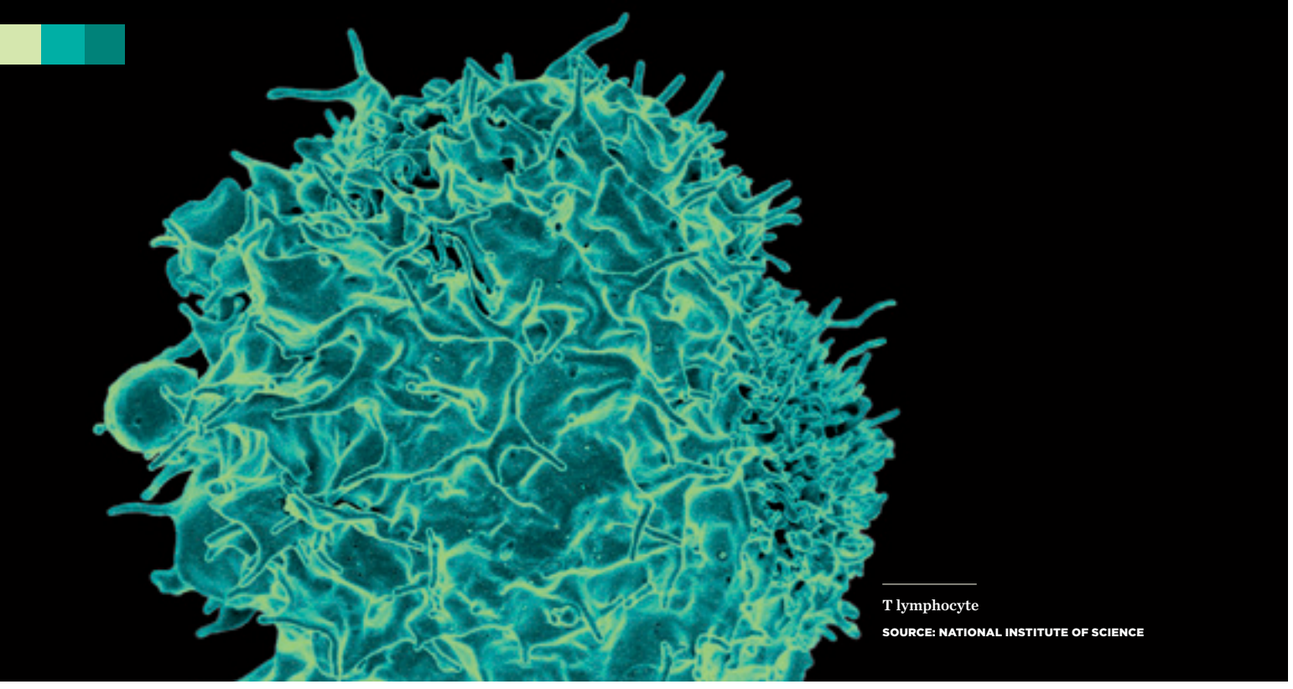
Nikoletta Lendvai

Alexander Lesokhin

COLLABORATING TEAMS

Cardiology Service
Case Management
Colorectal Service
Critical Care Medicine Service
Dental Service
Dermatology Service
Endocrinology Service
Gastroenterology & Nutrition Service
Gastric & Mixed Tumor Service
General Internal Medicine Service
Geriatrics Service
Gynecology Service
Head & Neck Service
Hepatopancreatobiliary Service
Infectious Diseases Service
Integrative Medicine Service
Interventional Radiology Service
Music/Art Therapy
Neurology Service
Neurosurgery
Nursing
Nutrition
Occupational Therapy
Ophthalmic Oncology Service
Orthopaedic Service
Pain & Palliative Care Service
Pathology
Diagnostic Molecular Pathology
Hematopathology
Pathology Diagnostic Services, Cytology
Surgical Pathology Diagnostic Services
- Bone & Soft Tissue Pathology
- Dermatopathology
- Gastrointestinal Pathology

Physical Therapy
Plastic & Reconstructive Surgical Service
Psychiatry Service
Pulmonary Service
Radiation Oncology
Radiology
Rehabilitation Medicine Service
Renal Service
Social Work
Surgery
Thoracic Service
Urgent Care Center
Urology Service



T lymphocyte

SOURCE: NATIONAL INSTITUTE OF SCIENCE

IMMUNOTHERAPY DRUG APPROVED FOR TREATMENT OF HODGKIN LYMPHOMA

BY JIM STALLARD

The immunotherapy drug nivolumab is giving hope to Hodgkin lymphoma patients after standard treatments don't work.

PATIENTS WITH HODGKIN LYMPHOMA whose disease returns after standard treatments have faced a shortage of effective therapies. The FDA has now approved the immunotherapy drug nivolumab for these patients. About two-thirds of patients in a clinical trial responded to the drug, and the benefit appears to be lasting. Nivolumab blocks a molecule called PD-1 and is the first such immunotherapy approved for Hodgkin lymphoma.

Hodgkin lymphoma, a type of blood cancer, is usually curable with current therapies. But patients whose disease doesn't respond to these treatments face difficult odds and — because the disease often strikes people in their twenties and thirties — many of them die at a relatively young age.

Today, their outlook is much brighter. The FDA has approved the immunotherapy drug nivolumab (Opdivo®) for use in Hodgkin lymphoma patients who have exhausted all other treatments. It is only the second drug in the last four decades to be approved for relapsed Hodgkin lymphoma — and the first in a new generation of immunotherapy drugs to be approved for the disease.

Two out of three patients with relapsed Hodgkin lymphoma responded to nivolumab, with minimal side effects.

The approval is based on results from an international clinical trial led by Memorial Sloan Kettering medical oncologist, Anas Younes, which showed about two-thirds of Hodgkin lymphoma patients responded to nivolumab, with minimal side effects. Results from the trial are being published in Lancet Oncology. (*The study is currently in press.*)

"After decades with no new treatments, we now have two highly active drugs that may be combinable."

Anas Younes, Chief, LYMPHOMA SERVICE

"The FDA approval of this new therapy addresses an urgent medical need for these young men and women," says Dr. Younes, who is Chief of MSK's Lymphoma Service. "It greatly enhances our treatment strategies going forward."

MSK medical oncologist Alexander Lesokhin, who played a critical role in the clinical testing of nivolumab, echoes this optimism. "This is great news for Hodgkin lymphoma patients and for the advancement of immunotherapies in blood cancers," he says. "This is a wonderful milestone that helps validate our ongoing efforts at MSK to develop the next generation of immunotherapy treatments."

Nivolumab is a type of immunotherapy drug called a checkpoint inhibitor, which blocks the actions of a molecule called PD-1 on the surface of immune cells. This "releases the brakes" on the immune system, allowing it to mount a stronger attack against cancer. MSK played a critical role in the clinical development of these drugs.

Nivolumab has already been proven effective against solid tumors such as melanoma, lung cancer, and kidney cancer. This FDA approval is the first for a PD-1 inhibitor to treat blood cancer.

RECENT ADVANCES IN HODGKIN LYMPHOMA AFTER SLOW PROGRESS

Hodgkin lymphoma is a cancer of the lymphatic system, which originates in white blood cells. Usually patients are successfully treated with chemotherapy alone or a combination of radiation and chemotherapy.

Patients whose Hodgkin lymphoma returns after initial treatment typically receive intensive chemotherapy — which wipes out the cancerous cells — followed by a transplant of their own blood-forming stem cells (called an autologous transplant) to rebuild their immune system.

Despite such demanding therapy, the disease progresses in some people. For these patients, no new treatments existed until 2011, when the FDA approved a drug called brentuximab vedotin, an antibody linked to a toxic chemical similar to chemotherapy.

Although brentuximab vedotin represented an important advance, most patients treated with it eventually saw their lymphoma return, requiring further therapy. The clinical trial led by Dr. Younes tested whether nivolumab would be effective in patients whose Hodgkin lymphoma returned or progressed despite receiving an autologous stem cell transplant followed by brentuximab vedotin.

In the trial, among 95 patients whose cancer returned after this treatment, 65% responded to nivolumab — meaning they had complete or partial remission of their disease. Among this subset of patients, the response lasted a median of 8.7 months.

Dr. Younes added that ongoing trials are testing whether giving patients who have failed other treatments a combination of nivolumab and brentuximab vedotin will be even more effective.

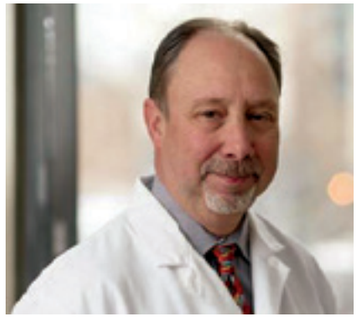
"After decades with no new treatments, we now have two highly active drugs that may be combinable — that's why everyone in the field is getting excited," he says. "It could become the building block for new treatment strategies for patients with this disease." He added that MSK is developing several new combinations with nivolumab and other similar immune therapy drugs for the treatment of patients with Hodgkin and non-Hodgkin lymphoma. ■

HIGHLIGHTS

- The FDA approved nivolumab for Hodgkin lymphoma.
- The drug is a type of immunotherapy.
- The approval is for patients whose disease resists standard treatments.
- It's the first PD-1 inhibitor approved for Hodgkin lymphoma.

LINK: https://www.mskcc.org/blog/first-immunotherapy-drug-approved-treatment-hodgkin-lymphoma

CRAIG MOSKOWITZ, MD, SETS INTERNATIONAL STANDARD OF CARE FOR LYMPHOMA



WHEN INFANTS JOIN THEIR MOTHERS in Craig Moskowitz's exam room, the Memorial Sloan Kettering physician-scientist knows his work has made an impact.

Over the course of his 23-year career — spent entirely at MSK — 63 of Dr. Moskowitz' patients have given birth after treatment for aggressive lymphoma. Now cured, the women have gone on to live largely normal lives, enjoying huge blessings in the form of tiny footprints.

"That, to me, is what it's all about," says Dr. Moskowitz, the Steven A. Greenberg Chair in Lymphoma Research and Clinical Director of the Division of Hematologic Oncology.

But Dr. Moskowitz' footprint in the lymphoma realm has been anything but small. Specializing in the care of Hodgkin's lymphoma and poor-risk diffuse large B-cell lymphoma (DLBCL), the lifelong New Yorker's research efforts have changed the international standard of care for lymphoma.

Dr. Moskowitz has held a razor-sharp focus on lymphoma since the start of his career during the early HIV/AIDS era, when a link emerged between HIV and the development of specific cancers, including DLBCL. Also an attending physician in MSK's Lymphoma and Adult BMT Services, he spotted a void in research to improve outcomes of patients with DLBCL and Hodgkin's and decided to fill it.

As Dr. Moskowitz describes it, his research can be divided into two tracks. One has focused on improving "salvage" therapy for patients with recurrent or stubborn disease that's not responding to standard therapy, by incorporating high-dose therapy and autologous stem cell transplantation along with newer drugs.

A second approach has involved developing strategies to optimize the treatment of newly diagnosed DLBCL according to the likelihood of a patient's disease recurring, using insights gleaned by studying those with relapsed cases. Therapy is then individually tailored to each patient's individual risk factors before treatment — including clinical, molecular or pathologic features of their lymphoma, as well as imaging test results.

"The research-based treatment I do is trying to improve on the standard of care in a curative setting," he says, noting that many of his patients are referred by physicians aware of his prominence. "In a palliative setting, patients are coming because they need hope."

CHAIN OF SUCCESSES EARNS ACCOLADES

Triple board-certified in internal medicine, medical oncology, and hematology, Dr. Moskowitz has won multiple awards recognizing his research, which proved noteworthy from his earliest years in the field. In the mid-1990s, he created what is known as the ICE chemotherapy regimen (combining ifosfamide, carboplatin, and etoposide), which triggered a major response in 66% of relapsed non-Hodgkin's lymphoma patients eligible for a potentially curative stem cell transplant in his study.

The ICE regimen, with many variations, is now the most common chemotherapy regimen used worldwide in this patient group.

Building on that success, Dr. Moskowitz — named one of *New York Magazine's* Top Doctors in 2015 and 2016 — spent about four years studying the combination of ICE and rituximab (Rituxan) after autologous stem cell transplantation in patients with relapsed or stubborn DLBCL. These efforts resulted in rituximab, a mouse-human monoclonal antibody directed against the B-cell antigen, being approved worldwide for maintenance therapy after stem cell transplant.

His achievements continue to pile up. Dr. Moskowitz was lead investigator of a study in the *Journal of Clinical Oncology* that fueled the March 2017 FDA approval of the immunotherapy drug pembrolizumab (Keytruda) for patients with classical Hodgkin's lymphoma who relapse after treatment with three or more lines of therapy.

"My research has really expanded as opposed to evolved," explains Dr. Moskowitz, who has lectured worldwide on lymphoma and stem cell transplantation. "I try to make small, incremental changes in the research pathway with every new study. Each tries to improve on the ICE chemo — by adding novel agents, incorporating novel imaging, or incorporating more molecular techniques."

THANKS TO MSK, SURVIVAL RATES CLIMBING

Striking a balance between all his responsibilities is a tenuous task for Dr. Moskowitz, who sees patients twice a week, mixing clinical duties with research and administrative commitments. Typically leading between five and seven studies at any given time, he also mentors junior faculty members — a role he particularly relishes.

Dr. Moskowitz also serves as one of three chairs heading MSK's Research Council, which reviews all studies being conducted by investigators here. This pivotal role, too, enhances his perspective on the rest of his duties.

"You get to see all the new agents being introduced in all types cancers, see others' study trial designs, and get to understand what may be successful and what may not," he says. "I find that appealing. It's a lot of extra work, but it sparks ideas."

As his career continues, Dr. Moskowitz is highly gratified to see compelling results from his untiring efforts. In 1994, during his fellowship in hematology/oncology at MSK, the cure rate for relapsed Hodgkin's lymphoma was about 45%, but now stands at approximately 65% — an improvement directly attributable to his and colleagues' research. Additionally, overall survival for lymphoma patients with failed stem cell transplants, who cannot be cured, was previously around 30 months; it's now seven to eight years.

But reaping these advances has unquestionably been a plodding process, one that wouldn't work well with a sense of impatience. Dr. Moskowitz is circumspect when assessing the long-term nature of achieving true progress in lymphoma treatment.

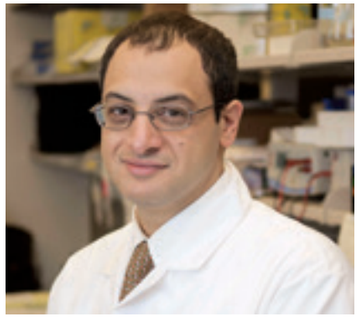
"It's an honor to take care of lymphoma patients. I'd rather crawl our way through this ... but it also turns out it's the right thing to do," he says. "It builds on what you've done before. When you explain it to patients and physicians and you publish what you've done, they can see the natural progression in your line of thinking."

"We're the end of the food chain," he adds. "If someone comes to see me, I have to figure it out. I can't ask anyone else." ■

OMAR ABDEL-WAHAB, MD

ASSISTANT ATTENDING PHYSICIAN
LEUKEMIA SERVICE

ASSISTANT MEMBER
HUMAN ONCOLOGY & PATHOGENESIS PROGRAM (HOPP)



OMAR ABDEL-WAHAB'S ARRIVAL at Memorial Sloan Kettering in 2007 quickly became a value-add proposition: A fellowship here in hematology-oncology offered the education he sought, but Dr. Abdel-Wahab stayed to lend pivotal new insights into the genetic basis for leukemias and other blood cancers.

While he can make his work sound quite simple, it's some of the most intricate research being done into hematological malignancies – including myeloproliferative neoplasms (MPNs), myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML) — anywhere in the world. The physician-scientist is happily involved in bench-to-bedside experiments he feels wouldn't be possible at many other institutions.

"We have a team here in the Leukemia Service of people devoted to patient care nearly 100%, and those like myself who are more devoted to the lab side, and we work together," he explains. "Most hospitals don't have this critical mass of people needed to make such an effort."

As a member of the Human Oncology and Pathogenesis Program, Dr. Abdel-Wahab has helped identify and characterize several new genetic abnormalities in blood cancers, with his advances offering promise in discovering novel targeted therapies. He was a key collaborator in 2015 research with Fred Hutchinson Cancer Research Center in Seattle that uncovered how a single mutation can trigger MDS, in which the bone marrow overproduces certain nascent blood cells but can't convert them to healthy cells.

He was also involved in seminal research on the rare blood cancers known as hairy cell leukemia and histiocytosis, identifying frequent mutations activating the MAP kinase pathway, which regulates communications within and between cells. The work resulted in clinical trials of the drug vemurafenib — already FDA-approved to target BRAF gene mutations in late-stage melanoma — for both of these malignancies.

The recipient of the Josie Robertson Young Investigator Award, among other honors, Dr. Abdel-Wahab discusses MSK's global prominence in leukemia care in this interview, as well as the interplay between clinical and research work.

How does your work with patients inform your research efforts?

First and foremost, it keeps me aware of what the critical questions and deficits are that we need to improve on for clinical care. I recognize from that work how much we do need new therapies for leukemias. In MDS, for example, no matter what we offer patients with standard care, there are very few who are cured from the disease. It's a strong motivator for the research. Also, we do a lot work introducing new therapeutic approaches in clinic, so understanding what's realistic in terms of giving these new drugs to patients would be hard to appreciate without the clinical background.

How does your work in the HOPP program enhance your overall focus?

HOPP is really one of the most important parts of MSK and why I'm so happy here. It's entirely a department of physician-scientists, so it's people like myself who interface between clinical care and the more basic research world. It's rare to have that, because in most institutions you have little interface between the two. We all have different backgrounds and different clinical interests and research focuses, but all speak kind of the same language. We're all physicians who understand the importance of basic research to improve clinical care.

What breakthroughs in understanding leukemia and its potential new therapies are you most proud of?

We discovered about five years ago that nearly 50% of patients with MDS have mutations in an RNA splicing factor. When DNA is transcribed to RNA to make protein, the RNA has to be processed a certain way, so the discovery of these mutations was a curious finding. With the discovery of these mutations, we've shown how this process goes awry in MDS. The details of that were unclear previously, and we were the group that came to understand how that process actually caused the disease and were involved in developing a therapeutic strategy to target the mutation. It's the basis for a clinical trial now going on here and elsewhere.

Why should leukemia patients seek care at MSK instead of another institution?

We have a focused interest in clinical care, clinical research, and scientific research in leukemias, and we have more specialists focused on this than available at almost any institution in the United States. So when a patient comes here, they get physicians who are most knowledgeable about the newest advances for leukemia care. That's really important when you have a disease that's relatively rare compared to other diseases, and for many forms of leukemia, unfortunately the outcomes are still not where we'd like them to be.

What are the biggest challenges remaining in leukemia research?

It's a huge challenge going from discovering drugs to getting them into patients in clinical trials. For a long time, the strategy for trying new drugs is that we're giving them after patients have already relapsed — they've been through a lot, and may be very sick, so the standard of care may not work well for them. Trying to change the historical paradigm to give them something brand new is one of the challenges.

What excites you most about your work?

Two things drive me most: One, I'm really interested in trying to make observations fundamental for research that are important for leukemia and blood cancers, but also important for understanding cancer development, period. There's much we still don't understand about the basic biology of cancer. By studying patient samples, we can learn things we would not stumble on otherwise.

Second, I love actually identifying something that makes a difference for patients in terms of treatment. We really need to improve treatment options for many forms of leukemia. It would be ideal if we developed curative therapies for patients that could improve outcomes. ■

BETWEEN THE MOON AND NEW YORK CITY: VICE PRESIDENT BIDEN LEADS MSK CANCER MOONSHOT ROUNDTABLE

BY MATTHEW TONTONOZ

MSK HOSTED THE VICE PRESIDENT and members of the New York City cancer community for a roundtable discussion devoted to brainstorming ideas for the cancer moonshot initiative. Key areas of concern were clinical trial participation and data sharing.

Prepping the launch pad for his cancer moonshot initiative, Former Vice President Joe Biden held a roundtable discussion at Memorial Sloan Kettering yesterday with nine members of the New York City cancer community, including several MSK doctors and nurses. MSK President and CEO Craig Thompson moderated the conversation.

The visit was the latest in Mr. Biden's efforts to "change cancer as we know it" through an ambitious national effort dubbed the cancer moonshot. "We're thrilled that you agreed to be at mission control," Dr. Thompson said in his opening remarks.

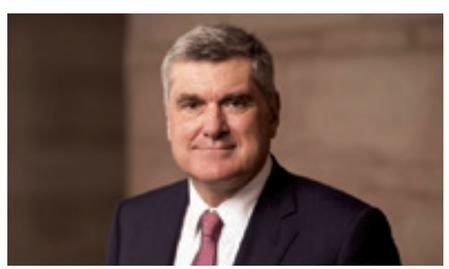
During the hour-long conversation, the vice president homed in on several key topics that have emerged since President Barack Obama announced the moonshot initiative in early 2016: increasing access to and enrollment in clinical trials, collecting and sharing cancer data, and breaking down barriers to scientific collaboration.

SHARING THE WEALTH

Noting that most cancer patients in the United States receive care in their local communities, the vice president asked the assembled guests what creative approaches they are taking to bring the latest cancer insights to the community setting.

"We're thrilled that you agreed to be at mission control."

Craig B. Thompson, MSK PRESIDENT AND CEO



MSK gynecologic surgeon, Carol Brown, pointed to efforts to enlist community oncologists as co-investigators on clinical studies. She said this would help to increase both awareness and incentives to enroll patients in clinical trials — thereby addressing the gap in care that can separate academic medical centers from community oncologists. Dr. Thompson offered up MSK's growing network of outpatient locations in New Jersey, Westchester, and Long Island as another way MSK has sought to elevate the quality of care in the community setting.

Dr. Brown, who is Director of MSK's Office of Diversity Programs in Clinical Care, Research, and Education, also discussed efforts to reduce disparities in healthcare outcomes among minorities by increasing the percentage of minority populations that enroll in clinical trials. She noted that trials offer some of the most promising therapeutic options, yet rates of participation, especially in underserved and minority communities, are low.

Nationally, the average patient enrollment on clinical trials is 3 to 5%. At MSK, nearly one-third of patients participate in clinical trials. One way MSK has managed to achieve such high levels of enrollment is through efforts to automatize the process that alerts doctors to possible trials for their patients. Dr. Thompson told the vice president that MSK leaders including Physician-in-Chief José Baselga, physician-scientist Charles Sawyers, and head of clinical research Paul Sabbatini would be on board to help disseminate this model to other centers.

DATA TSUNAMI

For about three decades, National Cancer Institute–designated cancer centers — comprised of MSK and 68 other academic centers — have helped to shape and distribute best care practices to the wider oncology community. The challenge in recent years, as Dr. Thompson noted, is the "tsunami" of new information emerging every day that could potentially change clinical practice. Guidelines issued in print and updated every six months often are outdated as soon as they are published.

The vice president homed in on several key topics: increasing access to and enrollment in clinical trials, collecting and sharing cancer data, and breaking down barriers to scientific collaboration.

Lindsay Saunders, Research Fellow, with Vice President Joe Biden and Ross Levine, MD.

Potential solutions to this quandary are systems designed to analyze large data sets and distill simple lessons. MSK's partnership with IBM Watson and its participation in Project GENIE are two such efforts. Another is Flatiron Health, with which MSK is also collaborating. Flatiron founder Nat Turner, who participated in the roundtable, noted that big data systems are equipped to help answer some of the most burning questions in oncology today, such as why only a small subset of patients respond to current immunotherapy drugs.

According to Mr. Turner, no one institution — including MSK — has enough information to be able to answer this question. That's why his company has recently partnered with the Food and Drug Administration to gain access to data from thousands of patients at multiple centers. Mr. Turner believes that solving this problem in immunotherapy is where "big data" is going to have some of its first big breakthroughs.

BE MORE LIKE NASA

Near the end of the roundtable discussion, Mr. Biden returned to a topic obviously close to his heart: data sharing. He reported being "stunned" to find out how many barriers currently hinder the free sharing of information among researchers and centers. He pointed to pay walls at scientific journals that put the results of publically funded research out of reach of those unable or unwilling to pay, and to duplicative research efforts at different centers that seemingly reinvent the wheel. He contrasted this situation with that of astronomers who routinely collaborate on common goals and share their data freely and immediately — a fitting comparison, given the moonshot analogy.

The vice president ended the roundtable with a warning and a request: "We don't go away easily," he said. "We'll be calling and asking for help."

Earlier in the day, Mr. Biden took a tour of leukemia researcher Ross Levine's lab at MSK. Dr. Levine's lab is one of several that make up a new Center for Epigenetics Research at MSK. Epigenetics, MSK scientists believe, has the potential to revolutionize the treatment of several cancers, including leukemia. ■

Complete list of roundtable participants: Syndy Benjamin, Joe Biden, Carol Brown, Jill O'Donnell-Tormey, Sue Posthumus, Robert Sidlow, Mary Solomon, Mark Souweidane, Craig Thompson, Nat Turner

Additional reporting contributed by Julie Grisham.

LINK: https://www.mskcc.org/blog/between-moon-and-new-york-city-vice-president-biden-leads-msk-cancer-moonshot-roundtable

WITH WIT AND AFFECTION, VETERAN BMT NURSE, PAMELA GRANT-NAVARRO, BEARS WITNESS TO SERVICE'S EVOLUTION

WHEN PAMELA GRANT-NAVARRO, RN, MSN,OCN, BMTCN, started her nursing career at Memorial Sloan Kettering 30 years ago, she gave herself a deadline: She would work here for only two years before finding a position closer to home on Long Island. No way would she commute two hours to work each way for very long, she vowed.

But she's still here. Now Grant-Navarro, a clinical nurse IV in the Adult Bone Marrow Transplant (BMT) Service, jokes that she's also given MSK her firstborn child. Her 25-year-old daughter is set to begin her own nursing career here later this year.

Why did she stay? It all goes back to the "pure nursing" she witnessed at MSK while still a nursing student. Tragically, Grant-Navarro's sister had been diagnosed with soft cell sarcoma during that period, and the budding nurse noticed the stark contrast between workplace cultures in local community hospitals — where she did clinical rotations — and MSK, where her sister was treated.

"There was no comparison," Grant-Navarro says. "I viewed Memorial as pure nursing – nurses here aren't worried about green jello or delivering specimens. They're in patient rooms dealing with patient care. There's a different sense of responsibility and autonomy here."

"I know there's no other place like this," she adds with her characteristic warmth and humor. "I'm still a believer. I drank the Kool-Aid."

'NO-TIARA-AND-SASH ROLE' KEEPS BMT UNIT HUMMING

Grant-Navarro's long tenure here has offered her a front-row seat to — and integral role in — the BMT Service's evolution and prominence. Hailed for performing the world's first successful bone marrow transplant between a patient and an unrelated donor, MSK physicians have since completed more than 4,000 bone marrow and stem cell transplants.

About 450 such transplants were performed at MSK in 2016, with a goal to extend this to 600 transplants annually in coming years. Facilitating this volume, however, requires an astuteness and agility akin to playing chess for Grant-Navarro, whose primary role is finding beds for incoming patients as they embark on their transplants.

With 25 beds currently in the BMT unit and 50 patients needing spaces at any given time, the job isn't at all simple.

"I'm very fortunate to have crazy, no-tiara-and-sash role, but I manage the flow of all the admissions to make sure we have the beds for them to come in," she says. "Every single day, my immediate focus is who's being admitted or discharged, and who we can safely move depending on the overall needs of the organization."

Construction is underway to double the size of the BMT unit, but in the meantime Grant-Navarro and her colleagues carefully coordinate with nurses on other floors and units to safely handle BMT's overload. Because the transplant process is tricky and fraught with particular complications — including greatly heightened risks of infection — placing patients in just any other unit isn't an option, she says.

Close communication is needed with nurses in other units to ensure they're equipped to serve BMT patients and are aware of any special needs.

"I wouldn't be able to go to the Neuro floor and take care of someone with a fresh craniotomy, because I don't know the particulars of that patient population or how to pregame to make sure nothing goes awry with the patient," she explains. "In the same way, that's what we're trying to ensure when our patients go off the floor."

"I'm going to those nurses and educating them," Grant-Navarro adds. "But a lot of hands are in the kitchen, so it does require great communication. I serve as a liaison between our Service to make sure the kind of complicated care needs of this population are still being served no matter where they reside off our primary floor."

COLLABORATION FUELS TOP OUTCOMES

Teaming with all other types of MSK clinicians, not just nurses, is one of the facets of her job that Grant-Navarro relishes most. There's an unspoken level of trust, she says, and the knowledge that each can tap the strengths of the other at any time.

"This isn't the nursing you see in the movies or in some other hospitals — I'm not waiting around for an order written by someone else to carry out," she says. "In a second, I can have a physician, nurse practitioner, pharmacist and physician assistant at my elbow. It really is a collaboration."

With the rise of electronic health records and other forms of advanced documentation in recent years, Grant-Navarro has augmented her own skills to match these needs. She earned a degree in nursing informatics "because I could see that data collection was really what was going to drive what we did next," she explains, "and I wanted to make sure it was done right. The nurses are able to really be present in each patient's room because all the rest is supporting our ability to do that."

The long-term nature of patient care in BMT — with many patients remaining hospitalized for 45 days or longer — affords Grant-Navarro the opportunity to forge deeper relationships with them. This isn't just personally fulfilling, but also gives her the time to teach patients in-depth concepts about their disease and treatment — such as infection prevention measures — that can help keep them safer in the immediate post-transplant period.

Outcomes for BMT patients at MSK are among the top in the United States, with the one-year survival rate for allogeneic, or donated, bone marrow transplants the best in the tri-state region, according to an independent study conducted by the U.S. National Marrow Donor Program.

"It gives me a source of comfort to have so much time to teach people and know they are safe when they go home," she says. "You feel an obligation to the patients and your peers. This is 30 years of people showing up here in the same way. This culture — you can't really buy that." ■

JODI MONES, MD

ASSOCIATE ATTENDING PHYSICIAN
HEMATOLOGY SERVICE

WANTING TO BREAK THE FAMILY MOLD set by her physician father and grandfather, Jodi Mones actually tried not to pursue medicine as a career. But ultimately, her love of science won out — an allure that worked to the benefit of Memorial Sloan Kettering, where Dr. Mones is a benign hematologist.

Arriving at MSK in January 2016 after practicing for 10 years at Montefiore Medical Center in the Bronx, Dr. Mones experienced tantalizing exposure to the atmosphere here during medical residency and fellowship rotations years earlier. When the opportunity arose to join MSK's faculty, she couldn't resist.

"In terms of academic and cutting-edge medicine, there's nothing like it," says Dr. Mones, who is board-certified in both hematology and medical oncology. "There's so much cutting-edge medicine that goes on here that you don't see anywhere else."

Dr. Mones quickly assumed pivotal roles at MSK, serving as co-investigator with several other faculty members — including Hematology Service Chief Gerald Soff — in a compelling international clinical trial comparing the anti-clotting drug rivaroxaban (brand name Xarelto) with placebo for preventing blood clots in cancer patients.

In this interview, Dr. Mones discusses the teamwork crucial to tailoring patient care and her enthusiasm for training medical fellows in benign hematology, among other topics.

Why did you decide to specialize in benign hematology?

The physiology of the way blood functions is pretty amazing. I love the fact that you can look at a blood or bone marrow smear and the pathology is there at your fingertips. Many oncologists never see the cancer they're treating, but in hematology, a lot of times you see what's going on in front of you as well as see the patient. There's a lot of unity in it.

What are the most prominent hematological issues facing cancer patients?

A high percentage experience some type of blood issue related or unrelated to their malignancy or treatment. A big problem is deep vein thrombosis (DVT) and pulmonary emboli (PEs), when blood clots lodge in the lung. Patients who undergo surgery and have prolonged hospitalizations face a very high risk of blood clots, so a lot of what we do is manage and treat clotting. Between those whose clot is found incidentally, say, during an EOD (evidence of disease) scan, and those who have symptomatic blood clots, with swelling in their legs or shortness of breath or chest pain, many cancer patients deal with blood clots. In fact, approximately 20% of DVTs/PEs are in patients with cancer.

Another major issue is low blood counts, including red and white blood cells and platelets. If platelets drop too low, oncologists can't continue a patient's chemotherapy at the optimal dose and schedule. We're running a clinical trial looking at the platelet-boosting drug romiplostim, known as Nplate, which can help patients to more quickly resume full-dose chemotherapy. We're looking to see if Nplate changes survival rates, but don't have all the data yet.

Why are vigilance and treatment of benign blood issues in cancer patients crucial to overall outcomes?

Our whole priority here is to cure patients of cancer. If they can't get the treatment they need because their platelet levels are too low, or they're on blood thinners and can't have necessary surgery, then the goal of getting rid their cancer becomes much more difficult. I see my job as basically facilitating what the surgical and medical oncologists need to do.

How might the clinical trial on rivaroxaban help change the standard of care for patients facing higher risks of blood clots?

Since blood clots represent the second leading cause of death for cancer patients, the research is particularly vital to benign hematology care. It's a multi-center, randomized clinical trial comparing rivaroxaban with placebo for the prevention of blood clots in cancer patients deemed at high risk due to their type of cancer or other factors such as BMI. It's called the CASSINI Study, and MSK is one of the highest enrolling sites internationally.

We know from prior studies that proactively preventing blood clots in cancer patients works. But in the past, that was done with injectable medication – and getting patients to inject themselves when they don't even

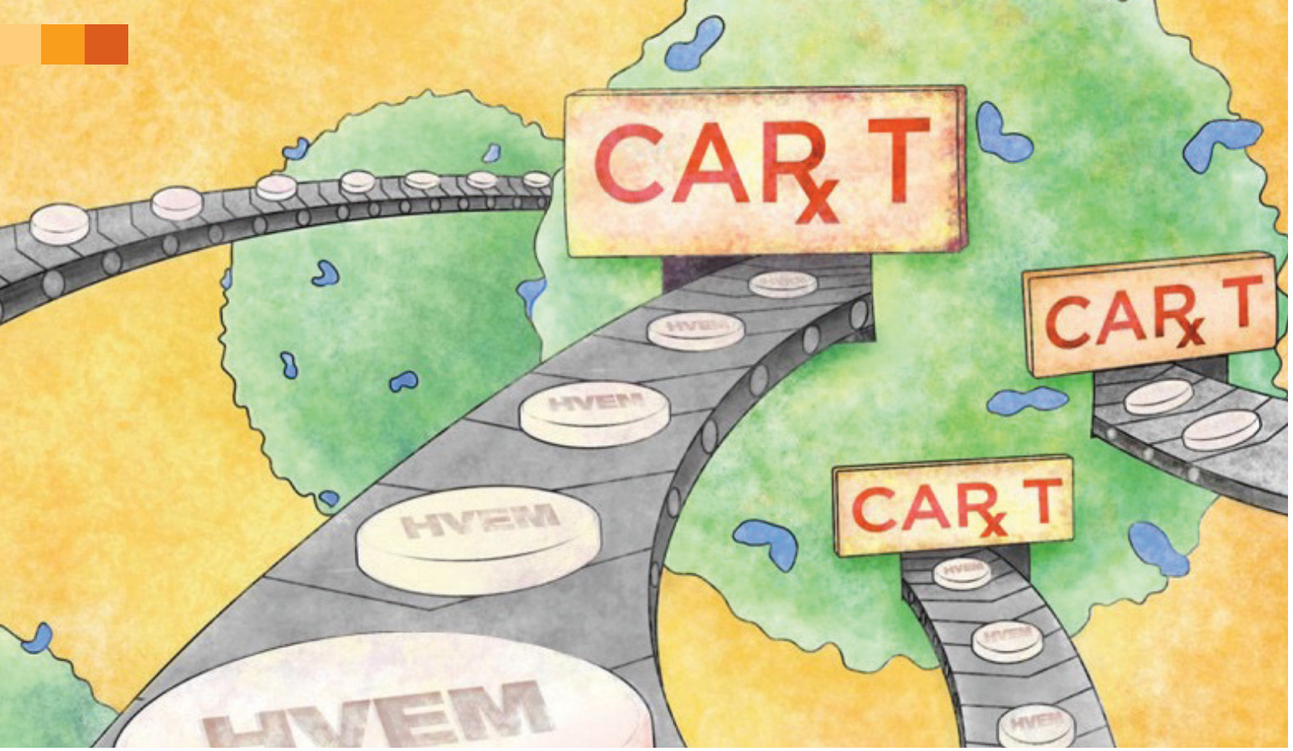
have a blood clot is a hard sell. However, most patients would take an oral drug like rivaroxaban. So I think if we get the data to back that up it will really make a big difference for patients.

You took initiative this year to incorporate benign hematology rotations into the training MSK's first-year medical fellows receive. Why?

Fewer fellows are comfortable with benign hematology or want to do it, but the population of cancer patients is growing, so there's going to be a shortage of us fairly soon. Typically, the fellows here don't do any benign hematology rotations, not in their first year, so some would graduate without having any benign hematology experience. I have them rotate with me so when they go out into the world of oncology, they have some background and experience in managing basic benign hematology issues like blood clots. This way, they know when to refer patients appropriately and what questions to ask. It may be the only exposure to benign hematology they have their entire career – which is fine – but it's important that they're coming into our clinic, at least for a few weeks. The fellows seem to like it and get to see things from a different perspective.

What are the most gratifying parts of your job?

I especially like the problem-solving or trouble-shooting aspects. Among my personal favorites is dealing with breast cancer patients, often young women who may need to go on Tamoxifen to treat their cancer or help prevent a recurrence. But some have a family or personal history of blood clotting that may preclude Tamoxifen use. I help risk-stratify these patients to determine if they can go on Tamoxifen or something else, or if Tamoxifen is the best choice from an oncology perspective, how I can make that safer by adding a low-dose blood thinner or aspirin. I give this information to the breast oncologist, who makes decisions about which therapy the patient should be on, and tell them how I can make it as safe as possible. It's like the art of medicine in a lot of ways. ■



Human CAR T cells have been engineered to produce a protein that could treat lymphoma.

NEW IMMUNOTHERAPY APPROACH TURNS CELLS INTO "MICRO-PHARMACIES"

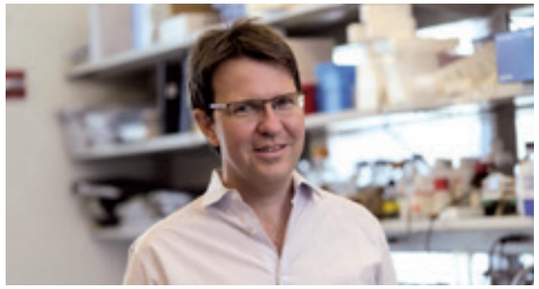
BY JIM STALLARD

RESEARCHERS HAVE MODIFIED CAR T CELLS to produce a protein called HVEM that could treat lymphoma. When injected, the cells naturally zero in on the location of the cancer cells and churn out HVEM continuously for several days. This new immunotherapy approach could potentially transform the way blood cancers are treated.

Memorial Sloan Kettering researchers have developed a potentially powerful lymphoma treatment using modified immune cells that function as on-site "micro-pharmacies," churning out proteins for therapeutic effect. In experiments with human tumors transplanted into mice, the new immunotherapy approach produced significant responses, raising hopes that this technique could someday offer an effective way of treating this disease and possibly other cancers.

The technique represents a new twist on a form of immunotherapy called chimeric antigen receptor (CAR) T cell therapy, which has demonstrated remarkable results in patients with other blood-related cancers. CAR T cell therapy involves removing immune T cells from a patient, genetically altering them to fight cancer, and giving them back to the patient in vast numbers.

The researchers identified a critical pathway that is disrupted in approximately 75 percent of follicular lymphomas, a subset of B cell lymphoma.



"This form of treatment could be very effective because the CAR T cells continuously produce the protein right where it is needed."

Hans-Guido Wendel, CANCER BIOLOGIST

Historically, this form of therapy has aimed to give immune cells the information they need to better recognize tumor cells as foreign and attack them. The new technique illustrates an untapped potential of CAR T cells to act as targeted delivery vehicles by revamping them to produce anticancer agents.

"This form of treatment could be very effective because the CAR T cells continuously produce the protein right where it is needed," says MSK cancer biologist Hans-Guido Wendel, who led an international team developing the novel technology that included Karin Tarte of the University of Rennes, France. "It could increase the on-target therapeutic activity and also reduce side effects of cancer treatments because it's restricted to the tumor sites."

DISRUPTED CROSSTALK LEADS TO LYMPHOMA

The researchers devised the innovative approach after making an important discovery about the biology of lymphomas, which usually arise in white blood cells called B cells and are characterized by uncontrolled growth. The researchers identified a critical pathway that is disrupted in approximately 75 percent of follicular lymphomas, a subset of B cell lymphoma.

The pathway involves an interaction between two receptors on the surface of B cells, proteins called HVEM and BTLA. Normally, these receptors communicate with each other to keep B cells' growth at a normal rate. If this communication is disrupted — if either receptor is not functioning properly — the cells will proliferate out of control.

Dr. Wendel and colleagues found that the gene for HVEM is mutated in most follicular lymphomas, producing a faulty HVEM protein that perturbs the interaction with the BTLA receptor that sits on the surface of the cancerous B cells. This accessible location suggested that it might be possible to deliver the HVEM protein therapeutically and restore its cancer-suppressing function.

"The challenge became finding a way to get HVEM to the cancer cells," Dr. Wendel says. "It's a big protein that's very difficult and expensive to manufacture, and if you tried injecting it, you would need a much higher concentration because it binds in a lot of places you don't want it to. So we decided to see if we could engineer T cells to make the protein instead and also deliver it to the tumor cells."

CAR T CELLS DRAWN TO THE CANCER SITE

The research team used human CAR T cells engineered to seek out cells expressing the CD19 protein, which is made by all B cells, both cancerous and normal. CD19 CAR T cells naturally home in on B cells and have recently produced stunning results in treating chemotherapy-resistant leukemia.

The research team modified the CD19 CAR T cells so that they would continuously produce the HVEM protein. "The CAR T cells pump out the protein for several weeks in one specific area — which is near the cancer cells," Dr. Wendel says.

When injected into mice that contained implanted grafts of human follicular cell lymphoma, the cells produced therapeutic responses that were far more significant than when using control CD19 CAR T cells that did not produce HVEM.

The researchers reported their results online today in the journal *Cell*.

"This shows a feasible way to put the brakes back on lymphoma cells by restoring the HVEM-BTLA interaction," Dr. Wendel says.

He adds that additional studies are needed to validate the effectiveness of this approach. Darin Salloum, a postdoctoral research fellow in Dr. Wendel's lab, is further modifying the CAR T cells to produce altered versions of the HVEM protein in the hopes of making the treatment even more effective. Ultimately, pharmaceutical or biotechnology companies can license the technology to conduct a clinical trial.

"Potentially, engineered T cells that function as 'micro-pharmacies' and deliver a range of anticancer drugs could transform the way we treat lymphomas and possibly other blood cancers as well," Dr. Wendel says. ■

LINK: https://www.mskcc.org/blog/new-immunotherapy-approach-turns-cells-micro-pharmacies

TIM PETERSON, PharmD, BCOP

CLINICAL PHARMACY SPECIALIST
LYMPHOMA/MYELOMA

AS A BORN AND BRED MIDWESTERNER, Tim Peterson's move to the City that Never Sleeps has proven to be somewhat of a culture shock. But when he steps through the doors of Memorial Sloan Kettering each day — where Dr. Peterson is a Clinical Pharmacy Specialist in lymphoma and myeloma — past and present merge in a highly pleasing way.

After earning his PharmD at University of Minnesota in 2013 and completing his PGY-1 residency at University of Iowa Hospitals, Dr. Peterson arrived at MSK in 2014 as a second-year resident in Adult Oncology Pharmacy. He was drawn to MSK because of its stellar research reputation, deciding to stay despite the steep learning curve required to adapt to New York City's very different way of life.

"It was a striking change going from a small town in the Midwest to Manhattan," he recalls. "It means I'm no longer saying hello to everyone I cross on the street. From the subway to MSK, I'm in Manhattan, but once I get here, it's like a small-town feel again."

Dr. Peterson is now one of 40 clinical pharmacy specialists in Department of Medicine, 21 of which work within the Division of Hematological Oncology. Rotating between inpatient and outpatient duties, Dr. Peterson has happily settled into specializing in lymphoma and myeloma — two areas in which drug therapy options are rapidly expanding, requiring increasing cooperation between oncologists and pharmacists.

"I had a longstanding interest in clinical oncology," he says, "and knew that most cutting-edge treatment regimens and decisions are based on what's done at institutions such as MSK."

In this interview, Dr. Peterson details his path into pharmacology and what keeps him enthused on the job.

What led you to become a pharmacist specializing in hematological cancers?

Both of my brothers, who are significantly older than I, are specialized physicians, so I was exposed to the healthcare realm my entire life and knew I wanted to be in it. But I also knew I wanted a role with more opportunities to spend time with and counsel patients than physicians sometimes have. On top of that, as someone personally affected by cancer in my family, I was able to witness diagnosis, initial treatment, follow-up, relapse, and so on, and the specific ways pharmacists can come into play to support the oncology team. With hematological malignancies, I think there are a lot more opportunities for pharmacists to get involved in interventions for infectious disease and supportive care measures. These patients tend to be very complicated, needing profound immune support and having difficulties with opportunistic infections, and we can help manage adverse effects.

Why is pharmacotherapy such a crucial part of cancer care for both inpatients and outpatients?

An important aspect with a lot of hematological malignancies is being able to assess the combinations of chemotherapy and targeted agents we're able to use, especially because — with increasing research into targeted therapies and immunotherapies — we are finding synergistic effects. With all the new regimens available, we're sometimes able to replace conventional chemotherapy but also to combine therapies. It's an exciting time to identify, based on genetic and epigenetic research, what sorts of agents we can combine with standard care, and this comes into the realm of both inpatients and outpatients.

"With hematological malignancies, I think there are a lot more opportunities for pharmacists to get involved in interventions for infectious disease and supportive care measures."

"I had a longstanding interest in clinical oncology," he says, "and knew that most cutting-edge treatment regimens and decisions are based on what's done at institutions such as MSK."

How much teamwork is required between you and other faculty members to ensure drugs are both prescribed and carried out accurately and effectively?

It's definitely a very highly collaborative practice. We have a mechanism in place here called CDTM, or collaborative drug therapy management, which allows us as clinical pharmacists to change the doses of medications on behalf of physicians relative to patients' organ function. So we dose-adjust for physicians and can send prescriptions and updated prescriptions to outside pharmacies as well.

What excites you most about your work?

My favorite part is probably the actual patient interactions and being able to see the success stories in person. Since I rotate between inpatient and outpatient, I'm able to see patients when they're not feeling their best, or are very ill, maybe having been in the ICU. But later, based on the care provided here, they're discharged, and then I see them in clinic when they're feeling better. I'm able to form professional and personal relationships with patients I see on a repeated basis. It's the most valuable part of my job. ■

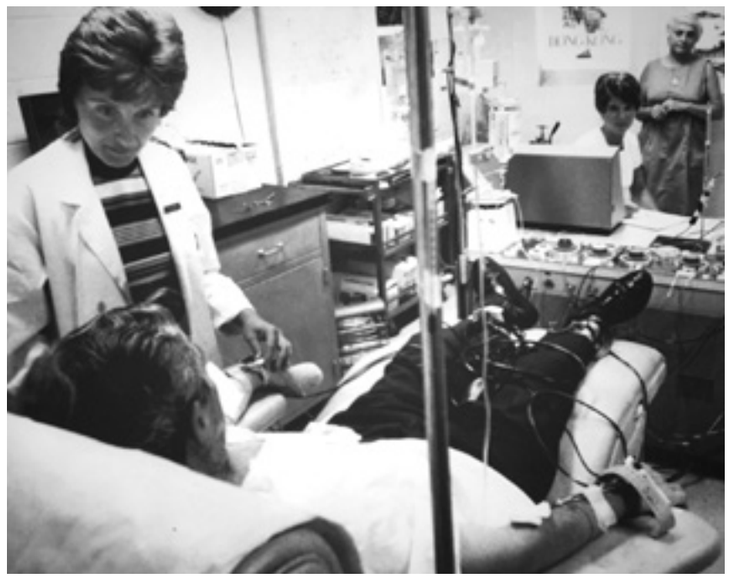
REMEMBERING LILIAN REICH, MD (1937-2016)

BY EILEEN WALSH

LILIAN REICH, MD was a pioneer in the use of apheresis technology for the treatment of cancer and hematologic diseases. After receiving her medical degree in Argentina at the Buenos Aires Medical School, she came to New York in 1961. She completed a fellowship in neurophysiology at Mount Sinai Hospital and an internship and residency at French Hospital. She joined the staff at Memorial Hospital in 1968 as a fellow in the Department of Medicine — Hematology, Immunohematology and Blood Bank. In 1970, she was appointed Assistant Director of Transfusion Service and Hematology and an Assistant Attending Physician in 1975. In 1980, Dr. Reich was appointed Associate Blood Bank Director and in 1994, she was appointed Attending Physician, Hematology and Oncology. Also in 1980, she was appointed Associate Director, Transfusion Service at the Hospital for Special Surgery.

Throughout her career, Dr. Reich contributed to over 130 published papers. Her research resulted in many advances in the treatment of leukemia, myeloma and other hematologic diseases and in the field of bone marrow transplant. As Medical Director of the Donor Room, she implemented the use of apheresis technology for therapeutic plasma exchange as therapy for diseases such as Waldenstrom macroglobulinemia, Thrombotic thrombocytopenic purpura, and Myasthenia gravis. Apheresis technology also contributed to the growth of bone marrow transplant therapy by enabling collection of hematopoietic progenitor cells from the blood. With Dr. Reich's leadership, the donor room expanded its services to keep pace with apheresis cellular collections for emerging immune therapies such as Car-T cells and treatments such as extracorporeal photopheresis. Dr. Reich also supervised the Donor Room's collection of thousands of blood components annually to be used for the treatment of MSK patients.

Dr. Reich enjoyed teaching and was also an Assistant Professor in Medicine at Cornell Medical School. She taught blood and bone marrow morphology and non-malignant hematology to fellows pursuing hematology boards. She mentored and inspired countless physicians at MSK. She had a wonderful sense of humor and used it in her teaching and lectures. She could be counted on to brighten up any meeting she was involved in with her laughter.



Dr. Reich treating a patient with one of the first apheresis instruments.

"Dr. Reich truly touched each and every one of her patient's lives."

Dr. Reich treated thousands of patients over her 55 year career as a physician. She always considered quality of life when advising treatment and took pride that she was able to maintain many patients for years, enabling them to enjoy their lives while living with cancer. She would always return from her clinic visits with a gift of flowers or chocolate (two of her favorite things) from at least one patient. She truly touched each and every one of her patient's lives.

Dr. Reich loved to travel, she loved the opera and she loved dogs. She was an avid bridge player and competed in tournaments for many years. She enjoyed her family life with her husband, children and grandchildren.

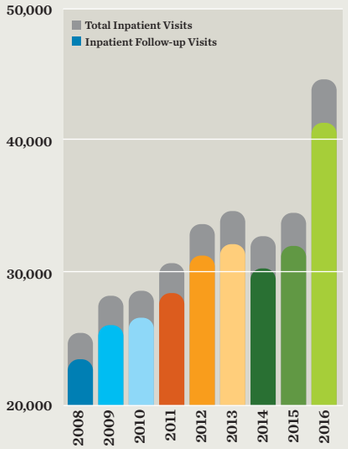
The Donor Room has had many staff members over the years. Dr. Reich made a point of getting to know each and every one. She participated in social events and always loved a party. Everyone benefited from her knowledge as she was always happy to answer any questions. She was a mentor and a friend to everyone.

Dr. Reich will always be remembered as a skilled and dedicated physician and one who truly loved the practice of medicine. She will also be remembered for her laughter, kindness, and generosity. She will be greatly missed by the MSK community.

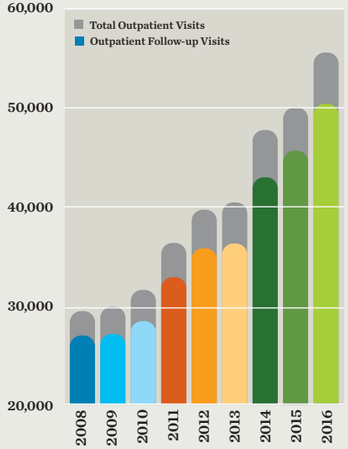
Eileen Walsh, a Nurse Leader, worked with Dr. Reich since October 1993, and says "I will always be grateful for having the opportunity to work beside her for so long and she has taught me a great deal. She was a very special person and will be greatly missed by all." ■

2016 DIVISION OF HEMATOLOGIC ONCOLOGY METRICS

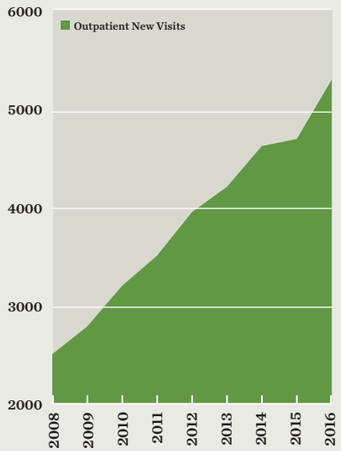
INPATIENT VISITS



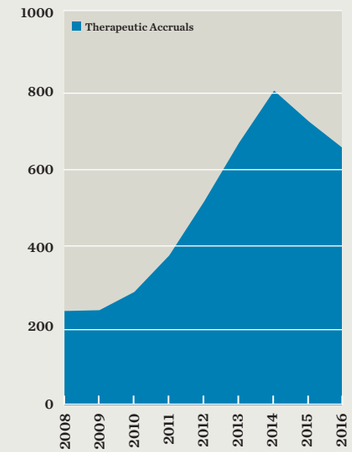
OUTPATIENT VISITS



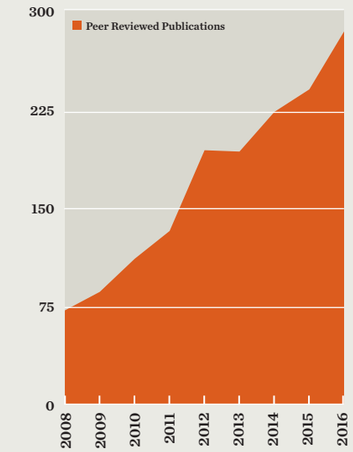
OUTPATIENT NEW VISITS



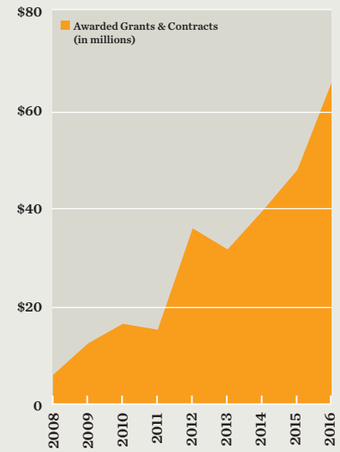
CLINICAL TRIAL ACCRUALS



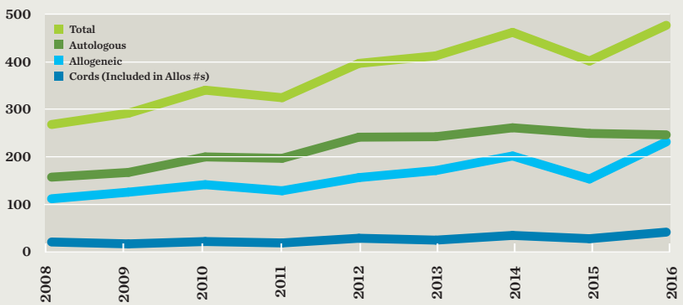
PEER-REVIEWED PUBLICATIONS



AWARDED GRANTS & CONTRACTS



ADULT BONE MARROW TRANSPLANTS



EXPANSION OF THE REGIONAL SITES

IN SEPTEMBER 2016, MSK Commack completed phase one of a $73 million expansion of services for our patients on Long Island. Some highlights of the new three story space include a sun-drenched chemotherapy suite, which features 18 private infusion rooms that boast floor-to-ceiling windows; increased capacity of CT and MRI scans; and the addition of an interventional radiology suite. The new waiting areas house a variety of seating options for patient and caregiver comfort and feature curated artwork. The expansion's second phase is expected to be complete by the end of 2017.

TOP: Memorial Sloan Kettering Commack, **BOTTOM:** Memorial Sloan Kettering Basking Ridge

HEMATOLOGIC ONCOLOGY FACULTY CURRENTLY PRACTICING IN THE REGIONAL NETWORK

Philip Caron	MSK Westchester*
Pamela Drullinsky	MSK Rockville Centre*
Audrey Hamilton	MSK Basking Ridge*
Paul Hamlin	MSK Basking Ridge
Hani Hassoun	MSK Westchester
Neha Korde	MSK Basking Ridge MSK Monmouth†
Sham Mailankody	MSK Commack
Matthew Matasar	MSK Commack
Colette Owens	MSK Monmouth*
Andrew Zelenetz	MSK Westchester

* Primary location † Starting 2017

MSK's presence in New Jersey also continues to grow. In December 2016, MSK Monmouth opened in Middletown, providing convenient access for residents of southern New Jersey and the Jersey Shore. In 2018, MSK Bergen is scheduled to open in Montvale, NJ to serve the northern half of the state as well as residents of New York's Orange and Rockland counties. MSK Basking Ridge recognized its tenth anniversary in 2016, and it's easy to see the enormous impact the facility has had on the community. When the 85,000-square-foot space opened in 2006, medical oncology and radiation oncology were its hallmarks. Today, patients can undergo outpatient surgical consultations on site as well as take advantage of acupuncture, genetic testing, nutritional counseling, and other support services. The Basking Ridge location also enrolls more patients in MSK's network of cutting-edge clinical trials than any other outpatient site. ■

EXPERT CANCER CARE CLOSE TO HOME

MSK BASKING RIDGE
136 Mountain View Boulevard
Basking Ridge, NJ 07920

MSK BERGEN
(Opening 2018)
225 Summit Avenue
Montvale, NJ 07645

MSK COMMACK
650 Commack Road
Commack, NY 11725

MSK HAUPPAUGE
800 Veterans Memorial Highway
Hauppauge, NY 11788

MEMORIAL SLOAN KETTERING CANCER CENTER
1275 York Avenue
New York, NY 10065

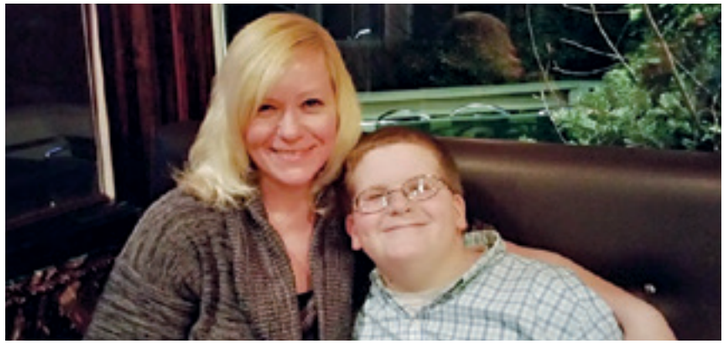
MSK MONMOUTH
480 Red Hill Road
Middletown, NJ 07748

MSK ROCKVILLE CENTRE
1000 North Village Avenue
Rockville Centre, NY 11570

MSK WESTCHESTER
5000 Westchester Avenue
West Harrison, NY 10604

READY TO FIGHT, BUT MY DOCTOR SAYS TO WAIT: WATCHFUL WAITING AFTER A LYMPHOMA DIAGNOSIS

BY MAUREEN SALAMON & MEREDITH BEGLEY



Doctors for Nancy Hughes, pictured here with her son, recommended a watch and wait approach after she was diagnosed with follicular non-Hodgkin's lymphoma.

THE WATCH AND WAIT APPROACH TO TREATMENT, also called active surveillance, is common treatment for lymphomas that pose no immediate threat to a patient's health. This hands-off method has been proven to work just as well as active treatment in select patients, and negates the risk of side effects.

When 47-year-old Nancy Hughes was diagnosed with follicular non-Hodgkin's lymphoma in 2007, she went into fight mode — but her doctor had another idea.

Memorial Sloan Kettering hematologic oncologist John Gerecitano instead recommended the "watch and wait" approach, in which Nancy, from Hampton Bays, New York, would be monitored regularly and put on chemotherapy only if her disease progressed.

"I remember thinking, this is insane. I have cancer, you have to get rid of it," the mother of two recalls. "And I think that's everybody's initial response."

That's a response Dr. Gerecitano often finds himself receiving whenever he advocates a watch and wait approach for lymphoma patients.

"This recommendation, especially in lymphoma, doesn't mean we're telling patients there's no treatment for them," he says. "We know from the data that harm will not come from waiting."

Also called active surveillance, watch and wait is a common treatment strategy at MSK and other top cancer institutions for lymphomas that pose no immediate threat to a patient's health.

"Some lymphomas can be treated like chronic conditions such as diabetes or high blood pressure, where we manage them over time," says Dr. Gerecitano, who recently led a trial for Venetoclax, a new FDA-approved lymphoma drug.

Even though that's good news, the plan can still lead to tremendous anxiety. Many patients are skeptical about holding off on active treatment.

"It causes understandable anxiety when you tell patients they have cancer and that they should sit on the sidelines," he says. "We live in a culture in which cancer is seen as an enemy that has to be actively fought."

But the surveillance is called "active" for a reason. Usually, patients are first assessed every three to six months. Once doctors understand the disease's growth pattern, they can sometimes space patients' visits further apart — but they're always carefully monitored.

MONITORING CAN SAFELY LAST FOR YEARS

At MSK, lymphoma experts typically recommend active surveillance for around 30% of lymphoma patients. Others are advised to start immediate treatment with chemotherapy, radiation, or surgery. But the hands-off approach has been proven to work just as well in select patients, and also negates the risk of side effects from treatment, Dr. Gerecitano says.

"These are lymphomas that are unlikely to cause an immediate threat to a patient's overall health," he says, adding that some lymphomas often take two to five years to cause problems severe enough to tackle with active treatments.

HELPING PATIENTS COPE WITH ANXIETY

Despite the evidence, convincing some patients that watch and wait is the best approach is still extremely challenging.

While Nancy initially wanted to eliminate the cancer as quickly as possible, she says she "knew during the first meeting" that she could trust Dr. Gerecitano.

"I just had the utmost faith in his decision-making," she recalls.

Dr. Gerecitano also tells patients that prudently waiting to launch active treatments allows for "the accrual of better weapons. Almost every year there are breakthroughs in the treatment of lymphomas."

To respond to patients' fears, MSK doctors typically schedule longer office visits so they have time to fully explain their recommendations. "When we sit and tell patients all of the information, most feel comfortable with active monitoring," he says. "We find that investing this time is worth it if we can spare patients the unnecessary side effects of chemo or prevent them from developing treatment resistance."

To help patients cope with the potential emotional strain of waiting, MSK also offers patient support groups, an online community, and individual and family counseling.

Dr. Gerecitano recommends that his patients stay physically active, not only to decrease the risk of lymphoma-related blood clots but also to keep their energy levels up. "It's important to get in the best place mentally and physically during that time," he says. "This will help them when it is time to fight."

TIME HEALS

Nine years after her diagnosis — with the disease still posing little threat — Nancy has made peace with her treatment plan.

"I think just as with anything else, time makes it better," she says. "When you go in for your appointments, those can be a little anxiety producing. But as time as progresses it just gets easier to process." ■

LINK: https://www.mskcc.org/blog/ready-fight-my-doctor-says-wait-watchful-waiting-after-lymphoma-diagnosis

HIGHLIGHTS

- Watch and wait patients are carefully monitored and more active treatments are introduced if the disease progresses.
- This approach can be challenging for patients, so MSK offers patient support groups, an online community, and individual and family counseling.

"This recommendation, especially in lymphoma, doesn't mean we're telling patients there's no treatment for them."

John F. Gerecitano, ONCOLOGIST

TOM BROKAW REPORTS ON HIS CANCER JOURNEY

Veteran news anchor Tom Brokaw shared his cancer experience with MSK staff.

ESTEEMED JOURNALIST TOM BROKAW is, unsurprisingly, used to dealing with the facts. But the former anchor of *NBC Nightly News* told a standing room audience of Memorial Sloan Kettering doctors, nurses, and staff that after his diagnosis with multiple myeloma, he struggled to accept the news.

"Half of me was thinking about [getting back to work], and the other half of me was saying, 'You've got cancer,'" he said. "I was trying to come to grips with my new life." Mr. Brokaw shared his experiences with MSK staff as part of the Art of Medicine program. The lecture series, run by medical oncologist Terri Gilewski, is designed to highlight the human dimensions of illness from the perspectives of current and former patients, doctors, and caregivers. He was diagnosed with multiple myeloma in 2013 after suffering from severe back pain. His treatment journey began at the Mayo Clinic, but he ultimately transitioned his care to a team led by MSK medical oncologist Heather Landau. The unflappable personality that served him well on dangerous reporting assignments in combat zones also helped him when he faced a threatening disease. "The conceit of an anchorman is that we think we're going to live forever," he said. Nevertheless, he acknowledged, "at every step of the way, as lucky as I was, it was harder than I thought it was going to be." Mr. Brokaw was adamant about how vital it is for patients to have someone to help them navigate those challenges. He spoke about the importance of having his wife of more than 50 years, Meredith, and his eldest daughter, Jennifer, an emergency room physician in San Francisco, on his team. Having a doctor in the family who could speak on his behalf — translating his level of pain from a downplayed "three" to a more realistic "seven," for example — was invaluable. "I was so lucky to have her," Mr. Brokaw said. "She was my advocate." ■

"The conceit of an anchorman is that we think we're going to live forever."

Tom Brokaw, JOURNALIST

Heather Landau

MSK researchers are studying the role of bacteria called bacteroidetes in drug-induced colitis.

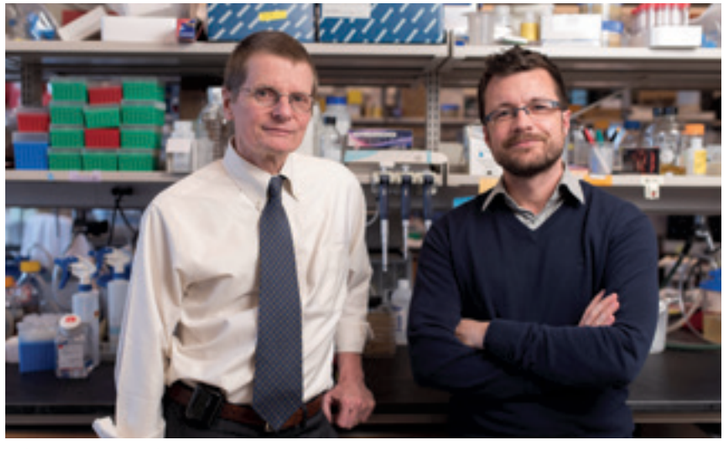
MICROORGANISMS IN THE GUT CAN AFFECT CANCER OUTCOMES

BY JULIE GRISHAM

STUDIES THAT ANALYZE THE MICROBIOME — the community of organisms that live in the body — in cancer patients are revealing new findings about the connection between bacteria and health in cancer patients.

When most people hear "bacteria," they think of disease-causing germs. But everyone has an ecosystem of bacteria inside them, and most of these microbes are not dangerous. They help keep us healthy by performing jobs including processing nutrients we get from food, thwarting tooth decay, and preventing harmful bacteria from gaining control.

Cancer treatment can throw the balance of microbes out of whack, leading to potentially serious consequences. Memorial Sloan Kettering investigators such as Eric Pamer, Head of the Division of Medical Subspecialties, are examining the relationship between cancer and the microbiota (the microbes that live on and within us). Dr. Pamer's team, together with MSK computational biologist Joao Xavier and collaborators from Yale University, received a grant earlier this year from the National Institutes of Health to investigate the connection between the microbiota and infections in cancer patients.



Eric Pamer, Joao Xavier

DECODING SIDE EFFECTS FROM IMMUNOTHERAPY

One study led by physician-scientist Jedd Wolchok and Dr. Pamer, published in February in *Nature Communications*, looked at how the balance of bacteria relates to colitis, an intestinal disorder, in people given the immunotherapy ipilimumab.

The drug, used mainly to treat melanoma, takes the brakes off the immune system, enabling immune cells to attack cancer. But when these cells are unleashed, side effects arise: In one-third of patients, the cells also attack the lining of the colon. Until this study was published, we didn't know why.

The researchers analyzed fecal samples from patients before treatment and again afterward to look for a connection between colitis and certain strains of bacteria. They found patients who had higher levels of the bacterial phylum called bacteroidetes before treatment did not get colitis, suggesting that these bacteria provided some kind of protection.

Although still in the early stages, this research suggests that it may be possible to use bacteroidetes to prevent colitis in patients most likely to get it.

THE ROLE OF THE MICROBIOTA IN BONE MARROW TRANSPLANTATION

Dr. Pamer's team also collaborates with Marcel van den Brink and Robert Jenq and other members of MSK's Bone Marrow Transplantation (BMT) Service. Having intestinal microbiota that are out of balance causes side effects and affects outcomes after BMT.

One complication is graft-versus-host disease (GVHD) — when immune cells from the donor graft attack tissue in the recipient, especially the intestinal lining. MSK studies have demonstrated that microbiota play a role in GVHD.

Antibiotics that prevent infections while patients recover from BMTs also can destroy beneficial bacteria and allow harmful ones to dominate. Research from the team suggests that, in order to keep levels of healthy bacteria high, some antibiotics may be better treatments than others.

Having intestinal microbiota that are out of balance causes side effects and affects outcomes after BMT.

MSK studies have demonstrated that microbiota play a role in GVHD.

Recent studies have found that which antibiotics are given to patients after BMT can influence their outcomes, including how likely they are to get GVHD. Researchers are using mice to study how these antibiotics affect the microbiota and determine the effect that gut microorganisms have on GVHD.

Dr. van den Brink, who is also co-director of the Parker Institute for Cancer Immunotherapy, presented research on the link between the microbiota and cancer at the American Association for Cancer Research annual meeting in this spring.

TECHNOLOGY ADVANCES THE FIELD

One advance that has enabled this research is faster, more detailed gene sequencing. Sequencing technology allows characterization of all the bacteria types that live in the gastrointestinal tract by analyzing the microbiome, the combined genes of all the microbiota.

Computational biologists also create tools to make sense of the millions of DNA sequences that come from this analysis. ■

HIGHLIGHTS

- One study has shown how microbes may trigger colitis in patients receiving the immunotherapy drug, ipilimumab.
- The balance of microorganisms also can play a role in graft-versus-host disease, a serious complication of bone marrow transplants.
- Advances in gene sequencing and computational biology have advanced microbiome research.

Enrico Velardi, Marcel van den Brink, Sophie Lieberman

LINK: https://www.mskcc.org/blog/microorganisms-gut-can-affect-cancer-outcomes

MOLECULAR GENETICIST, ELLI PAPAEMMANUIL, AT FOREFRONT OF REVEALING BIOLOGICAL UNDERPINNINGS OF CANCER

WHEN THE INEVITABLE cocktail party question arises about what Elli Papaemmanuil, PhD, does for a living, the molecular geneticist offers acquaintances the short answer. "I run a multidisciplinary team with a common research interest: to understand how mutations in DNA lead to cancer and how we can use that information to understand cancer biology and define the best treatment options for patients."

Dr. Papaemmanuil, recruited by Memorial Sloan Kettering in 2015 from her post at University of Cambridge in England, fully recognizes the yawning gap between characterizing the genomics of cancer and actually developing effective new therapies to treat it. Motivated as a young girl by the launch of the Human Genome Project in 1990, the Greek native's research has always focused on uncovering the genetic drivers of leukemia and various other cancers.

At MSK, Dr. Papaemmanuil wears multiple hats. She's an Associate Member of Epidemiology and Biostatistics; a Joint Appointee in the Sloan Kettering Institute in cancer biology and genetics; and Assistant Attending in the Computational Oncology Service. Her work here also extends to the global stage, where she leads an international group to better classify myeloid neoplasms such as acute myeloid leukemia (AML) or myelodysplastic syndromes (MDS).

Dr. Papaemmanuil and her colleagues use in-depth, state-of-the-art genome profiling studies on large patient groups of 1,000 or more, which have revealed hundreds of novel genes and biological pathways that lead to cancer. Bioinformatics capabilities and statistical tools help her to integrate genomic, clinical, and patient-specific factors to develop diagnostic and prognostic models of care.

"Some of the best scientists in our field are members of the MSK community," says Dr. Papaemmanuil, who earned her PhD from University of London and received the European Hematology Association Young Investigator and ASH Scholars Award.

"My goal was always to do impactful and innovative research, and MSK is a fantastic place to do that with other researchers to focus not only on genomics, but integrate biology and translational cancer research in a way we can bridge back into the clinic as directly as possible," she adds. "This was probably one of the best moves of my life."

NOTABLE RESEARCH REVEALS VARIATIONS IN AML

Even in her relatively short tenure at MSK, Dr. Papaemmanuil feels she's been able to design experiments she "never would have dreamt of before." Rather than focusing on a single project, as she did during postdoctoral studies, she finds herself immersing herself in many research pools simultaneously.

"For example, I'm working very closely with Pediatrics in trying to understand disease evolution from primary disease, to the effects of treatment, to the risk of developing secondary malignancies," she explains. "I'm also working very closely with other areas, establishing functional models of disease biology to cell-based systems, and also investigating the potential of immunotherapy. These are all areas I never would have conceived of before and are very much the product of collaborative relationships within MSK."

Most notably, Dr. Papaemmanuil's efforts have produced one of the largest studies ever

"We can support science that's very much controlled and statistically powerful, using the opportunity to learn from patient samples themselves."

to link mutations with outcomes in AML. Published recently, the work sequenced 111 genes across 1,540 AML patients in Germany. The results suggested the existence of 11 additional molecular subsets of AML that were not widely recognized previously, adding to established AML subsets.

The grim prognosis associated with two of the AML subgroups, in particular, adds to the urgency to characterize gene mutations in these pathways and integrate that knowledge into initial diagnosis for these patients.

"AML is a disease that's affecting an increasingly older population, so it's a growing healthcare concern," she says. "Therapies haven't really changed and the five-year survival is 25%."

"We're able to risk-stratify 85% of patients now, compared to about 50% before, and have a good sense of what their response to therapy will be," Dr. Papaemmanuil adds. "Incorporating information from mutations found, we'll be able to deliver truly patient-tailored care treatment decisions. We could predict patient outcomes from chemotherapy as well as bone marrow transplant, and recommend which patients would benefit from which therapy."

SHARED DATABASE PROPELS STATISTICAL POWER OF RESEARCH

Dr. Papaemmanuil's exhaustive research has also led to other key insights. Among them, she has noticed a major overlap between AML and MDS, a type of cancer in the blood-forming cells that can also evolve into AML.

"When a patient presents in clinic and is classified as having [AML, MDS or another myeloid neoplasm], that dictates very much what treatment they receive," she notes. "My research has led me to see the opportunity to redefine how we diagnose each of those subsets."

This knowledge also led Dr. Papaemmanuil to orchestrate an international group of researchers who are combining 12,000 biological samples across the spectrum of myeloid neoplasms to better define them based on genetic markers.

"Hopefully this will lead to better therapies and better survival because diagnosis will be based on these markers instead of empirical information," she says.

Creating a unified, easily shared database linking researchers with information gleaned from patient leukemia specimens has been one of Dr. Papaemmanuil's highest priorities. Known as the LeukGen project, MSK launched the first portion of this information pipeline in early 2016 and has since analyzed more than 6,000 specimens.

"Now if one MSK researcher, for example, performs research on a particular mutation, we can link to all the specimens in the biobank that have that mutation and accelerate science," she explains. "We can support science that's very much controlled and statistically powerful, using the opportunity to learn from patient samples themselves."

Dr. Papaemmanuil feels a certain awe — as well as humility and gratitude — to be part of a large web of scientists trying to reveal the genetic secrets of cancer development and progression.

"When the data comes through … it's a whole new world that unravels in front of us," she says. "It's very powerful to be part of the process of understanding how the data we generate delivers new information that directly impacts our understanding of disease biology as well as how that translates in the clinic."

"The science we do always builds upon what the entire scientific community has contributed to, and each of us adds a little block to the larger knowledge," she adds. "A single researcher or team is never the start or end of any scientific endeavor." ■

AMERICAN SOCIETY OF HEMATOLOGY (ASH) MEETING 2016

SAN DIEGO, CA

THE 58TH ANNUAL MEETING of the American Society of Hematology took place in San Diego, California from December 3-6, 2016. Faculty from the Division was well-represented with over 140 abstracts, 71 of which were selected for oral presentation.

The 9th annual ASH reception for the Division of Hematologic Oncology was hosted by the Memorial Hospital Alumni Society at the Hilton San Diego Bayfront. It was attended by MSK alumni, current faculty, fellows, and colleagues from other institutions as well as invited guests of the Division of Hematologic Oncology.

Prior to the ASH Meeting, Dr. Marcel van den Brink and Dr. Edmund Waller (Emory University, Winship Cancer Center) co-chaired the 5th Annual BMT Winter Workshop at the University of California San Diego. The workshop was attended by over 160 physicians and scientists and consisted of short presentations regarding unpublished recent research on Hematopoietic Stem Cell Transplantation. ■

CLOCKWISE, FROM TOP, LEFT TO RIGHT: Sergio Giralt, James Young, Marcel van den Brink, Adam Boruchov, Katharine Hsu; Colette Owens, Stephanie Thermozier, Melody Smith; Leyla Shune, Guenther Koehne, Susan Prockop; Esperanza Papadopoulos, Kathy Hsu; Jacob Soumerai, Hugo Castro-Malaspina

SIX MYTHS ABOUT DONATING BONE MARROW AND STEM CELLS

BY JULIE GRISHAM

MANY PEOPLE ARE RELUCTANT to join the bone marrow donor registry because they fear being called upon to donate. Here we address several myths about donating your bone marrow or stem cells to cancer patients in need.

What would you do if you found out that your bone marrow was a match for someone who needed it — even a complete stranger?

Bone marrow and stem cell transplants are a lifesaving treatment for many people with blood cancers like leukemia and lymphoma, as well as some other blood diseases.

During a transplant, patients are given high doses of chemotherapy and sometimes radiation to wipe out their cancer. These powerful treatments also destroy the blood-making cells, however. So the next step is for healthy blood stem cells to be infused into the body, enabling the patients to grow new blood cells and recover from the treatment.

Although some patients can use their own stem cells to rebuild the blood, many patients — especially those with leukemia whose blood stem cells may themselves be cancerous — need a donor to provide the cells that will enable them to recover.

One way that donors are found is through the National Marrow Donor Program, a group that maintains a registry to match unrelated volunteer donors with patients in need. Many people are reluctant to join this registry because they don't understand what's involved or how important their donation may be. We spoke to Parastoo Dahi, a hematologist and medical oncologist at Memorial Sloan Kettering who specializes in stem cell transplantation, about some of the myths surrounding bone marrow and stem cell donation.

Medical oncologist, Dr. Parastoo Dahi (left) specializes in treating patients with stem cell transplants.

Myth 1:
Stem cell donations always come from the bone marrow.

"We still commonly use the term 'bone marrow transplant,' but more often than not, what we really mean is a transplant using stem cells that are removed from the bloodstream rather than the marrow," Dr. Dahi says.

The doctor performing the transplant will decide which procedure will be used to extract the stem cells based on what he or she thinks will be best for the recipient. But the majority of donations are taken from the blood, not the bone marrow.

Myth 2:
Making a stem cell donation is difficult and painful.

With stem cell donation from the blood, there is very little pain involved. It is very similar to donating blood platelets. The main difference is that for a few days before the donation, donors need to take an injection called filgrastim (Neupogen®), which stimulates the bone marrow to produce extra blood-forming stem cells. They may experience some bone pain or a low-grade fever while taking filgrastim, but the side effects usually are not severe and go away after the donation process is complete.

Bone marrow donation, the less common form of donation, is a surgical procedure done in an operating room. Donors are given general anesthesia so they don't feel any pain as the bone marrow is removed, or aspirated, from both sides of their pelvis.

"The procedure takes an hour or two, and usually donors can go home within a few hours of waking up," Dr. Dahi says. "They may have some pelvic and hip pain, as well as some bruising, for a few days, but most donors can immediately go back to their regular activities. The achiness can generally be controlled with over-the-counter pain medications."

Myth 3:
Stem cell donation is inconvenient.

Leading up to the time of the stem cell donation, most people are able to give themselves injections of filgrastim at home, so they don't need to go to the doctor every day.

On the day of the donation, the donor is hooked up to what is called an apheresis machine. The blood is collected from one arm, sent through a machine that removes the stem cells, and returned to the other arm. Donors can read or watch movies during the donation process.

Dr. Dahi says the process takes three to four hours, and the donor may need to return a second day, depending on how many cells are retrieved.

In the cases of both bone marrow and blood stem cell donation, the donor cells can be retrieved at a local hospital or blood donor room and shipped to where they are needed. The donor and recipient may live in different states, or even in different countries.

Myth 4:
Most patients can find a stem cell donor in their own family, so there's no reason to join the registry.

The process by which the donor and recipient are matched is called HLA (human leukocyte antigen) typing. It's not related to blood type but instead has to do with the immune proteins that we all inherit at birth from both of our parents. "The immune system uses these proteins to understand which cells belong to your body and which do not," Dr. Dahi explains. "An optimal match means that eight out of eight markers are the same."

According to Dr. Dahi, about one-quarter of patients have a sibling who is a perfect match. This means that about 75% of cancer patients must rely on potential donors from the registry.

Even if a sibling is perfectly matched, there may be medical reasons why they are unable to donate. Medical restrictions include infections such as HIV and hepatitis, autoimmune diseases such as lupus, bleeding problems, and a history of cancer. "It's important to make sure that the process is safe for both the donor and the patient," she says.

Myth 5:
There are plenty of people already in the stem cell donor registry, so my contribution isn't needed.

Not everyone who needs a donor is able to find one. "For members of minority groups, there can be major problems finding donors because they tend to be underrepresented in the registry," Dr. Dahi says. "Different ethnic groups have different HLA types, so a patient's best chance of finding a donor is someone within their own ethnic group." It may be even harder for people of mixed ethnic backgrounds to find donors, because their HLA makeup can be more complex.

For patients who are unable to find matched donors, there are other options, including a donation from a family member who is a half-match (called a haploidentical transplant) or using stem cells from donated umbilical cord blood, which don't require a full match. "We don't want patients to delay their treatment if they don't have a perfect match," she adds, "but it's still the standard to go with a donor who is a perfect match whenever possible."

Myth 6:
Getting into the stem cell donor registry is a hassle.

Joining the registry is easy. You can go to www.bethematch.org to order a collection kit that will be sent to your house or to find a local drive in your area. Once you get the kit, all it requires is wiping a cotton swab on the inside of your cheek, sealing it in a provided container, and mailing it back.

Because the most successful donors are between the ages of 18 and 44, the National Marrow Donor Program asks that people between the ages of 45 and 60 make a $100 contribution to cover the costs of testing their swab. ■

HIGHLIGHTS

- The majority of stem cell donations are taken from the blood (not the bone marrow).
- Donors and recipients are matched with a process called HLA typing.
- Three-quarters of people who need transplants do not have a matched sibling.
- It is especially hard for members of minority groups to find matched donors.

LINK: https://www.mskcc.org/blog/six-myths-about-donating-bone-marrow-stem-cells

‘CULTURE OF SUPPORT AND PARTNERSHIP’ DEFINES KEY OPERATIONS ROLE

AS THE CHILD OF EASTERN EUROPEAN IMMIGRANTS whose English was limited, it fell to Tanya Gelfand to act as her grandfather’s healthcare proxy when he was treated for cancer at Memorial Sloan Kettering more than a decade ago. Despite the challenging circumstances — Gelfand’s grandfather later died — spending so much time at MSK marked her in such positive ways that she’s now Administrative Manager of the Division of Hematologic Oncology.

Gelfand, who holds a master’s in public administration from New York University, has worked in a variety of administrative support roles in MSK’s Department of Medicine over the last 10 years. In her current position, she serves as administrative partner to Division Head Marcel R.M. van den Brink, MD, PhD, working closely with him to bolster the Division’s projects and initiatives as well as overseeing and mentoring other administrative support personnel.

“I made it my personal mission to come back and work at MSK,” says Gelfand, who also considered pursuing a law career. “I was so impressed by the empathy, care, and attention everyone provided to my grandfather here that the year after he passed, I applied for an entry-level job. It was something I really wanted to be part of myself.”

Gelfand’s key operations role is part of an intricate network of more than 70 administrative support staff in the Division supporting its nearly 70 faculty members in their own multi-faceted roles. One initiative affecting all is the planned relocation in 2019 to the David H. Koch Center for Cancer Care, which is currently under construction along the FDR Drive between East 73rd Street and East 74th Street. After the move, all Division personnel will be housed under the same roof for the first time, and Gelfand’s duties encompass smoothing that huge transition for the academic offices.

> **“I made it my personal mission to come back and work at MSK.”**

“There isn’t such a thing as a typical day for me because spontaneous things come up all the time, but ultimately my job is to partner in overseeing the division from an administrative position and support any ongoing projects,” she explains. “The common thread is the culture of support and partnership here.”

STEPPING-STONE EXPERIENCES CHARACTERIZE CAREER TRAJECTORY

Rising quickly through the ranks in the Department of Medicine over the last decade, Gelfand started out as a physician office assistant offering day-to-day support to doctors, scheduling appointments and performing other routine clerical duties. About two years later, she was promoted to physician office specialist, giving her exposure to management duties and overall supervisory experience for the first time. Another bump in duties occurred when Gelfand assumed an administrative coordinator position where she served as a direct supervisor to those in entry-level roles. She’s held her current position since July 2015.

“Ultimately I wanted to be in a managerial capacity. The way I learned and like to mentor is by having some direct knowledge of the role,” she says. “So it was important to start where I did — I wanted to know firsthand what operations entail from there on up.”

Gelfand’s daily tasks now vary by the hour, including directly supervising five staff members who oversee more than 70 direct reports of their own. She also meets and collaborates with staff and faculty to help spearhead disparate projects ranging from recruitment to data analytics.

“For example, one of the Division’s Service Chiefs is trying to figure out optimal support for his Service, so there have been a lot of meetings and thinking about the best way to map out his program,” she explains. “Another big initiative is access, collaborating closely with multiple departments and interdisciplinary teams to ensure optimal and streamlined access to our Division’s high-quality care.”

Gelfand finds she needs to stay agile in order to readily jump from one priority to the next.

“It’s operations, so I can plan my whole schedule fully and the next morning something very different comes up that necessitates flexibility,” she says. “For example, a recent big snowstorm required me to reprioritize half a day to make sure our calls would be answered and the few staff that came in would be supported. That’s definitely the challenge of being a manager, and it’s important to be OK with change because that’s part of the job and culture.”

EXCITING CHANGES LOOMING

Another major challenge of her role is not getting caught in “analysis paralysis,” spending prolonged time in meetings at the expense of taking action, Gelfand notes. Along those lines, she’s enthused by the reflection provoked within the entire Department of Medicine by the naming of its new chairman, Philip W. Kantoff, MD, in late 2015 and Senior Director, Jean Jordan.

“We’re going through this re-thinking period of what is the best way for each role to function,” she says. “It’s an opportunity to reflect, re-evaluate, and innovate, so it’s a very exciting time for us.”

The Division’s upcoming relocation, while adding considerably to Gelfand’s to-do list, also prompts excitement. Besides creating a central hub for Hematologic Oncology, Gelfand feels the move will enhance collaboration — “already a strong suit at MSK, but I think this will make it that much better,” she says.

“One thing I find such a privilege is that while I don’t provide direct patient care, I still feel that’s part of my mission,” she says. “I really am super-honored to work with and be surrounded by brilliant people. The clinicians here are simply amazing and they’ve dedicated their lives to caring for patients. To be even a small piece of that motivates me greatly.” ■

THE MORTIMER J. LACHER LECTURE & FELLOWS CONFERENCE

LEFT: LEFT TO RIGHT: Santosha Vardhana, Michael Scordo, Neha Mehta-Shah, Anthony Daniyan, Connie Batlevi, Jacob Soumerai; **TOP RIGHT:** Dr. Mortimer J. Lacher; **BOTTOM RIGHT:** Dr. Kenneth Offit

THE SEVENTH ANNUAL MORTIMER J. LACHER LECTURE AND FELLOWS CONFERENCE was hosted by the Division of Hematologic Oncology on April 15, 2016. The event honors Dr. Lacher, 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. In 1965, he published a seminal report with John R. Durant describing the success of combining vinblastine and chlorambucil to treat Hodgkin disease.

Dr. Lacher is the co-founder and current President of The Lymphoma Foundation and currently serves as a Consultant in MSK’s Department of Medicine. The Lymphoma Foundation provides annual funding for Medical Oncology/Hematology fellows at MSK as well as specific projects in the laboratories of MSK physician-scientists.

The Seventh Annual Mortimer J. Lacher Lecture, “Genomic Susceptibility to Lymphoid Malignancies,” was delivered by Kenneth Offit, MD, MPH, Chief of the Clinical Genetics Service and Vice Chairman of Academic Affairs, Department of Medicine, Memorial Hospital; Member, Program in Cancer Biology and Genetics, Sloan Kettering Institute; and Professor of Medicine and Public Health at Weill Cornell Medical College. ■

The 2016 Lacher Fellows are listed below along with their abstracts:

Jacob Soumerai, MD (Mentor: Dr. Andrew Zelenetz, MD, PhD)
An evaluation of the CLL-IPI score and comprehensive prognostic factor analysis in patients with R/R CLL in Idelalisib phase 3 randomized studies

Michael Scordo, MD (Mentors: Dr. Sergio Giralt, MD & Dr. Craig Sauter, MD)
Towards making an effective therapy safer — A comprehensive toxicity assessment of patients with CNS lymphoma consolidated with autologous stem cell transplantation using thiotepa, pharmacokinetically-targeted busulfan, cyclophosphamide conditioning

Neha Mehta-Shah, MD (Mentor: Dr. Steven Horwitz, MD)
A phase Ia/IIb trial of the combination of romidepsin, lenalidomide and carfilzomib in patients with relapsed/refractory lymphoma: Phase I results

Anthony Daniyan, MD (Mentor: Dr. Renier Brentjens, MD, PhD)
The development of a genetically engineered dendritic cell-based immunotherapy platform for the treatment of chronic lymphocytic leukemia

Carla Hajj, MD Mentor (Dr. Joachim Yahalom, MD, FACR)
Early stage follicular lymphoma treated with first-line radiation therapy alone: a 15 years experience

Santosha Vardhana, MD, PhD (Mentor: Dr. Craig Thompson, MD)
Metabolic rewiring as a mechanism of resistance to nutrient deprivation in naïve stem cells and cancer cells

Connie Batlevi, MD, PhD (Mentor: Dr. Anas Younes, MD)
Genomics in Lymphoma Management

NURSING AND PHYSICIAN ASSISTANT ACCOMPLISHMENTS 2016

LEFT: Joanne Taylor, Sergio Giralt, Pamela Grant-Navarro, and Holly Wallace; **RIGHT:** Nursing NP — **TOP ROW:** Coleen Ranaghan, Bernadette Cuello, Michelle Abboud, Tara Wolff ; **BOTTOM ROW:** Nicole LeStrange, Mary Shannon McGinnis, Megan Heavey Scott

TWO ABSTRACTS AT ASBMT IN 2016

- **Age-Stratified Comparison of Incidence of Falls and Mental Status Changes in Older Adult Transplant Patients (Podium)**

  Catherine Featherstone, MSN, FNP-BC
  Heather M. Hylton, MS, PA-C

  Biol Blood Marrow Transplant 2016;22(3):S106. Abstract received recognition as one of three Advanced Practice Professionals Best Abstracts and was accepted for an oral presentation (given by Cathy Featherstone, NP) at the 2016 BMT Tandem Meetings BMT Clinical Education Conference.

- **A Multidisciplinary Approach to Improving Communication Across the Care Continuum (Poster)**

  Catherine Featherstone MSN, FNP-BC
  Nicole Krist MSN, CNS, AOCNS, BMTCN

FOUR ABSTRACTS AT ONCOLOGY NURSING SOCIETY (ONS) CONFERENCE IN 2016

- **Chemotherapy Admissions: Opportunity to Improve the Patient Experience (Podium)**

  Elena Lubimov
  Caroline Srikumar
  Carlos Rojas
  Donna Miale Mayer
  Mary Dowling

- **The Clinical Protocol Coordinator: Essential role in the Integration of Phase 1 Clinical Trials on a Hematology Oncology Unit (Poster)**

  Jacqueline Patterson
  Connie McKenzie
  Kristen Battiato
  Diane Llerandi
  Donna Miale Mayer
  Mary Dowling

- **Quiet! Noise Reduction on a Hematology Oncology Unit. (Poster)**

  Marybeth Leo
  Danielle Donlon
  Lindsay Lachkey
  Megan Hanley
  Kerry King
  Colleen McGlynn

- **Remember to Wear Your PPE: Safe Handling of Antineoplastic Agents on A Hematology Oncology Unit. (Podium)**

  Kristen Battiato
  Jacqueline Patterson
  Liza Sanchez
  Connie McKenzie
  Melanie McCormick
  Mary Dowling

- **The Future is Here: What You Need to Know About Biosimilars. (Poster)**

  Sharon Lynch, BSN, RN, OCN

- **Engaging Patients via Online Portals (Clinical Lectureship Award Presentation)**

  Elizabeth S. Rodriguez, DNP, RN, OCN

PROMOTIONS

- **Clinical Nurse IV**

  Maggie Brennan, BSN, RN, OCN
  Barbara Morcerf, BSN, RN, BMTCN

- **Clinical Nurse III**

  Kimberly Ford, BSN, RN, BMTCN
  Anna Custodio, BSN, RN, OCN
  Katie Hambright, BSN, RN, OCN
  Lindsay Donofrio, BSN, RN, OCN

- **Clinical Nurse II**

  Christa Percoco, BSN, RN

- **Hematology Clinical Nurse Specialist (M12)**

  Jacqueline Patterson

CERTIFICATIONS

- **Bone Marrow Transplant Certified Nurse (BMCTN)**

  Andrea Arvidson, BSN, RN, BMTCN
  Suzanne McEnrue, RN, BMTCN
  Jason Chan, BSN, RN, BMTCN

- **Oncology Certified Nurse (OCN)**

  Genie Karen, BSN, RN, OCN
  Jay Mallari, BSN, RN, OCN

ACCOMPLISHMENTS AND HONORS

- **Amanda Copeland,** Clinical Nurse Specialist, Lymphoma Research Outpatient was promoted to Director of Clinical Research Nursing.

- **Elaina Preston, MPH, MSHS, PA-C** and **Dr. Nancy Kernan** were invited faculty members for an on demand CME/CE program *Discerning Sinusoidal Obstruction Syndrome (Veno-Occlusive Disease) in HCT* which launched in June 2016: **http://www.medscape.org/viewarticle/864133.**

- **Elaina Preston, MPH, MSHS, PA-C, Whitney Quitta, MS, PA-C, Catherine Bender, MPAC, PA-C, Teresa Scardino, PA-C, MPAS, Nadia Kralovic, MS, PA-C,** and **Heather Hylton, MS, PA-C** served as primary preceptors for 10 PA students who rotated in Adult BMT and Medical Oncology during calendar year 2016.

- **Heather Hylton, MS, PA-C** was an invited faculty member for the ASCO University *Team-Based Care* course which launched in 2016.

- **Heather Hylton, MS, PA-C** received the inaugural Advocate of the Year Award from the American Society of Clinical Oncology in 2016.

PUBLICATIONS/ POSTERS/PRESENTATIONS

- **Hylton H, Scardino T.** Improving Access to Care: The Physician/Physician Assistant Team. *Physician Assistant Clinics.* 2016;1(3):489-97. (Publication)

- Tetzlaff E, **Hylton H,** and Wong Y. "An Exploratory Study of Provider Characteristics and their Association with Burnout and Career Satisfaction among Physician Assistants in Oncology. Survey-based national study". *Abstract accepted for poster presentation at the 2016 Annual Meeting of the American Society of Clinical Oncology.*

- **Heather Hylton, MS, PA-C** presented "How to Integrate New Advanced Practice Providers into Clinical Oncology Practice" as part of the *Practical Tips to Engage Trainees, Advanced Practice Providers, and Patients* session at the American Society of Clinical Oncology Annual Meeting in 2016.

SERVICE

- **Nadia Kralovic, MS, PA-C** served on the United Hospital Fund Outpatient Antibiotic Stewardship Initiative in 2016.

- **Catherine Bender, MPAC, PA-C** served as a volunteer on a regular basis with the New York Cares organization in 2015.

- **Heather Hylton, MS, PA-C** was appointed to the American Academy of PAs' Commission on the Health of the Public and as the American Academy of PAs' Medical Liaison to the American Society of Clinical Oncology in 2016. ■

PHARMACY ACCOMPLISHMENTS 2016

CLOCKWISE, FROM TOP LEFT: Tim Peterson, Salma Afifi , Kristen Poppiti, Thu Dang, Laura Tang; Andrew Lin, Carmen Lau, Kristen Beyer, Meagan Griffin, Valkal Bhatt, Anthony Proli II; Ryan Daley, Amber King, Larry Buie, Troy Horvat

PUBLICATIONS IN 2016

- **Ogunniyi A, Rodriguez M,** Devlin S, et al. Upfront use o plerixafor and granulocyte-colony stimulating factors (GCSF) for stem cell mobilization in patients with multiple myeloma: efficacy and analysis of risk factors associated with poor stem cell collection efficiency. *Leuk Lymphoma* 2017;58(5):1123-1129.

- **Horvat TZ, Pecoraro JJ, Daley RJ, Buie LW, King AC,** et al. The use of Erwinia asparaginase for adult patients with acute lymphoblastic leukemia after pegaspargase intolerance. *Leuk Res* 2016;50:17-20.

- **Bhatt V, Lin A, Beyer K, Proli A,** et al. Analysis of Cyclosporine A levels supports new dosing guidelines in adult double-unit cord blood transplant recipients to optimize immunosuppression early post-transplant. *Biol Blood Marrow Transplant* 2016;22(8):1533-4.

- **Bhatt V,** Shune L, Lauer E, et al. Autoimmune Hemolysis and Immune Thrombocytopenic Purpura After Cord Blood Transplantation (CBT) May be Life-threatening and Warrants Early Therapy with Rituximab. *Bone Marrow Transplant.*

continued on page 30

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2016;51(12):1579-83.

- Reiss SN, **Buie LW,** Adel N, Goldman DA, Devlin SM, and Douer D. Hypoalbuminemia is significantly associated with increased clearance time of high dose methotrexate in patients being treated for lymphoma or leukemia. *Ann Hematol* 2016 Aug 20 [Epub ahead of print].
- Bates JS, **Buie LW,** Amerine LB, Savage SW, Eckel SF, Patel R, Valgus JM, Rao K, Daniels R. Expanding care through a layered learning practice model .*Am J Health Syst Pharm* 2016 Sep 23 [Epub ahead of print].
- **Afifi S**, Michael A, Lesokhin A. Immunotherapy: A new approach to treating multiple myeloma with daratumumab and elotuzumab. *Ann Pharmacother*. 2016;50(7):555-68.
- **Afifi S,** Devlin S, Duck E, et al. Upfront plerixafor plus G-CSF versus cyclophosphamide plus G-CSF for stem cell mobilization in multiple myeloma: efficacy and cost analysis study. *Bone Marrow Transplant*. 2016;(51(4):546-52.
- **King AC, Peterson TJ, Horvat TZ, Rodriguez M, Tang LA.** Venetoclax. Ann Pharmacother. 2016 Dec 1 [Epub ahead of print].
- **Dang TO, Ogunniyi A, Barbee MS,** et al. Pembrolizumab for the treatment of PD-L1 positive advanced or metastatic non-small cell lung cancer. *Expert Rev Anticancer Ther.* 2016;16(1):13-20.

POSTER PRESENTATIONS IN 2016

- **Proli A**, Tamari R, Zheng J, Jakubowski AA, et al. Impact of Busulfan Exposure on Transplant Outcomes for Patients with Advanced Myelodysplastic Syndrome Undergoing CD34 Selected Allogeneic Hematopoietic Stem Cell Transplantation. American Society of Blood and Marrow Transplantation Annual Meeting. Honolulu HI. February 2016.
- **Bhatt V, Lin A, Beyer K, Proli A,** et al. Analysis of Cyclosporine A levels supports new dosing guidelines in adult double-unit cord blood transplant recipients to optimize immunosuppression early post-transplant. American Society of Blood and Marrow Transplantation Annual Meeting. Honolulu HI. February 2016.
- **Bhatt V,** Palazzo M, Kilroy K, et al. Low Dose Unfractionated Heparin (UFH) Prophylaxis Is a Feasible Strategy for the Prevention of Hepatic Sinusoidal Obstruction Syndrome (SOS) after Myeloablative Adult Allogeneic Hematopoietic Stem Cell Transplantation (HSCT). American Society of Blood and Marrow Transplantation Annual Meeting. Honolulu HI. February 2016.
- **King AC,** Hsu M, Mauro MJ, Rampal RK. Treatment-related infections and risk factors in patients with myeloproliferative neoplasms treated with ruxolitinib. American Society of Hematology 58th Annual Meeting. San Diego CA. December 2016.
- **Dang TO,** AI N, Gerecitano JF, et al. Incidence of Infectious Complications Associated with Bendamustine and Anti-CD20 Monoclonal Antibody Combination at Memorial Sloan Kettering Cancer Center (MSKCC). American Society of Hematology 58th Annual Meeting. San Diego CA. December 2016.
- **Lau C, Bhatt V,** Barker J, et al. Incidence, Severity, Day 100 Treatment Efficacy and Therapy Toxicity of Cytomegalovirus (CMV) Infections with Early Pre-Emptive Therapy in Adult Cord Blood (CB) Transplant Recipients. American Society of Hematology 58th Annual Meeting. San Diego CA. December 2016.
- **Poppiti K, Lin A,** Hilden P, Castro-Malaspina H, et al. Outcomes of rituximab for EBV viremia/post-transplant lymphoproliferative disease in CD34+ selected allogeneic hematopoietic stem cell transplantation. American Society of Hematology 58th Annual Meeting. San Diego CA. December 2016.

NATIONAL PRESENTATIONS IN 2016

- **Salma Afifi:**

Invited speaker: "Multiple Myeloma Debate: Chemotherapy versus autologous hematopoietic stem cell transplantation" at the Hematology/Oncology Pharmacy Association (HOPA) 12th Annual Meeting in Atlanta, GA.

- **Thu Oanh Dang:**

Invited speaker: "Pre-phase treatment strategy for elderly patients with lymphoma" at the Hematology/Oncology Pharmacy Association (HOPA) 12th Annual Meeting in Atlanta, GA.

- **Larry Buie:**

Invited speaker: "Relapsed and refractory adult B-Cell acute lymphoblastic leukemia (ALL) at the Hematology/Oncology Pharmacy Association (HOPA) 12th Annual Meeting in Atlanta, GA.

- **Valkal Bhatt:**

Invited speaker: "Clinical Application of Chimeric Antigen Receptor (CAR) T-Cell Therapy in Hematopoietic Cell Transplantation (HCT)". American Society of Blood and Marrow Transplantation Annual Meeting. Honolulu HI. February 2016.

Invited speaker: "Clinical Application of Chimeric Antigen Receptor (CAR) T-Cell Therapy in Hematopoietic Cell Transplantation (HCT)". International Society for Cellular Therapy North America 2016 Regional Meeting. Memphis TE. October 2016.

NATIONAL COMMITTEE REPRESENTATION

- **Larry Buie:**

Served as the Chair-Elect of the Hematology Oncology Practice and Research Network for the American College of Clinical Pharmacy (ACCP) Practice and Research Network.

- **Valkal Bhatt:**

Served on the American Society of Blood and Marrow Transplantation Pharmacy Special Interest Group Education Working Committee and the Cord Blood Committee.

AWARDS & HONORS

- **Larry Buie**

Fellow of the American Society of Health-System Pharmacists (ASHP).

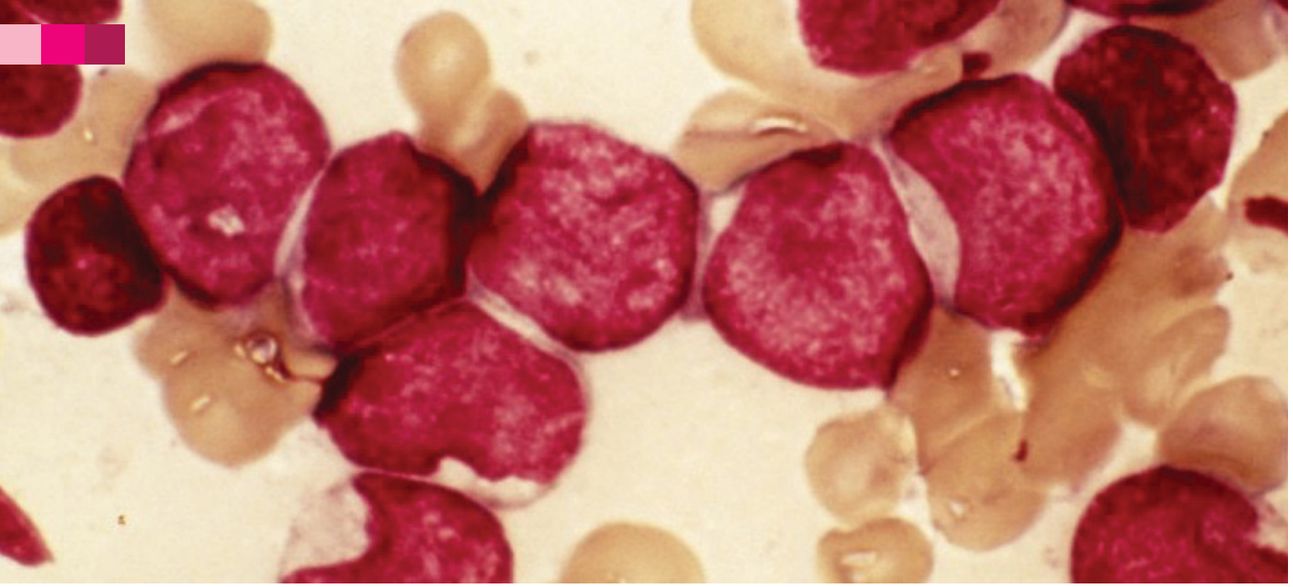
BOARD CERTIFICATION IN ONCOLOGY PHARMACY (BCOP) & PHARMACOTHERAPY (BCPS)

- **Tony Proli II, Andrew Lin, Valkal Bhatt, Larry Buie, Ryan Daley, Thu Dang,** and **Troy Horvat** successfully continued their board certification in oncology pharmacy (BCOP).
- **Valkal Bhatt** successfully continued his board certification in pharmacotherapy (BCPS).
- New BCOP certifications for 2016 included **Laura Tang, Tim Peterson,** and **Amber Ki.** ■

SURVIVORSHIP

THE 21ST ANNUAL CELEBRATION for the survivors of Blood and Marrow Transplant (BMT) was held on October 26th, 2016. This event brought together over 450 recipients of bone marrow transplant, and their loved ones, including family members, friends, donors, doctors, nurses, and other MSK staff who played a vital role in their transplantation and recovery. The evening to honor the strength, courage, and continued success began with short speaking program followed by live jazz music, food, and drinks. The festive atmosphere keeps participants coming back year after year to see fellow survivors and members of their care team who supported them through their transplant process. ■

LEFT TO RIGHT: Hugo Castro-Malaspina; Richard O'Reilly; David Chung



AML develops when cells in the bone marrow become cancerous and produce abnormal white blood cells.

NEW RESEARCH SHOWS AML IS NOT ONE DISEASE, BUT ELEVEN OR MORE

BY JIM STALLARD

DOCTORS CARING FOR PEOPLE with acute myeloid leukemia (AML) must base treatment decisions on patients' prognosis and likelihood of response to therapy. A large new study reveals that AML is actually 11 or more distinct disease subtypes — each caused by particular genetic changes and associated with specific outcomes. This is a critical step in helping doctors identify which patients need aggressive therapies or could benefit from a clinical trial.

Acute myeloid leukemia (AML), an aggressive blood cancer, has proved to be tricky for doctors to assess and treat. Patients vary widely in their response to treatment, and clinicians have found it nearly impossible to predict who will do well and who will fare poorly.

A new study analyzing more than 100 genes known to cause the disease reveals a major reason for this disparity: AML is not one disorder but at least 11 distinct subtypes caused by specific genetic changes. This discovery could change the way patients are diagnosed and treated.

"These findings help us understand how AML develops as mutations occur — what the critical events are that fine-tune the leukemia," says Memorial Sloan Kettering molecular geneticist Elli Papaemmanuil, who co-led the study, which was published today in the New England Journal of Medicine (NEJM). "This is the first step in helping us to identify who needs aggressive treatments and to choose who might benefit from clinical trials."

"These findings help us understand how AML develops as mutations occur."

Elli Papaemmanuil, MOLECULAR GENETICIST

"This is the basis for scientific studies to unlock new ideas about this disease and to test new therapeutic ideas."

Ross L. Levine, LEUKEMIA RESEARCHER

HIGHLIGHTS

- AML is aggressive and difficult to treat.
- A large study shows AML is actually at least 11 different diseases.
- Each AML subtype has a distinct molecular profile.
- The research will help doctors tailor AML treatment to each patient.

The study was conducted in collaboration with the Wellcome Trust Sanger Institute and a team of international colleagues. It involved analyzing leukemia-associated genes in 1,540 AML patients enrolled in three clinical trials in Europe — the largest AML patient group ever used for this type of genetic study. Researchers looked for common genetic themes behind development of the disease. They found that patients fit into at least 11 major groups, each with different assortments of genetic changes and distinctive clinical features.

"For the first time, we untangled the genetic complexity of AML genomes into distinct genetic subgroups, reflecting paths leading to specific subtypes of AML," Dr. Papaemmanuil explains. "This enables us to understand the biology of AML types and to use that information to develop clinical approaches such as combination therapies for clinical trials based on the mutation patterns."

MUTATIONAL PROFILES AND AML SUBTYPES

AML is characterized by the rapid growth of abnormal white blood cells. It develops when precursor cells in the bone marrow become cancerous as a result of a series of errors in the DNA. This usually requires mistakes in several key genes controlling blood-cell production. The disease affects people of all ages and often requires months of intensive inpatient chemotherapy.

Although in recent years researchers have identified a handful of AML mutations that play a significant role in driving the disease, most patients have a number of additional mutations that may or may not be important. The new study clarifies how the interplay between many of these mutations can affect the disease's progression.

MSK leukemia researcher Ross Levine, in an accompanying NEJM editorial, cited Robert Frost's "The Road Not Taken" in describing how distinct paths — initiated by varying mutations — lead to different disease destinations. The study, he wrote, provides "an unprecedented understanding of the different roads that lead to AML and how the specific path from normal blood cell to leukemia has important biologic and clinical implications."

In the study, full knowledge of the genetic makeup of a patient's leukemia greatly improved clinicians' ability to predict whether that patient would be cured with current treatments.

Because the study was so large, it allowed researchers to tease out genetic interactions that were not previously recognized. For example, the analysis showed patterns not just in the combination of mutations that occur but also in how one mutation can lead to a subsequent aberration.

"Once you expand to a large cohort, you identify relationships, not just in the combination of which mutations come together but also in the order in which they're acquired," Dr. Papaemmanuil says.

"This work provides us with a blueprint for how leukemia develops," Dr. Levine adds. "It shows that how that blueprint is written really matters for the patient."

VALIDATING GENOMIC ANALYSIS

The study illustrates the promise of improving cancer care through genomic analysis of patient-derived samples.

The Marie-Josée and Henry R. Kravis Center for Molecular Oncology, established at MSK in 2014, is taking this approach by correlating molecular information from tumors with clinical data, including patients' outcomes and responses to therapy.

More specifically, MSK's newly established Center for Hematologic Malignancies seeks to use this type of molecular data to better understand how leukemia develops — and then to apply those findings to crafting better therapies.

"This gives us a framework to go back to the lab and understand how all this wiring contributes to leukemia — to really look under the hood," Dr. Levine says. "This is the basis for scientific studies to unlock new ideas about this disease and to test new therapeutic ideas." ■

LINK: https://www.mskcc.org/blog/new-research-shows-aml-not-one-disease-11-more

SUSAN AND PETER SOLOMON DIVISIONAL GENOMICS PROGRAM

INITIATED IN 2010, the Susan and Peter Solomon Divisional Genomics Program at MSK is a collaborative, multidisciplinary program comprised of clinical and research experts that has pioneered efforts to develop genomics platforms to look for genetic mutations in the tumor samples of patients with different blood cancers. Led by three Co-Directors: Marcel van den Brink, Ross Levine and Elli Papaemmanuil, the program has invested in new and innovative technologies that have contributed to discovery and translational research in hematologic malignancies, including DNA/RNA sequencing and proteomic approaches, which allows MSK to invest in our clinical and laboratory investigators and to recruit additional world leaders in blood cancer research.

Peter and Susan Solomon

The program's initial efforts led to rapid, cost-effective mutational studies for MSK patients with acute myeloid leukemia (AML), myelodysplastic syndromes, and myeloproliferative neoplasms. In collaboration with Foundation Medicine, the program also developed research-based genomic tests for all patients with hematologic malignancies, including a state-of-the-art DNA/RNA sequencing test, which is used to comprehensively profile samples from leukemia, lymphoma and myeloma samples. This test is now offered world-wide, and has allowed our investigators to lead the field by bringing genomic testing to the clinical setting and by defining specific roles for genomic testing in the care of patients with blood cancers. ■

In 2016, the Solomon Divisional Genomics Program organized its first formal Funding Opportunity Announcement. Seven unique projects were selected for funding including:

Scott Lowe, PhD: *"Genomic and Epigenetic Characterization of Complex karyotype-AML"*

Heather Landau, MD: *"Genomic Analyses of Malignant Plasma Cells from Independent Sites of Osseous and Extraosseous Disease in Patients with Multiple Myeloma (MM)"*

Alan Hanash, MD, PhD: *"Somatic mutations in AML predict adverse outcome in patients undergoing allogeneic stem cell transplant"*

Eric Lai, PhD:*"Genomic analyses of novel Slicer- dependent miRNA pathways in blood and leukemia"*

Elli Papaemmanuil, PhD: *"The Impact of Oncologic Therapy on the Evolution of Clonal Hematopoiesis and Subsequent Hematologic Malignancy"*

Lia Palomba, MD: *"Dissecting the mechanisms of response to checkpoint blockade vs sequential low-dose radiotherapy plus checkpoint blockade in follicular lymphoma"*

Suhail Chaudhry, MD, PhD: *"Epigenomic and single cell transcriptomic characterization of thymic epithelial cell regeneration after damage"*

HEMATOLOGIC ONCOLOGY TISSUE BANK

FRONT: Amber Turner, Juliann Orfini, Keimya Sadeghi
MIDDLE: Haivy Luu, Jessica Schulman, Amanda Ciardiello
BACK: James Young, MD, Sean Quach, Jason Mironidis

THE DIVISION OF HEMATOLOGIC ONCOLOGY established the Hematologic Oncology Tissue Bank (HOTB) in 2010 to support the many different research projects of Memorial Hospital and Sloan Kettering Institute investigators.

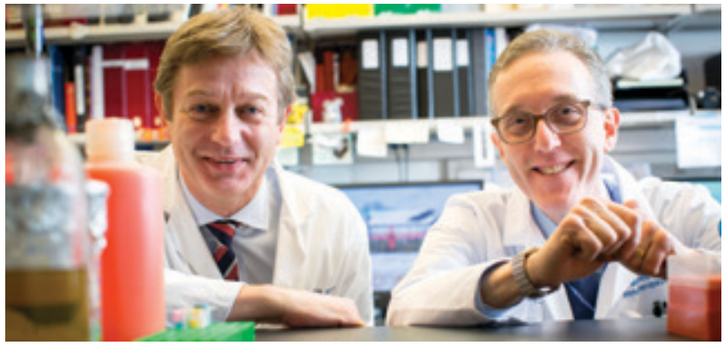
The HOTB is a centralized, comprehensive resource for banking of human biological specimens to support research using primary human cells and tissue. This facility provides appropriate cell and tissue-based specimens from patients with hematologic and lymphoid malignancies for investigator-initiated experimentation *in vitro*. Comparable materials are also available from healthy volunteers, although these are more limited in quantity and scope.

When the bank was created, about 150 samples were processed each month. Sample processing has steadily increased with no signs of slowing down; currently the HOTB processes more than 2,500 samples per month. The HOTB currently has an inventory of more than 170,000 aliquots, including peripheral blood components (plasma, serum, granulocyte pellets and mononuclear cells), buccal swabs for DNA, bone marrow mononuclear cells, skin, and lymphoid tissue.

Research specimens are collected from the following services: Leukemia, Lymphoma, Multiple Myeloma, Bone Marrow Transplant, Pediatrics, DTC, ITC, Dermatology as well as the MSK Regional Network Sites. In addition to tissue banking, the HOTB also supports specimen processing for over 35 clinical trials within MSK. 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.

The bank has become an invaluable resource for biospecimens linked to annotated clinical data, containing samples collected both before and after treatment from patients with lymphoid and hematologic malignancies. ■

PARKER INSTITUTE FOR CANCER IMMUNOTHERAPY



Marcel van den Brink and Jedd Wolchok describe the impact of the Parker Institute for Cancer Immunotherapy on research efforts at Memorial Sloan Kettering.

IN APRIL 2016, MSK's leadership in cancer immunotherapy was recognized when it was named one of six founding centers of the newly created Parker Institute for Cancer Immunotherapy, established by tech entrepreneur Sean Parker. The Institute is geared toward accelerating breakthrough immunotherapy treatments for patients.

The Parker Institute for Cancer Immunotherapy (PICI) is an unprecedented collaboration among 300 of the country's leading immunologists at six academic cancer centers, all dedicated to a single mission: harnessing the power of the immune system to fight — and cure — cancer.

By encouraging cooperation, data sharing, and industry partnership, the Parker Institute aims to eliminate the intellectual silos that stifle progress by giving researchers the incentive to work together on common goals.

Serial tech entrepreneur Sean Parker first made a name for himself in the early 2000s as the brains behind Napster and Facebook. In recent years, Mr. Parker has turned his entrepreneurial zeal — and the considerable wealth he has accumulated as a result — to addressing pressing matters of public health.

In April 2016, the Parker Foundation, of which Mr. Parker is the founder and president, announced the creation of PICI, a network of scientists and research centers geared toward unlocking the power of the immune system to fight cancer. The new institute is enabled by a $250 million grant from the Parker Foundation.

MSK is one of six founding centers, along with the University of Texas MD Anderson Cancer Center; Penn Medicine; Stanford Medicine; the University of California, Los Angeles; and the University of California, San Francisco. Funding for the Parker Institute comes from a $250 million grant from the Parker Foundation, established by tech entrepreneur and philanthropist Sean Parker.

By providing the resources and central coordination needed to advance research objectives, the Parker Institute empowers its team of scientists to pursue their boldest research ambitions.

MISSION AND SCOPE

The Parker Institute's mission is to accelerate the development of breakthrough immune therapies capable of turning cancer into a curable disease.

It will work to achieve this goal by:

- Bringing together the best scientists, clinicians, and industry partners to build a smarter and more coordinated cancer immunotherapy research effort
- Building a better funding and research model that overcomes the logistical hurdles that can slow research breakthroughs, and invests more strategically in projects that have big potential

The Parker Institute provides its members with easy access to advanced bioinformatics, intellectual property, sequencing, immune monitoring, industry-owned drugs, cell manufacturing, genetic engineering, and clinical trials management.

An innovative funding model allows proceeds from commercialized products to feed back into laboratory support so that the effort is self-sustaining. ■

MSK CENTER FOR HEMATOLOGIC MALIGNANCIES

ESTABLISHED 2016

THE MSK CENTER FOR HEMATOLOGIC MALIGNANCIES provides a venue to accelerate scientific discovery, support investigations into new research directions, and serve as an intersection for translational research between laboratory and clinical investigators with a shared interest in hematologic malignancies.

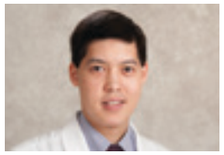
Dr. Ross Levine, who holds the Laurence Joseph Dineen Chair in Leukemia Research, and joint appointments in the Human Oncology and Pathogenesis Program (HOPP) and the Department of Medicine, serves as the inaugural Director of this new center.

The past decade has seen remarkable advances in the biology and treatment of blood cancers. Molecular-based therapies for specific disease subtypes have led to new treatment approaches and continued innovation in stem cell transplantation, which have had major impacts on patients at MSK and worldwide. Our world-renowned laboratory scientists and clinical investigators strive daily to make further paradigm-changing discoveries that improve outcomes for patients with blood cancers. Our leadership in the field means we are able to support emerging research and move discoveries from the lab to the patient's bedside. ■


Connie Batlevi, MD, PhD


Sheng Cai, MD, PhD


David Chung, MD, PhD


Stephen Chung, MD


Jacob Glass, MD, PhD


Alan Hanash, MD, PhD


Katharine Hsu, MD, PhD


Jodi Mones, MD

APPOINTMENTS

CONNIE BATLEVI, MD, PHD

IN JULY 2016, Connie Batlevi joined the Lymphoma Service as an Assistant Attending (L1) Physician. Dr. Batlevi received her MD/PhD in 2010 from University of Massachusetts Medical School in Worcester, MA. She completed her medicine internship and residency at Mount Sinai Hospital, Mount Sinai School of Medicine in New York, NY. She first joined MSK in 2012 as a Fellow in Hematology and Medical Oncology and focused her training and research in lymphoma under the mentorship and guidance of Dr. Anas Younes. She develops early phase clinical trials for B cell lymphoma.

SHENG CAI, MD, PHD

IN DECEMBER 2016, Dr. Sheng Cai joined the Leukemia Service as an Instructor. Dr. Cai received his MD and PhD from Washington University School of Medicine in St. Louis and completed his residency in internal medicine at New York Presbyterian-Weill Cornell Medical Center. He then joined the research-track medical oncology fellowship program under the mentorship of Dr. Scott Armstrong, during which he was awarded a two-year MSK Clinical Scholars Biomedical Research Fellowship, an ASCO Young Investigator Award, and a Leukemia & Lymphoma Society Career Development Award. His laboratory-based research, now under the guidance of Dr. Ross Levine, investigates the mechanisms of action of novel leukemia-directed epigenetic therapies, with the ultimate goals of reaching a deeper understanding of how leukemias develop and improving clinical outcomes for patients.

JACOB GLASS, MD, PHD

IN JULY 2016, Dr. Jacob Glass joined the Leukemia Service as an Assistant Attending L1 Physician. Dr. Glass received his MD and PhD from Albert Einstein College of Medicine in New York City. He completed his internal medicine residency at New York Presbyterian Hospital and his Hematology/Oncology fellowship at MSK. During his fellowship, Dr. Glass worked under the joint mentorship of Drs. Ari Melnick and Olivier Elemento to better define the DNA methylation features that characterize various AML subtypes. In parallel, he also worked on the use of fitness trackers and other smart devices in the clinic to deliver personalized care with greater precision. Dr. Glass joins the Leukemia Service and Center for Epigenetics Research with a clinical focus on treating patients with AML, MDS, and CLL. His research will examine the epigenetic features contributing to malignancy, and in particular how to use epigenetic information to better characterize poorly defined leukemias. He will also continue to work toward developing a platform to utilize fitness trackers and similar devices in the clinical setting.

JODI MONES, MD

IN JANUARY 2016, Dr. Jodi V. Mones joined MSK as an Associate Attending on the Hematology Service in the Division of Hematologic Oncology. Dr. Mones received her MD from New York Medical College. She completed her residency in Internal Medicine as well as her fellowship in Hematology/Oncology at New York Presbyterian Hospital/Weill Cornell Medical Center. Prior to joining our faculty, she was an Attending Physician at Montefiore Medical Center. Dr. Mones has a specific interest in benign hematology and will provide consultation for patients with thrombosis, bleeding disorders, cytopenias and a full range of hematologic disorders related to cancer. Her clinical expertise includes acquired and inherited hematologic disorders, thrombosis, abnormal bleeding, hemoglobinopathies and chemotherapy-induced blood disorders.

COLETTE OWENS, MD

DR. COLETTE OWENS joined the Monmouth Medical Oncology Service as an Instructor in August 2016. Dr. Owens received her MD from the Rutgers-Robert Wood Johnson Medical School and completed her residency in Internal Medicine at the Columbia University Medical Center in New York, NY. She completed her Hematology and Medical Oncology fellowship training at MSK. Dr. Owens' clinical practice focuses on lymphoma and genitourinary medical oncology. She began her practice at MSK's Basking Ridge location before moving to MSK Monmouth after it opened in December 2016.

JONATHAN PELED, MD, PHD

IN JULY 2016, Dr. Jonathan Peled joined the Adult BMT Service as an Assistant Attending L1 Physician. Dr. Peled received his MD and PhD degrees from the Medical Scientist Training Program at Albert Einstein College of Medicine and completed a residency in Internal Medicine at Massachusetts General Hospital in Boston, MA. He then completed a Hematology-Oncology Fellowship at MSK. Dr. Peled's research focuses on the role of the intestinal microbiota and how it affects transplant outcomes. He also provides consultation in bone marrow transplantation.

GUNJAN SHAH, MD

DR. GUNJAN SHAH joined the Adult BMT Service as an Assistant Attending L1 Physician in August 2016. Dr. Shah received her MD from the Temple University School of Medicine and a Masters in Pharmacology from Thomas Jefferson University. She completed a residency in Internal Medicine at the Thomas Jefferson University Hospital in Philadelphia, PA and her Hematology-Oncology Fellowship at Tufts University Hospital where she served as Chief Fellow. She then completed her Bone Marrow Transplant Fellowship at MSK. Her clinical practice and research will focus on transplantation for lymphoma and myeloma, as well as cost and comparative effectiveness in the hematologic malignancies.

ERIC SMITH, MD, PHD

IN JULY 2016, Eric Smith, MD, PhD joined the Myeloma Service as an Assistant Attending L1 Physician. Dr. Smith received his MD and PhD from the Mount Sinai School of Medicine and completed a residency in Internal Medicine at Mount Sinai Hospital in New York, NY. He then completed his Medical Oncology Fellowship at MSK. His fellowship research resulted in the invention and validation of novel CAR T cell therapy vectors for multiple myeloma (MM). These vectors have since been licensed, and through his efforts, the first-in-human study is enrolling patients at MSK. Dr. Smith will continue his pre-clinical work to understand the biology of CAR T cell function in the MM microenvironment, as well as to develop next generation CAR vectors for MM.

PROMOTIONS

DAVID CHUNG, MD, PHD

DR. DAVID CHUNG was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician on the Adult BMT Service in the Department of Medicine with a secondary appointment on the Myeloma Service, and Assistant Professor of Medicine at Weill Cornell Medical College. He is also an Assistant Attending Physician at The Rockefeller University Hospital. After receiving his MD and PhD degrees from Georgetown University, he completed an internship and residency in internal medicine at the University of California at Los Angeles. He joined MSK as a Medical Oncology/Hematology Fellow in 2004 and was appointed to an Instructor faculty position on the Adult BMT Service in 2008. Dr. Chung is actively involved in translational studies, primarily in the areas of cellular immunotherapy, post-transplant immune reconstitution, and immune-based mechanisms of disease evasion/relapse. He has developed a growing clinical practice focused on stem cell transplantation for myeloma while working in Dr. James Young's laboratory. His research in the Young lab has yielded important insights into dendritic cell biology, which in turn have been translated into clinical vaccine trials for melanoma and multiple myeloma using mRNA-electroporated autologous Langerhans-type dendritic cells.

STEPHEN CHUNG, MD

DR. STEPHEN CHUNG was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician on the Leukemia Service and Assistant Professor of Medicine at Weill Cornell Medical College. Dr. Chung received his MD from Washington University in St. Louis and completed his housestaff training at Massachusetts General Hospital. He joined MSK in 2009 as a fellow working under the mentorship of Dr. Christopher Park in the Department of Pathology and Dr. Martin Tallman on the Leukemia Service. He was appointed to an Instructor faculty position in 2012 on the Leukemia Service. In the laboratory, Dr. Chung studies molecular alterations in the hematopoietic (blood-forming) stem and progenitor cells that underlie the development of acute myeloid leukemia (AML) and the myelodysplastic syndromes (MDS). His ultimate objective is to improve our understanding of what causes these diseases, as well as the mechanisms by which they may become resistant to standard therapies. He is also interested in identifying novel alterations in cell surface protein expression in these diseases to identify new therapeutic targets and to develop new diagnostic tests. His work has led to the identification of CD99 as a marker of and therapeutic target on disease stem cells in AML and MDS. He has also contributed to studies furthering our understanding of the cell of origin of lymphoid malignancies.

ALAN HANASH, MD, PHD

DR. ALAN HANASH was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician on the Adult BMT Service at Memorial Hospital and Assistant Professor of Medicine at Weill Cornell Medical College. He received his MD and PhD from the University of Miami School of Medicine

continued on page 38


Ariela Noy, MD

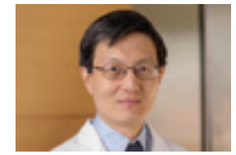

Colette Owens, MD


Jae Park, MD


Jonathan Peled, MD, PhD


Raajit Rampal, MD, PhD


Gunjan Shah, MD


Alan Shih, MS, PhD


Eric Smith, MD, PhD

continued from page 37

and completed a residency in internal medicine at the University of Chicago in Chicago, IL. He first joined MSK in 2008 as a Hematology/Oncology Fellow. Dr. Hanash is only the second member of the Division of Hematologic Oncology in the last ten years to go from trainee to independent laboratory-based faculty. His research focuses on the immunology of hematopoietic transplantation and immune-mediated mechanisms of tissue damage and regeneration. He is the recipient of an ASH Scholar Award, the Amy Strelzer Manasevit Research Program Fellowship, and his own R01 funding from the NIH, and his senior-authored manuscript on IL-22-mediated regulation of the intestinal stem cell compartment was the first manuscript on bone marrow transplant immunology published in Nature in over 30 years.

KATHARINE HSU, MD, PHD

DR. KATHARINE HSU was promoted to the rank of Member at MSK and Attending Physician at Memorial Hospital as well as Professor of Medicine at the Weill Cornell Medical College. Dr. Hsu is also jointly appointed in the Immunology Program at the Sloan Kettering Institute. She received her BS and MS degrees from Stanford University and her MD and PhD degrees from Weill Cornell Medical College. She then completed her internship and residency in Internal Medicine at Brigham and Women's Hospital, Harvard University. In 1997, she started a Hematology/Oncology fellowship at MSK, and she joined the Adult BMT Service faculty as an Instructor in 2002. Dr. Hsu's basic research is primarily based on the use of human tissue and human leukemia blasts and/or cell lines. Part of this is related to the fact that the KIR genes, so vital to human natural killer cell function, are essentially unique to humans. Therefore, the relevance of natural killer cells to human leukemia necessitates testing of human cell systems in vitro. Translation of her in vitro findings to the in vivo setting of transplantation is a hallmark of Dr. Hsu's work and certifies the relevance of her work to human disease.

ARIELA NOY, MD

DR. ARIELA NOY was promoted to the rank of Member at MSK, Attending Physician on the Lymphoma Service at Memorial Hospital, and Professor of Clinical Medicine at the Weill Cornell Medical College. Dr. Noy earned her MD from the University of Pennsylvania School of Medicine in Philadelphia, PA and completed an internship and residency at Columbia Presbyterian Medical Center in New York, NY. She first joined MSK in 1993 as a Hematology/Medical Oncology Fellow. In 1997, she was appointed to a faculty position as Clinical Assistant on the Lymphoma Service. Dr. Noy is best known for her leadership role in the AIDS Malignancy Consortium (AMC) Lymphoma Working Group and is widely recognized as an international leader in this field. She played an integral role in the development of autologous and allogeneic bone marrow transplantation trials for HIV patients with lymphoma in collaboration with the BMT Clinical Trial Network. Outside of HIV, her work led to a recognition of the correlation of lymphoma aggressivity with PET scan intensity and more recently to the 2017 FDA approval of ibrutinib, an oral targeted therapy for the treatment of marginal zone lymphoma. At MSK, she is also a member of the Department of Medicine and the Department of Radiology Quality Assurance Committees and the Fertility Preservation Committee.

JAE PARK, MD

DR. JAE PARK was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician on the Leukemia Service at Memorial Hospital and Assistant Professor of Medicine at Weill Cornell Medical College. Dr. Park received his MD from the Johns Hopkins University School of Medicine and completed his housestaff training in the Harvard system. He joined MSK as a fellow under the mentorship of Dr. Renier Brentjens. Dr. Park has become an authority in one of the most exciting novel therapeutic strategies in hematologic malignancies: chimeric antigen receptor (CAR) T cell therapy. Our institution has become internationally recognized for this promising treatment and Dr. Park has contributed greatly to this distinction.

RAAJIT RAMPAL, MD, PHD

DR. RAAJIT RAMPAL was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician on the Leukemia Service at Memorial Hospital and Assistant Professor of Medicine at Weill Cornell Medical College. Dr. Rampal earned his MD and PhD degrees from Stony Brook University School of Medicine. He completed an internship and residency in internal medicine at the University of Chicago and first joined MSK in 2009 as a Hematology/Medical Oncology Fellow. In 2013, he was appointed to an Assistant Member L1 faculty position on the Leukemia Service. Dr. Rampal's research focus is the development of new and innovative approaches to treating myeloproliferative neoplasms (MPNs) and leukemia. He seeks to understand the genetic and epigenetic events that contribute to the development and progression of leukemia and MPNs, and to utilize this information to develop new preclinical models and therapeutic strategies which can be rapidly translated into clinic trials. He is currently leading a multi-center effort to characterize genomic alterations in post-MPN AML, and is leading a multi-center phase I/II study for patients with accelerated-phase MPN and post-MPN AML.

ALAN SHIH, MD, PHD

DR. ALAN SHIH was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician on the Leukemia Service at Memorial Hospital and Assistant Professor of Medicine at Weill Cornell Medical College. Dr. Shih earned his MD degree from Weill Cornell Medical College and his PhD degree from Weill Cornell School of Medical Science of Cornell University. He then completed a residency in internal medicine/research at New York Presbyterian Hospital before joining MSK in 2009 as a Hematology-Oncology Fellow under the mentorship of Dr. Ross Levine. In 2013, he was appointed to an Instructor faculty position on the Leukemia Service. Dr. Shih's research focus is the molecular mechanisms of leukemogenesis. He develops mouse models of leukemia, specifically, defining the role of TET2 in hematopoietic transformation. He is working to understand how epigenetic modifications affect the development of leukemic cells, alter their differentiation program, reprogram the DNA, and lead to therapeutic resistance. In 2016, he was awarded a National Cancer Institute (NCI) Mentored Clinical Scientist Research Career Development Award (K08). ■

CLINICAL TRAINING & EDUCATION

PROGRAMS TRAIN THE LEADERS OF THE FUTURE

Memorial Sloan Kettering Cancer Center attracts applicants from all over the world for two distinguished fellowships in Medical Oncology/Hematology and Bone Marrow Transplantation. Education in benign hematology is also provided by the Hematology Service to international medical students, internal medicine residents, and hematology/oncology fellows.

MEDICAL ONCOLOGY/ HEMATOLOGY FELLOWSHIP

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 is the largest of its kind in the country, attracting more than 450 applicants each year for just 15 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 which has allowed our fellows to become leaders in our field in their own right.

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

BONE MARROW TRANSPLANTATION FELLOWSHIP

THE ADULT HEMATOPOIETIC Stem Cell 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, including experience with clinical research. The fellowship provides training in inpatient and outpatient settings, with a specific focus on the different subspecialties within hematopoietic stem cell transplantation, 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 19 fellows. Eighteen of the 19 graduates are now full time faculty on BMT services in academic centers in the U.S. and abroad. One graduate is working in industry as medical director for a CAR-T program.

To learn more, visit **http://www.mskcc.org/education/fellowships/fellowship/bone-marrow-transplantation.** ■

AWARDS & RECOGNITION 2016


Omar Abdel-Wahab


Connie Batlevi


Sheng Cai


Alan Hanash


Katharine Hsu


Malin Hultcrantz


Andrew Intlekofer


Scott James


Heather Landau


Ola Landgren


Ross Levine


Craig Moskowitz

THE FOLLOWING FACULTY MEMBERS received Steven Greenberg Lymphoma Research Awards:

Dr. Omar Adel-Wahab (2016), **Dr. Connie Batlevi** (2016), **Dr. Andrew Intlekofer** (2016, 2017), **Dr. M. Lia Palomba** (2016, 2017), **Dr. Hans Guido Wendel** (2016, 2017)

The following MSK faculty members and fellows in our Division received ASCO Young Investigator Awards:

Dr. Connie Batlevi: *"Autologous CD19 targeted CAR T-cells for consolidation post salvage chemotherapy in transplant ineligible patients with relapsed DLBCL"*

Dr. Sheng Cai: *"Targeting the histone demethylase LSD1 in acute myeloid leukemia"*

Dr. Scott James: *"Application of inhibitory chimeric antigen receptors (iCARs) in adoptive T cell immunotherapy of B cell leukemia"*

Dr. Santosha Vardhana: *"Mechanisms of response and resistance to checkpoint blockade in Hodgkin Lymphoma"*

The MSK Survivorship Nurse Practitioners Team was selected as the recipient of the 2016 ONS Team Achievement Award, one of the Pearl Moore "Making A Difference" Awards.

ADULT BMT

Dr. Katharine Hsu received the following grant awards in 2016:

- Alex's Lemonade Stand Foundation Innovation Award | Project title: *"Development of an anti-KIR3DL1 antibody to promote innate immunity against neuroblastoma".*
- LLS Scholar Award (R01) | Project title: *"Ensuring AML eradication in HLA-matched allogeneic stem cell transplantation by harnessing donor natural killer cell activity".*
- NIH R01 (AI125651) | Project title: *"KIR and HLA in cis and trans cooperatively shape human NK cell education".*
- FDA R01 (FD-R-005415-01) | Project title: *"Phase I study of humanized 3F8 MoAb (IND BB112594) and NK cells (IND BB-13399) for neuroblastoma".*

Dr. Alan Hanash received a Basic and Translational Immunology Grant funded by MSK's Ludwig Center for Cancer Immunotherapy for his project, *"Immune-mediated regulation of intestinal injury and regeneration,"* studying immune responses against intestinal stem cells.

Dr. Heather Landau received a 2016 MSK Society Research Grant award for her study: *"Identification of Genes that Regulate Light Chain (AL) Amyloid Pathogenesis and Clinical Outcomes."*

Dr. Melody Smith received the 2016 American Society for Blood and Marrow Transplantation (ASBMT) New Investigator Award for her project, *"CD 19 targeted donor T cells improve graft versus lymphoma activity and reduce graft versus host disease."*

LEUKEMIA

Dr. Omar Abdel-Wahab received a 2016 Prize for Young Investigators in Cancer Research from the Pershing Square Sohn Cancer Research Alliance (PSSCRA). His project seeks to identify novel transcripts, pathways, and therapeutic strategies to target spliceosomal-mutant malignancies in leukemias.

The **Leukemia Service** won the 2016 Teaching Excellence. This is the second time the service has received this award since 2011.

Dr. Ross Levine received a National Cancer Institute R35 Outstanding Investigator Award (OIA) for his project, *"Synergistic Role of Signaling and Epigenetics in Leukemic Transformation."* His work seeks to elucidate how mutations in signaling effectors and in epigenetic regulators contribute to leukemic transformation and to the response to anti-leukemic therapies.

Dr. Alan Shih received an NCI Mentored Clinical Investigator Award (CIA-K08).

Dr. Eytan Stein won the 2016 Paul Sherlock Housestaff Teaching Award.

LYMPHOMA

Dr. Connie Batlevi received an American Society of Hematology (ASH) Scholar Award, and a Lymphoma Clinical Research Mentoring Program Award from the Lymphoma Research Foundation (LRF).

Dr. Andrew Intlekofer received the Burroughs Wellcome Fund Career Award for Medical Scientists (CAMS) for his project: *"Investigating L-2-hydroxyglutarate production and its relevance to normal hematopoiesis and leukemogenesis."* He also received an NIH/NCI K08 Mentored Clinical Scientist Research Career Development Award.

At the 41st Annual Alumni Reception, the Memorial Hospital Alumni Society honored **Dr. Craig Moskowitz** and **Dr. Andrew Zelenetz** as Distinguished Alumni of the Year.

Dr. Ariela Noy published a trial that has led the FDA to approve the first ever drug specifically for marginal zone lymphoma:

> *Targeting BTK with ibrutinib in relapsed/refractory marginal zone lymphoma*
> Noy A, de Vos S, Thieblemont C, Martin P, Flowers CR, Morschhauser F, Collins GP, Ma S, Coleman M, Peles S, Smith S, Barrientos JC, Smith A, Munneke B, Dimery I, Beaupre DM, Chen R.
> *Blood* 2017; 129(16):2224-2232. PMID: 28167659; PMC5399483

Dr. Anas Younes was awarded a Leukemia and Lymphoma Society Specialized Center of Research (SCOR) Program Grant on *"Novel Immune Therapy of Lymphoma."* The central goal of this SCOR is to establish a collaborative team-science approach aiming at the development of new immune therapeutic strategies for diffuse large B cell lymphoma (DLBCL). Our ultimate goal is to translate our findings into novel clinical trials to improve the cure rate of patients with DLBCL.

Dr. Anas Younes and **Dr. Andrew Zelenetz** were awarded an MSK Specialized Program of Research Excellence (SPORE) in Lymphoma. The overall approach for this Lymphoma SPORE is to transform clinical practice by developing new treatments for diffuse large B cell lymphoma (DLBCL) and identify potential biomarkers that show how well these treatments are working.

HEMATOLOGY

Dr. Rekha Parameswaran received the MSK Hematology Teaching Attending of the Year Award in 2016.

Dr. Gerald Soff received MSK's 2016 Willett F. Whitmore Award for Clinical Excellence Award. "Dr. Soff is a tremendous clinician, with the dedication and compassion that makes every patient and family feel safe, comfortable, and well-looked-after while under his care," said MSK Physician-in-Chief José Baselga, quoting a colleague of Dr. Soff's."He is one of the most passionate and inspiring physicians and educators I have ever known. He makes me proud to be at MSK."

MYELOMA

Dr. Malin Hultcrantz received a grant from the Swedish Society of Medicine as well as the International Postdoc Award for her project titled, *"Mechanisms and Markers of Progression from MGUS to Multiple Myeloma."* She was also awarded a grant from the Karolinska Institute Foundations for her project, *"Genomic landscape of multiple myeloma."*

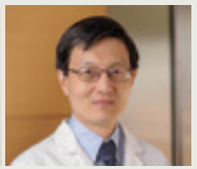
Dr. Ola Landgren received a Multiple Myeloma Research Foundation Translational Network Grant for his project, *"Mechanisms and makers of progression from MGUS to multiple myeloma."* He also received a grant from the Food and Drug Administration (FDA) Office of Minority Health for his project, *"Molecular Characterization of Racial Disparities and Outcome in Multiple Myeloma."*

Dr. Eric Smith received an SITC-EMD Serono Cancer Immunotherapy Clinical Fellowship for his project, *"Investigating and manipulating the interplay between the tumor microenvironment and Chimeric Antigen Receptor (CAR) T cell therapy to generate durable remissions in multiple myeloma."* He also developed and licensed CAR constructs targeting 3 antigens for multiple myeloma to Juno Therapeutics. ■


Ariela Noy


Lia Palomba

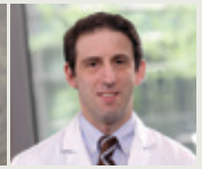

Rekha Parameswaran


Alan Shih


Eric Smith


Melody Smith


Gerald Soff


Eytan Stein


Santosha Vardhana


Hans Guido Wendel


Anas Younes


Andrew Zelentz

The MSK Survivorship Nurse Practitioners Team

The Leukemia Service

LEFT, TOP TO BOTTOM: Michael Mauro, Christina Muggeo

MEMORIAL SLOAN KETTERING CANCER CENTER
FRED'S TEAM
IMAGINE A WORLD WITHOUT CANCER

For more information, please visit:
www.fredsteam.org

FRED'S TEAM

FRED'S TEAM, named after a running legend Fred Lebow, is Memorial Sloan Kettering Cancer Center's (MSK) athletic fundraising program dedicated to bringing us closer to a world without cancer. By competing in marathons, half-marathons, triathlons, cycling races, and other endurance events worldwide, Fred's team participants fundraise to further MSK's pioneering research and support the Aubrey Fund for Pediatric Cancer Research.

Over 900 Fred's Team members took part in the 46th New York City Marathon on November 6th, 2016, and raised over $5.3 million dollars. In total, over $70 million has been raised since 1995.

In 2016, nearly $338,627.97 was received from Fred's Team participants to advance the work of physicians, scientists, and programs in the Division of Hematologic Oncology. ■

PARTICIPANTS FROM THE DIVISION INCLUDE:

Naomi Cazeau
Stephen Chung
Alan Hanash
Michael Mauro
Christina Muggeo
Roni Tamari
Marcel van den Brink

SWIM ACROSS AMERICA

Team Transplant: **LEFT TO RIGHT: FRONT:** Grace Chang, Lindsay Hall, Elyssa Johnson, Tamarah Strauss, Susan McCall, Nicole Magaldi (with daughter,Grace); **BACK:** John Sheehan, Dick Endris, Jim Young, Emily Panzner, Jim Norgaard, Honorata Zaklicki, Jeff Bodenmann, and Gary Ryan

SWIM ACROSS AMERICA
★ MAKING WAVES TO FIGHT CANCER ★

Swim Across America's webpage:
www.swimacrossamerica.org

Team Transplant's webpage:
http://www.swimacrossamerica.org/site/TR/OpenWater/LongIslandSound?team_id=18964&pg=team&fr_id=4364

SWIM ACROSS AMERICA (SAA) was established in 1987 by cancer survivor Jeff Keith and his childhood friend Matt Vossler, two former Run Across America participants who transitioned from running to swimming for a cure. Since the first fundraiser was held in Nantucket, Massachusetts, SAA has raised over $70 million to fund cancer research and clinical trials at world-renowned research institutes and organizations.

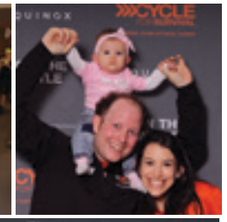
One of its major research beneficiaries is MSK, which has received $7 million in support of research that has led to historic breakthroughs in the burgeoning field of immunotherapy and cancer. Today, over 5000 recreational swimmers, masters swimmers, and even kayakers and boaters participate in 15 experiential open water swimming fundraising events and over 100 pool swim fundraisers.

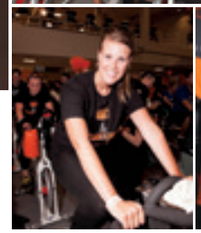
Dr. James Young, Attending Physician on the Adult Bone Marrow Transplantation (BMT) Service and avid distance swimmer, began swimming the Long Island Sound Open Swim in 2006. The Long Island Sound chapter was founded in 1992 and has grown to be the largest in the organization.

MSK's Team Transplant was founded in 2009 at the suggestion of Dr. Young's patient, a fellow swimmer who had undergone an allogeneic transplant for acute leukemia. The funds raised by Team Transplant support MSK's Adult BMT program. In July 2016, Team Transplant participated in its eight consecutive swim at the SAA Long Island Sound Open Swim and raised nearly $30,000.

Since 2009, Team Transplant has raised over $200,000 for much needed support of the research efforts that ensure the successful use of transplantation to cure patients with leukemia, lymphoma, multiple myeloma, and other cancers of the blood and bone marrow.

2017 will mark the 30th year anniversary of Swim Across America. Team Transplant will be swimming its ninth consecutive summer on July 29, 2017 in SAA's 25th Long Island Sound Open Swim. ■





CLOCKWISE FROM TOP LEFT: Miguel Perales; Payal Dixit, Alyssa Avalon, Caitlin Stacom, Beth Hoover, Gillian Moore, and Christopher Mazis; Aaron Viny, Aly Viny, and their daugther; Jort Van Der Schans, Kristina Caban, Suhail Chaudhry, Stephanie Benardis, Christina Muggeo, Melody Smith; Taylor Borrill

CYCLE FOR SURVIVAL

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 options. With support from our founding partner Equinox, Cycle for Survival had its biggest fundraising year so far in 2016. Raising $30 million this year—and more than $105 million during our first ten years—was only possible because of our dedicated community of riders, supporters, patients, researchers, and doctors. Over 27,000 people across 15 cities participated in 2016. Within six months of the annual events, all money raised goes directly to lifesaving research. 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. ■

CYCLE FOR SURVIVAL
MEMORIAL SLOAN KETTERING | EQUINOX

PARTICIPANTS FROM THE DIVISION INCLUDE:

BigJeffs CancerKickingCrew–NYC Sat
Carolyn Bernstein
Skylar Chwatt
Erik Coleman
Liza Deangelis
Adena Edwards
Christina Dominguez
Beth Epstein
Jason Feingold
Jessica Fink
Samantha Fink
Amy Friedlander
Eve Friedlander
Steven Friedlander
Jennifer Hartstein
Carol Hersh
Wendy Herzberg
Bonnie Karidis
Craig Moskowitz
Nadia Kralovic
Danielle Moskowitz
Robin Moskowitz
MJ Pedone
Josh Shapiro
Ron Sussman
Steve Sussman

Leukteam2016
Kelsey Alvarez
Yvette Bernal
Shaked Bornstein
Christina Bravo
Margaret Buff
Isabella Cazacu
Erika Chung
Morgan Coleman
Chris Famulare
Catherine Coombs
Ashley Foster
Talal Khawaja
Virginia Klimek
Amy Kong
Adam Kurnick
Rivky Litvin
Kelsey Malone
Michael Mauro
Janine Morice
Oby Nwankwo-Otti
Minal Patel
Adrienne Spears
Raajit Rampal
Diane Stopka
Anna Trakhtenberg
Kira Yasuda
Yasaman Zarbafian

Med Onc All Stars
Randi Ackerman
David Berliner
Janice Berliner
Kathleen Calivo
Caroilne Clark
Janet Cogswell
Ana Costa
Debbie Dobson
Joe Dougherty
Karen Dougherty
Meaghan Egan
Rachel Ezra
Anna Furevich
Kellee Greene
Paul Hamlin
Laurie Kerrigan
Donna McGuffy
Samantha Mellea
Jason Pablo
Bryan Pilipie
Jennifer Pilipie
Samantha Schrager
Jennifer Tota

MSKCC Fellows
Kathryn Arbour
Tim Bowler
Maria Ignez Braghiroli
Lara Dunn
Neha Mehta-Shah
Matt Pianko
Nitya Raj
Donya Sadi

T-Cell Racers
Nasrin Ahmed
Victoria Balonik
Erika Belmont
Briana Cadzin
Heather Coggins
Rebecca Green
Steven Horwitz
Christine Jarjies
Marissa Lyons
Shoshana Miller
Autumn Park
Stephen Randolph
Mark Scheuerman
Monica Shah
Tamir Sholklapper
Caroline Vilter
Janelle Walkley

Team HOPP
Shalu Arjomand
Emma Badini
Danielle Balsam
Jane Barnet
Natalie Barragan
Baselga Family
Mike Berger
Avery Bicks
Clare Bradley
Sarat Chandarlapaty
Mitchell Clark
Dominique Donnarumma
Laura Flink
Silvia Garriga
Holly Gottsegen
Emma Hatton
Danielle Hsu
Cliff Hudis
David Hyman
Liz & Dan Kaufman
Allison Krug
Lee and Laura Krug
Ross Levine
Tullia Lindsten
Randi Lipton
Sabina Lowitt
Javier & Monica Vargas Machado
Elizabeth Martin
Myra Melcer
Debra Mesnick
Paul Miranda
Mihal Nahari
Lisa Newman
Shraddha & Nayana Pancholi
Ederlinda Paraiso
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PUBLICATIONS

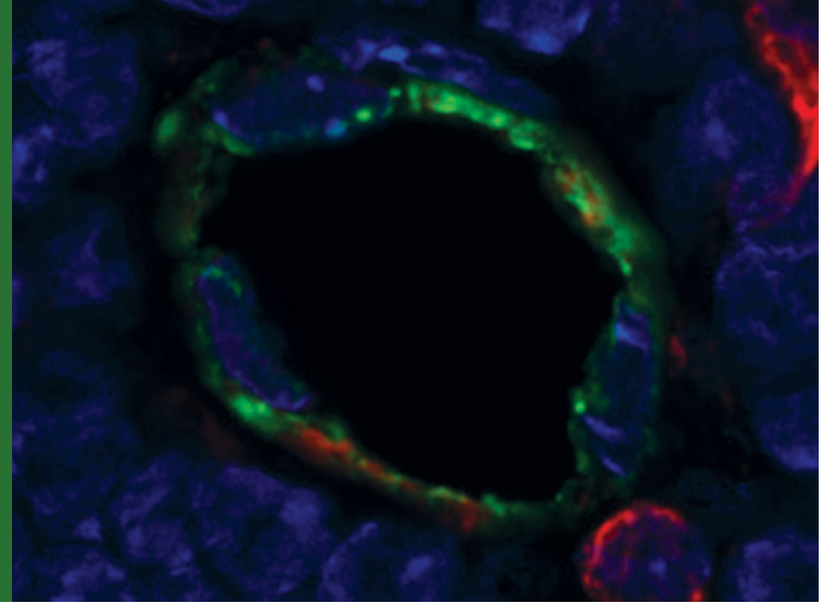


Image showing colocalization of the "damage-sensror" channel TRPA1 (red) with CD31 (green) in thymic endothelial cells, 63X. Confocal immunofluorescence microscopy.

CREDIT: KIMON ARGYROPOULOS, ENRICO VELARDI

THESE ARE A FEW PEER-REVIEWED PUBLICATIONS selected from the 282 total articles published by the Division of Hematologic Oncology faculty in 2016 and early 2017.

ADULT BMT

- **Intestinal Microbiota and Relapse After Hematopoietic-Cell Transplantation.**

  Peled JU, Devlin SM, Staffas A, Lumish M, Khanin R, Littmann ER, Ling L, Kosuri S, Maloy M, Slingerland JB, Ahr KF, Porosnicu Rodriguez KA, Shono Y, Slingerland AE, Docampo MD, Sung AD, Weber D, Alousi AM, Gyurkocza B, Ponce DM, Barker JN, Perales MA, Giraldt SA, Taur Y, Pamer EG, Jenq RR, van den Brink MRM.

  J Clin Oncol. 2017; 35(15):1650-1659. PMID:28296584

  Healthy gut bacteria have an important influence on many aspects of health. In this study of over 500 MSK patients, a certain group of gut bacteria were found to predict whether relapse of leukemia would occur after bone marrow transplantation. This paves the way for future studies that will optimize intestinal bacteria to improve patient health.

- **Increased GVHD-related mortality with broad-spectrum antibiotic use after allogeneic hematopoietic stem cell transplantation in human patients and mice.**

  Shono Y, Docampo MD, Peled JU, Perobelli SM, Velardi E, Tsai JJ, Slingerland AE, Smith OM, Young LF, Gupta J, Lieberman SR, Jay HV, Ahr KF, Porosnicu Rodriguez KA, Xu K, Calarfiore M, Poeck H, Caballero S, Devlin SM, Rapaport F, Dudakov JA, Hanash AM, Gyurkocza B, Murphy GF, Gomes C, Liu C, Moss EL, Falconer SB, Bhatt AS, Taur Y, Pamer EG, van den Brink MR, Jenq RR.

  Sci Transl Med. 2016; 8(339):339ra71. PMID:27194729; PMC4991773

  This study examined the records of 857 transplant patients and found that certain antibiotics were linked with development of graft-versus-host disease (GVHD), which can cause severe intestinal inflammation. In a mouse model, these antibiotics appeared to select for bacteria (shown in red in the image) that consume intestinal mucus (in green), damaging this important protective layer and exacerbating GVHD.

- **Allogeneic Hematopoietic Stem Cell Transplantation Is Underutilized in Older Patients with Myelodysplastic Syndromes.**

  Getta BM, Kishtagari A, Hilden P, Tallman MS, Maloy M, Gonzales P, Castro-Malaspina H, Perales MA, Giralt S, Tamari R, Klimek V.

  Biol Blood Marrow Transplant. 2017; pii: S1083-8791(17)30339-7. PMID:28336325

  A stem cell transplant is the only curative treatment option for myelodysplastic syndromes (MDS.) This study shows that patients may not undergo transplant because they are either not referred to a transplant specialist or because referral was delayed, particularly in patients over 65 years old.

- **Ex Vivo CD34$^+$-Selected T Cell-Depleted Peripheral Blood Stem Cell Grafts for Allogeneic Hematopoietic Stem Cell Transplantation in Acute Leukemia and Myelodysplastic Syndrome Is Associated with Low Incidence of Acute and Chronic Graft-versus-Host Disease and High Treatment Response.**

  Barba P, Hilden P, Devlin SM, Maloy M, Dierov D, Nieves J, Garrett MD, Sogani J, Cho C, Barker JN, Kernan NA, Castro-Malaspina H, Jakubowski AA, Koehne G, Papadopoulos EB, Prockop S, Sauter C, Tamari R, van den Brink MR, Avecilla ST, Meagher R, O'Reilly RJ, Goldberg JD, Young JW, Giralt S, Perales MA, Ponce DM.

  Biol Blood Marrow Transplant. 2017; 23(3):452-458. PMID: 28017734; PMC5398850

  CD34+ selected T-cell depletion is an approach to reduce a serious transplant complication known as graft-versus-host disease (GVHD) where the donor's immune system recognizes the recipient tissue as foreign, triggering an attack and causing inflammation that sometimes may be fatal. This study investigated the characteristics of GVHD after T-cell depleted transplant in patients with acute leukemia and myelodysplastic syndrome. It also found that T-cell depletion was associated with a low risk of acute and chronic GVHD and that survival without chronic GVHD or disease relapse was high. The skin was the organ most commonly affected in patients who developed GVHD and had a high response to therapy. These findings support the use of T-cell depletion for the prevention of GVHD.

- **KIR3DL1/ HL A-B Subtypes Govern Acute Myelogenous Leukemia Relapse After Hematopoietic Cell Transplantation.**

  Boudreau JE, Giglio F, Gooley TA, Stevenson PA, Le Luduec JB, Shaffer BC, Rajalingam R, Hou L, Hurley CK, Noreen H, Reed EF, Yu N, Vierra-Green C, Haagenson M, Malkki M, Petersdorf EW, Spellman S, Hsu KC.

  J Clin Oncol. 2017:JCO2016707059. PMID: 28520526

  Dr. Katharine Hsu and colleagues demonstrated that allele subtype combinations of the natural killer (NK) cell receptor, KIR3DL1, and its ligand HLA-B titrate the magnitude of inhibition signaled to NK cells. In patients receiving HLA-matched hematopoietic cell transplantation for the treatment of acute myelogenous leukemia, donors whose KIR3DL1 allele subtypes were predicted to inhibit weakly or not at all were associated with improved protection from leukaemia relapse. These findings now form the basis of a prospective, multicenter clinical trial led by Drs. Hsu and Shaffer, where HLA-equivalent donors are stratified based on KIR3DL1 allele subtypes, with those that predict the lowest inhibition prioritized for transplantation.

- **T cell exhaustion in multiple myeloma relapse after autotransplant: Optimal timing of immunotherapy.**

  Chung DJ, Pronschinske KB, Shyer JA, Sharma S, Leung S, Curran SA, Lesokhin AM, Devlin SM, Giralt SA, Young JW.

  Cancer Immunology Research. 2016; 4(1):61-71. PMID: 26464015; PMC4703436

  The rational development of immunotherapeutic interventions after autotransplant requires a comprehensive understanding of the post-transplant immunologic milieu. This study showed that the early post-transplant period is an opportune time to introduce immunotherapy and identified a unique population of immunologically quiescent or exhausted T cells associated with relapse after autotransplant. The exhausted T cells up-regulate expression of the immune inhibitory receptor, PD-1, and are a potential therapeutic target to revive anti-myeloma immunity and counteract relapse. The study also demonstrated the preservation of dendritic cell and T cell function after autotransplant and provides rationale for the early introduction of immunotherapeutic modalities like vaccines and immune checkpoint blockade agents to induce antitumor immunity after autotransplant.

- **Prospective Evaluation of Unrelated Donor Cord Blood and Haploidentical Donor Access Reveals Graft Availability Varies by Patient Ancestry: Practical Implications for Donor Selection.**

  Kosuri S, Wolff T, Devlin SM, Byam C, Mazis CM, Naputo K, Davis E, Paulson J, Nhaissi M, Wells DS, Dahi P, Giralt SA, Jakubowski A, Perales MA, Shaffer BC, Scaradavou A, Ponce DM, Barker JN.

  Biol Blood Marrow Transplant. 2017; 23(6):965-970. PMID: 28263918

  MSK's highly successful Cord Blood (CB) Transplant Program led by Dr. Juliet Barker continues to grow. The findings in this paper include the ability of CB to extend access to potentially curative transplants for minority patients.

- **Optimal Practices in Unrelated Donor Cord Blood Transplantation for Hematologic Malignancies.**

  Barker JN, Kurtzberg J, Ballen K, Boo M, Brunstein C, Cutler C, Horwitz M, Milano F, Olson A, Spellman S, Wagner JE, Delaney C, Shpall E.

  Biol Blood Marrow Transplant. 2017; 23(6):882-896. PMID: 28279825

  This paper investigates novel strategies to further improve the success and reduce the morbidity of these transplants. Dr. Juliet Barker leads the American Society of Blood and Marrow Transplant CB Special Interest Group and has recently published the national guidelines for CB transplants for patients with hematologic malignancies.

- **Cell-extrinsic MHC class I molecule engagement augments NK cell education programmed by cell-intrinsic MHC class I.**

  Boudreau JE, Liu X-R, ZhaoZ, Zhang A, Shultz LD, Greiner DL, DupontB, Hsu KC.

  Immunity. 2016. 45(2):280-9. PMID: 27496730.

  This study examines how interaction between HLA and their receptors on the NK cell surface interact to direct NK potency. Human NK cells can absorb HLA from surrounding tissue cells, altering NK education and responsiveness.

- **Phase II study of haploidentical natural killer cell infusion for treatment of relapsed or persistent myeloid malignancies following allogeneic hematopoietic cell transplantation.**

  Shaffer BC, Le Luduec JB, Forlenza C, Jakubowski AA, Perales MA, Young JW, Hsu KC.

  Biol Blood Marrow Transplant. 2016. 22(4): 705-9. PMID: 26772158.

  The findings in this paper show that NK cells from related individuals can be infused into leukemia patients safely, leading to disease response in some cases.

LEUKEMIA

- **DNMT3A mutations promote anthracycline resistance in acute myeloid leukemia via impaired nucleosome remodeling.**

  Guryanova OA, Shank K, Spitzer B, Luciani L, Koche RP, Garrett-Bakelman FE, Ganzel C, Durham BH, Mohanty A, Hoermann G, Rivera SA, Chramiec AG, Pronier E, Bastian L, Keller MD, Tovbin D, Loizou E, Weinstein AR, Gonzalez AR,

continued on page 46

continued from page 45

Lieu YK, Rowe JM, Pastore F, McKenney AS, Krivtsov AV, Sperr WR, Cross JR, Mason CE, Tallman MS, Arcila ME, Abdel-Wahab O, Armstrong SA, Kubicek S, Staber PB, Gönen M, Paietta EM, Melnick AM, Nimer SD, Mukherjee S, Levine RL.

Nat Med. 2016; 22(12):1488-1495. PMID: 27841873; PMC5359771

This work uncovered a novel mechanism by which leukemia cells can become resistant to chemotherapy, and provided a new link between the emerging field of cancer epigenetics and drug resistance in acute myeloid leukemia.

- **Modulation of splicing catalysis for therapeutic targeting of leukemia with mutations in genes encoding spliceosomal proteins.**

Lee SC, Dvinge H, Kim E, Cho H, Micol JB, Chung YR, Durham BH, Yoshimi A, Kim YJ, Thomas M, Lobry C, Chen CW, Pastore A, Taylor J, Wang X, Krivtsov A, Armstrong SA, Palacino J, Buonamici S, Smith PG, Bradley RK, Abdel-Wahab O.

Nat Med. 2016; 22(6):672-8. PMID: 27135740; PMC4899191

Mutations in gene controlling the process of RNA splicing are common in patients with myelodysplastic syndromes (MDS), chronic lymphocytic leukemia (CLL), and other forms of leukemia. This study identified that cells with mutations in RNA splicing factors are sensitive to drugs which alter the RNA splicing process further, providing an exciting potential new avenue to treat many common forms of leukemia.

- **Integrated genomic DNA/RNA profiling of hematologic malignancies in the clinical setting.**

He J, Abdel-Wahab O, Nahas MK, Wang K, Rampal RK, Intlekofer AM, Patel J, Krivstov A, Frampton GM, Young LE, Zhong S, Bailey M, White JR, Roels S, Deffenbaugh J, Fichtenholtz A, Brennan T, Rosenzweig M, Pelak K, Knapp KM, Brennan KW, Donahue AL, Young G, Garcia L, Beckstrom ST, Zhao M, White E, Banning V, Buell J, Iwanik K, Ross JS, Morosini D, Younes A, Hanash AM, Paietta E, Roberts K, Mullighan C, Dogan A, Armstrong SA, Mughal T, Vergilio JA, Labrecque E, Erlich R, Vietz C, Yelensky R, Stephens PJ, Miller VA, van den Brink MR, Otto GA, Lipson D, Levine RL.

Blood. 2016; 127(24):3004-14. PMID: 26966091; PMC4968346

This study reported the first clinical genomic assay which is able to detect all known genomic alterations in blood cancer, which can be used to clinically profile the genome of blood cancers and to improve diagnosis, prognostication and the use of novel therapies for patients with leukemia, lymphoma, and myeloma.

- **CD19-targeted CAR T-cell therapeutics for hematologic malignancies: interpreting clinical outcomes to date.**

Park JH, Geyer MB, Brentjens RJ.

Blood. 2016; 127(26):3312-20. PMID: 27207800; PMC4929923

Clinically meaningful responses have been seen in patients with B cell cancers treated with genetically modified T cells (called "CAR T cells") targeted to a B cell surface marker called CD19, though CAR T cell design and production and the ways in which clinical trials are run vary between centers. This review article discusses clinical results and side effects of CD19-targeted CAR T cell treatment for B cell leukemias and lymphomas at MSKCC and other centers in light of these differences, outlined major principles of current use, and highlighted ongoing challenges and opportunities in the field.

- **Mutational correlates of response to hypomethylating agent therapy in acute myeloid leukemia.**

Coombs CC, Sallman DA, Devlin SM, Dixit S, Mohanty A, Knapp K, Al Ali NH, Lancet JE, List AF, Komrokji RS, Padron E, Arcila ME, Klimek VM, van den Brink MR, Tallman MS, Levine RL, Rampal RK, Rapaport F.

Haematologica. 2016; 101(11):e457-e460. PMID: 27418649

This study investigated the relationship between somatic gene mutations affecting DNA methylation and response to hypomethylating agents in patients with AML. The study concluded that that there was no observable relationship between response to hypomethylating agents and IDH1/2 and TET2 mutations. However, the presence of DNMT3A mutations was found to predict response to hypomethylating agents in AML patients being treated in the frontline setting (but not the relapsed/refractory setting).

- **Stage-Specific Human Induced Pluripotent Stem Cells Map the Progression of Myeloid Transformation to Transplantable Leukemia.**

Kotini AG, Chang CJ, Chow A, Yuan H, Ho TC, Wang T, Vora S, Solovyov A, Husser C, Olszewska M, Teruya-Feldstein J, Perumal D, Klimek VM, Spyridonidis A, Rampal RK, Silverman L, Reddy EP, Papaemmanuil E, Parekh S, Greenbaum BD, Leslie CS, Kharas MG, Papapetrou EP.

Cell Stem Cell. 2017; 20(3):315-328.e7. PMID: 28215825; PMC5337161

In the present study, patient derived leukemic or myelodysplastic syndrome (MDS) cells were used to develop induced pluripotent stem cells representative of clonal as well as sub clonal cell fractions from the same patient. This delivers a first in kind experimental model for the characterization of co-operating gene mutations and the biological consequences of acquired mutations during disease progression in myeloid disease as well as the ability to test in primary patient cells the therapeutic potential of novel agents, targeting specific mutations or deregulated pathways in myeloid disease.

- **Genomic Classification and Prognosis in Acute Myeloid Leukemia.**

Papaemmanuil E, Gerstung M, Bullinger L, Gaidzik VI, Paschka P, Roberts ND, Potter NE, Heuser M, Thol F, Bolli N, Gundem G, Van Loo P, Martincorena I, Ganly P, Mudie L, McLaren S1, O'Meara S1, Raine K, Jones DR, Teague JW, Butler AP, Greaves MF, Ganser A, Döhner K, Schlenk RF, Döhner H, Campbell PJ.

N Engl J Med. 2016; 374(23):2209-21. PMID: 27276561; PMC4979995

In this study, targeted gene re-sequencing was performed in 1540 acute myeloid leukemia (AML) patients. Mutation sequencing data were combined with diagnostic, treatment and outcome data. Advanced statistical modeling analysis showed that AML is comprised by at least 11 distinct subtypes. Each subtype is defined by specific gene mutations, clinical presentation and response to therapy. Findings from this study will inform MDA diagnosis, classification and prognostication and will form the basis for the development of clinical algorithms to inform best clinical management of patients with AML.

- **Precision oncology for acute myeloid leukemia using a knowledge bank approach.**

Gerstung M, Papaemmanuil E, Martincorena I, Bullinger L, Gaidzik VI, Paschka P, Heuser M, Thol F, Bolli N, Ganly P, Ganser A, McDermott U, Döhner K, Schlenk RF, Döhner H, Campbell PJ.

Nat Genet. 2017; 49(3):332-340. PMID: 28092685

The researchers in this study analyzed gene mutations, demographic and clinical data in 1,540 patients to develop a patient tailored prognostic and predictive model in acute myeloid leukemia (AML). The research shows that incorporation of gene mutations delivers patient specific risk estimates and the model presented in this study delivers significantly improved risk estimates for 1 in 3 AML patients. This enables the characterization of patients with high risk disease that would benefit from higher intensity treatments thus enabling optimal and patient specific treatment decisions as well as patients that would not benefit from current standard of care therapies. Analysis of outcomes from stem-cell transplantation from this study shows that a patient tailored approach would reduce the total number of transplants by ~25% but would maintain the same overall survival rates within the test population.

LYMPHOMA

- **Safety, tolerability, and preliminary activity of CUDC-907, a first-in-class, oral, dual inhibitor of HDAC and PI3K, in patients with relapsed or refractory lymphoma or multiple myeloma: an open-label, dose-escalation, phase 1 trial.**

Younes A, Berdeja JG, Patel MR, Flinn I, Gerecitano JF, Neelapu SS, Kelly KR, Copeland AR, Akins A, Clancy MS, Gong L, Wang J, Ma A, Viner JL, Oki Y.

Lancet Oncol. 2016; 17(5):622-31.PMID: 27049457

This is the first clinical trial to test the safety and efficacy of the novel, chemically designed small molecule inhibitor that target both the phosphoinositide 3-kinase (PI3K)and histone deacetylases (HDAC) in lymphoma.

- **Idelalisib or placebo in combination with bendamustine and rituximab in patients with relapsed or refractory chronic lymphocytic leukaemia: interim results from a phase 3, randomised, double-blind, placebo-controlled trial.**

Zelenetz AD, Barrientos JC, Brown JR, Coiffier B, Delgado J, Egyed M, Ghia P, Illés Á, Jurczak W, Marlton P, Montillo M, Morschhauser F, Pristupa AS, Robak T, Sharman JP, Simpson D, Smolej L, Tausch E, Adewoye AH, Dreiling LK, Kim Y, Stilgenbauer S, Hillmen P.

Lancet Oncol. 2017; 18(3):297-311. PMID: 28139405

Idelalisib is a first in case PI3K delta inhibitor that was approved for the treatment of relapsed and refractory CLL and follicular lymphoma. This papers details the results of a randomized phase III trial in patients with relapsed/refractory chronic lymphocytic leukemia treated with a standard immunochemotherapy of bendamustine and rituximab (BR) with or without the addition of idelalisib. The addition of idelalisib to BR improved the progress-free and overall survival compared to the patients treated with BR plus placebo. There were more infectious toxicities and hematologic toxicity. However, the net benefit demonstrated in this study demonstrated that for patients being treated with BR addition of idelalisib provided important clinical benefits.

- **Nivolumab for classical Hodgkin's lymphoma after failure of both autologous stem-cell transplantation and brentuximab vedotin: a multicentre, multicohort, single-arm phase 2 trial.**

Younes A, Santoro A, Shipp M, Zinzani PL, Timmerman JM, Ansell S, Armand P, Fanale M, Ratanatharathorn V, Kuruvilla J, Cohen JB, Collins G, Savage KJ, Trneny M, Kato K, Farsaci B, Parker SM, Rodig S, Roemer MG, Ligon AH, Engert A.

Lancet Oncol. 2016; 17(9):1283-94.PMID: 27451390

This clinical trial established the benefit of Nivolumab for patients with relapsed Hodgkins lymphoma. Nivolumab is an immune therapy drug that enhances the patients own immune cells to fight their lymphoma.

- **Diffuse Large B-Cell Lymphoma Version 1.2016**

Zelenetz AD, Gordon LI, Wierda WG, Abramson JS, Advani RH, Andreadis CB, Bartlett N, Byrd JC, Fayad LE, Fisher RI, Glenn MJ, Habermann TM, Lee Harris N, Hernandez-Ilizaliturri F, Hoppe RT, Horwitz SM, Kaminski MS, Kelsey CR, Kim YH, Krivacic S, LaCasce AS, Lunning M, Nademanee A, Porcu P, Press O, Rabinovitch R, Reddy N, Reid E, Roberts K, Saad AA, Sokol L, Swinnen LJ, Vose JM, Yahalom J, Zafar N, Dwyer M, Sundar H.

J Natl Compr Canc Netw. 2016; 14(2):196-231.PMID: 26850490

The publication represents an update of the NCCN guidelines for the treatment of diffuse large B cell lymphoma (DLBCL). These guidelines are use to help oncologist in the US and around the world optimally manage patients with DLBCL, the most common lymphoma.

- **Clinicogenetic risk models predict early progression of follicular lymphoma after first-line immunochemotherapy.**

Jurinovic V, Kridel R, Staiger AM, Szczepanowski M, Horn H, Dreyling MH, Rosenwald A, Ott G, Klapper W, Zelenetz AD, Barr PM, Friedberg JW, Ansell S, Sehn LH, Connors JM, Gascoyne RD, Hiddemann W, Unterhalt M, Weinstock DM, Weigert O.

Blood. 2016; 128(8):1112-20. PMID: 27418643

Prior work has established that a combination of the follicular lymphoma international prognostic index (FLIPI) and the mutation pattern of 7 genes can enhance the identification of patients who have a poor outcome. The index called the m7-FLIPI identifies approximately 20% of patients with a poor outcome at diagnosis. Patients who have disease progression within 24 (PFS24) months of starting treatment also have a poor outcome. This paper examined if there was extensive overlap in the identification of poor risk patients identified by the m7-FLIPI and PFS24. The study shows that about 50% of the poor risk patients identified in the m7-FLIPI fail to achieve PFS24. There is clear enhancement in the detection of these poor risk patients; however, a more refined model may have better power to detect that patients destined to do poorly.

HEMATOLOGY

- **The patterns of anticoagulation control and the risk of stroke, bleeding and mortality in patients with non-valvular atrial fibrillation: comment.**

Mantha S, Moll S, Hilden P, Devlin S, Rose A.

J Thromb Haemost. 2016; 14(10):2083-2084.PMID: 27431450

This study applied a previously described mathematical pattern clustering method to the prediction of intracranial hemorrhage in a large dataset of patients on chronic anticoagulation with a vitamin K antagonist for prevention of stroke or systemic

continued on page 48

continued from page 47

embolism in the setting of non-valvular atrial fibrillation. The findings showed that using this sophisticated algorithm did not add value to the simpler approach of using solely the INR time in the therapeutic range.

- **Preoperative Chemoprophylaxis is Safe in Major Oncology Operations and Effective at Preventing Venous Thromboembolism.**

  Selby LV, Sovel M, Sjoberg DD, McSweeney M, Douglas D, Jones DR, Scardino PT, Soff GA, Fabbri N, Sepkowitz K, Strong VE, Sarkaria IS; MSKCC VTE Task Force.

  J Am Coll Surg. 2016; 222(2): 129-37. PMID: 26711793; PMC4729628

  Thrombosis remains a major adverse event following major surgery. This study demonstrates a significant reduction in the rate of peri-operative thrombosis with a small dose of pre-operative anticoagulation. Fortunately, this small dose of anticoagulation was not associated with an increase in significant bleeding.

- **Safe and effective use of rivaroxaban for treatment of cancer-associated venous thromboembolic disease: a prospective cohort study.**

  Mantha S, Laube E, Miao Y, Sarasohn DM, Parameswaran R, Stefanik S, Brar G, Samedy P, Wills J, Harnicar S, Soff GA.

  J Thromb Thrombolysis. 2017; 43(2):166-171. PMID: 27696084; PMC5318467

  Deep vein thrombosis and pulmonary embolism are common complications that arise in cancer patients. Low molecular weight heparin (LMWH) has been the standard anticoagulation to treat cancer associated thrombosis for over a decade. However, LMWH are painful, expensive, and associated with a significant residual risk of recurrent thrombosis and bleeding. In a Quality Assessment/Quality Improvement program, we introduced rivaroxaban, an FDA-approved oral anticoagulant to treat patients at MSK. This study analyzed 200 MSK patients who developed a cancer-associated thrombosis and whose full course of anticoagulation was with rivaroxaban. The study demonstrated that rivaroxaban was at least as safe and at least as effective as LMWH, thus providing a safe effective alternative to LMWH.

MYELOMA

- **Phase IB study of cabozantinib in patients with relapsed and/or refractory multiple myeloma.**

  Lendvai N, Yee AJ, Tsakos I, Alexander A, Devlin SM, Hassoun H, Korde N, Lesokhin AM, Landau H, Mailankody S, Koehne G, Chung DJ, Landgren O, Raje NS, Giralt S.

  Blood. 2016; 127(19):2355-6. PMID: 27020089 PMCID: PMC5003505

  MSK clinical researchers collaborated with colleagues at Massachusetts General Hospital Cancer Center to conduct this study evaluating cabozantanib, a small molecule that inhibits several pathways thought to be important for the growth of myeloma cells. The study found that while safe, when given by itself this drug did not seem to significantly affect myeloma in patients whose myeloma has come back multiple times.

- **Treatment of multiple myeloma with monoclonal antibodies and the dilemma of false positive M-spikes in peripheral blood.**

  Murata K, McCash SI, Carroll B, Lesokhin AM, Hassoun H, Lendvai N, Korde NS, Mailankody S, Landau HJ, Koehne G, Chung DJ, Giralt SA, Ramanathan LV, Landgren O.

  Clin Biochem. 2016. pii: S0009-9120(16)30312-5. PMID: 27664535; PMC5360528

  This is a study that characterized the effects of 3 monoclonal antibodies using for treatment of myeloma (daratumumab, isatuxumab and elotuzumab) and their impact on the interpretation of the serologic results of myeloma response. The study shows that the treatment of multiple myeloma patients with monoclonal antibodies results in a visible and quantifiable M-protein that has the potential to falsely indicate poor response to therapy.

- **Impact of Genes Highly Correlated with MMSET Myeloma on the Survival of Non-MMSET Myeloma Patients.**

  Wu SP, Pfeiffer RM, Ahn IE, Mailankody S, Sonneveld P, van Duin M, Munshi NC, Walker BA, Morgan G, Landgren O.

  Clin Cancer Res. 2016; 22(16):4039-44. PMID: 26847058

  The poor prognosis of multiple myeloma with t(4;14) is driven by the fusion of genes encoding multiple myeloma SET domain (MMSET) and immunoglobulin heavy chain; specific genes affected by MMSET and their clinical implications in non-MMSET myeloma remain undetermined. In this study, comprehensive analyses of MMSET-like gene signature suggested the involvement of p53 and MYC pathways. MMSET-like probes were associated with poor survival in non-MMSET myeloma. MMSET-like gene signature captures a subset of high-risk myeloma patients underrepresented by conventional risk stratification platforms and defines a distinct biologic subtype.

- **Monoclonal gammopathy-associated pure red cell aplasia.**

  Korde N, Zhang Y, Loeliger K, Poon A, Simakova O, Zingone A, Costello R, Childs R, Noel P, Silver S, Kwok M, Mo C, Young N, Landgren O, Sloand E, Maric I.

  Br J Haematol. 2016; 173(6):876-83. doi: 10.1111/bjh.14012. PMID: 26999424

  Pure red cell aplasia (PRCA) is a rare disorder characterized by inhibition of erythroid precursors in the bone marrow and normochromic, normocytic anemia with reticulocytopenia. Among 51 PRCA patients, we identified 12 (24%) patients having monoclonal gammopathy, monoclonal gammopathy of undetermined significance or smouldering multiple myeloma, with presence of monoclonal protein or abnormal serum free light chains and atypical bone marrow features of clonal plasmacytosis, hypercellularity and fibrosis. Thus far, three patients treated with anti-myeloma based therapeutics have responded with reticulocyte recovery and clinical transfusion independence, suggesting plasma cells play a key role in the pathogenesis of this specific monoclonal gammopathy-associated PRCA.

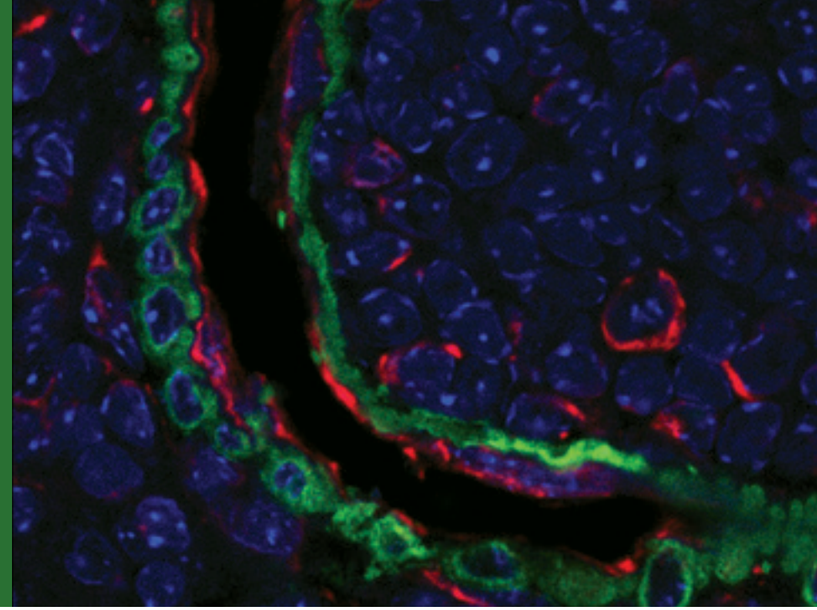
- **Role of MRD status in relation to clinical outcomes in newly diagnosed multiple myeloma patients: a meta-analysis.**

  Landgren O, Devlin S, Boulad M, Mailankody S.

  Bone Marrow Transplant. 2016; 51(12):1565-1568. PMID: 27595280

  This is a systemic review and meta-analysis of minimal residual disease (MRD) status and clinical outcomes in myeloma which demonstrated that that MRD negativity is associated with improved progression-free and overall survival. ■

CLINICAL TRIALS



Expression of the "damage-sensor" channel TRPA1 (red) by thymic endothelial cells. Vascular smooth muscle cells (Smooth Muscle Actin, Green) appear in the circumference of the vessel and are negative for TRPA1, 63X. Confocal immunofluorescence microscopy.

CREDIT: KIMON ARGYROPOULOS, ENRICO VELARDI

THESE ARE A FEW HIGHLIGHTED THERAPEUTIC CLINICAL TRIALS in the Division of Hematologic Oncology. For more information, please visit: https://www.mskcc.org/cancer-care/clinical-trials.

ADULT BMT

- **Selection of Allogeneic Hematopoietic Cell Donors Based on KIR and HLA Genotypes**

  IRB #: 15-059; PI: Katharine Hsu, Co-PIs: Nancy Kernan, Brian Shaffer

  This is a multi center trial that selects bone marrow donors based on genetics of the innate immune system to reduce the risk of leukemia relapse following bone marrow transplantation.

- **A Phase I Trial of High Dose Therapy and Autologous Stem Cell Transplantation Followed by Infusion of Chimeric Antigen Receptor (CAR) Modified T-Cells Directed Against CD19+ B-Cells for Relapsed and Refractory Aggressive B Cell Non-Hodgkin Lymphoma**

  IRB #: 12-117; PI: Craig Sauter, Co-PIs: Jae Park, Miguel-Angel Perales

  Given the efficacy of chimeric antigen receptor modified T cells (CAR-T) for acute lymphoblastic lymphoma at our center, we embarked on a clinical trial of CAR-T cells following autologous stem cell transplantation for poor risk aggressive B cell non-Hodgkin lymphoma. The clinical trial was completed with 15 patients treated demonstrating cytokine biomarkers predictive for toxicity. The results of this study were awarded podium presentations at the annual meetings of: the American Society of Hematology, the American Society of Clinical Oncology, the American Society of Blood and Marrow Transplantation and the International Conference for Malignant Lymphoma.

- **INCB 18424-271: A Single-Cohort, Phase 2 Study of Ruxolitinib in Combination With Corticosteroids for the Treatment of Steroid-Refractory Acute Graft-Versus-Host Disease**

  IRB #: 17-118; PI: Miguel-Angel Perales, Co-PIs: Doris Ponce, Barbara Spitzer

  This single arm, multicenter phase II study is exploring the use of a JaK1/JAK2 inhibitor, ruxolitinib, in patients with Steroid-Refractory Acute Graft-Versus-Host Disease. This is a patient population for which there are no standard treatments, as well as poor outcomes. Preliminary data suggests that the use of this drug may be beneficial in this indication. Ruxolitinib has been given the breakthrough designation by the FDA in the GVHD. Dr. Perales is closely involved in the planning of additional studies of this drug and similar drugs in the prevention and treatment of both acute and chronic GVHD.

- **A Randomized, Multi-Center, Phase III Trial of Calcineurin Inhibitor-Free Interventions for Prevention of Graft-versus-Host Disease (BMT CTN 1301)**

  IRB #: 14-263; PI: Miguel-Angel Perales, Co-PIs: Nancy Kernan, Esperanza Papadopoulos

  This is a multicenter phase 3 trial comparing 3 approaches to the prevention of graft-versus-host disease performed by the Blood and Marrow Transplantation Clinical Trial Network, which is sponsored by the NHLBI and NCI. One of the investigational approaches is the use of CD34 selection, and approach that was pioneered at MSK. This study has the potential to change the current standard of care for patients with acute leukemia and myelodysplastic syndrome who will undergo a stem cell

continued on page 50

continued from page 49

transplant. Dr. Perales is one of the national co-chairs of the study. This study has reached more than 60% of planned accrual, and is expected to complete accrual 6 months ahead of schedule.

- **Phase II Multicenter Trial of Single Autologous Hematopoietic Cell Transplant Followed by Lenalidomide Maintenance for Multiple Myeloma with or without Vaccination with Dendritic Cell (DC)/Myeloma Fusions (BMT CTN 1401)**

  IRB #: 16-1067; PI: David Chung, Co-PIs: Sergio Giralt, James Young

  This national trial is comparing the efficacy of a dendritic cell/myeloma fusion vaccine + granulocyte macrophage colony-stimulating factor (GM-CSF) adjuvant + lenalidomide maintenance therapy versus lenalidomide maintenance therapy alone or with GM-CSF following autotransplant, as part of upfront treatment of multiple myeloma. It is hypothesized that the dendritic cell/myeloma fusion vaccine will improve clinical responses in multiple myeloma after autotransplant.

- **A Phase I Study to Assess Safety and Tolerability of Tremelimumab in Combination with MEDI4736, Administered after High-Dose Chemotherapy and Autologous Stem Cell Transplant (HDT/ASCT)**

  IRB #: 16-1329; PI: David Chung, Co-PI: Alexander Lesokhin

  This trial is testing the safety and feasibility of dual immune checkpoint blockade in the setting of autotransplant for multiple myeloma. It is hypothesized that blocking two distinct arms of immunosuppression (CTLA-4 and PD-L1) should provide greater antitumor activity as compared with monotherapy with either agent, thus offering a novel approach to improve clinical outcomes after autotransplant by augmenting/reviving anti-myeloma immunity to target residual disease.

LEUKEMIA

- **A Phase 1, Multi-Label, Safety Study of AG-120 or AG-221 in Combination with Induction Therapy and Consolidation Therapy in Patients with Newly Diagnosed Acute Myeloid Leukemia with an IDH1 and/or IDH2 Mutation**

  IRB #: 16-012; PI: Eytan Stein, Co-PI: Martin Tallman

  The use of IDH1 and IDH2 inhibitors as single agents in patients with relapsed and refractory acute myeloid leukemia (AML) has been extremely successful, with overall response rates of 40-45%. This new clinical study builds on this experience and is evaluating the combination of standard-of-care induction chemotherapy with inhibitors of mutant IDH1 or IDH2 for patients with AML who have IDH1/IDH2 mutations.

- **A Phase I Trail of CD19-Targeted EGFRt/19-28z/4-1BBL "Armored" Chimeric Antigen Receptor (CAR) Modified T Cells in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia (CLL)**

  IRB #: 16-1570; PI: Jae Park, Co-PI: Craig Sauter

  Our previous clinical trial with the autologous T cells genetically modified to express a 2nd generation CD19-targeted chimeric antigen receptor (CAR) (19-28z) demonstrated that an overall response rate of 40-50% in patients with relapsed chronic lymphocytic leukemia (CLL) (IRB #06-138). While encouraging, the response rate was modest compared to the complete response rate of 80% in patients with acute lymphoblastic leukemia (ALL). Therefore, we have further modified and created an "armored" CAR T cells expressing 4-1BBL, designed to better stimulate the T cells and educate other immune cells to more completely eradicate CLL cells. This phase I clinical trial is currently enrolling patients with relapsed CLL to test the safety and efficacy of this new armored CAR T cells.

- **A Biomarker-Directed Phase 2 Trial of SY-1425, a Selective Retinoic Acid Receptor Agonist, in Adult Patients with Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS)**

  IRB #: 17-031; PI: Eytan Stein, Co-PI: Martin Tallman

  Approximately 30% of patients with AML harbor have a biomarker called a "RARA superenhancer." In pre-clinical studies, leukemia cells with this abnormality are very responsive to the drug SY-1425, also known as Tamibarotene. This study is evaluating the use of Sy-1425 in patients with the RARA superenhancer biomarker.

- **A Phase I, Multicenter, Open-label Study of Oral ABL001 in Patients with Chronic Myelogenous Leukemia or Philadelphia Chromosome-positive Acute Lymphoblastic Leukemia**

  IRB #: 14-168; PI: Michael Mauro, Co-PI: Ellin Berman

  MSKCC Study 14-168, the phase I study of ABL001 in Philadelphia chromosome positive leukemias, continues to show continued safety with broader study of different doses and in combination with available drugs (TKIs) for such patients, marking the first dual ABL kinase targeted approach and opening doors for its future development. MSKCC is planned to continue involvement in the study of ABL001, in comparison to current salvage therapy in chronic phase CML against bosutinib, and a proposed use to boost chances of treatment free remission.

- **A Safety and Tolerability Trial of Crenolanib and Chemotherapy with Cytarabine and Anthracyclines in Patients with Newly Diagnosed Acute Myeloid Leukemia with FLT3 Activating Mutations**

  IRB #: 15-084; PI: Martin Tallman, Co-PI: Eytan Stein

  The FLT3 inhibitor Crenolanib is quite effective in patients with AML with a FLT3 abnormality, that occurs in approximately 30% of patients with AML. This new clinical study builds on this experience and is evaluating the combination of standard-of-care induction chemotherapy with inhibitors of mutant FLT3 for patients with AML who have a FLT3 abnormality.

LYMPHOMA

- **A Phase 1b, Open-Label, Dose Escalation Study of ME-401 in Subjects with Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) or Follicular Lymphoma (FL)**

  IRB #: 16-1614; PI: Andrew Zelenetz, Co-PI: John Gerecitano

  Phosphoinositide 3-kinase (PI3K) is a key protein in pathways that regulate cellular growth. This protein comes in 4 different forms: α, β, γ and δ. The δ-isoform is particularly important in regulation of B-lymphocytes. ME-401 is a drug that specifically targets the enzyme PI3Kδ. We are determining the safety of this drug in patients with chronic lymphocytic leukemia and follicular lymphoma. If the drug is both safe and effective, it will be combined in two different cohorts with an anti-CD20 antibody and an inhibitor of Bruton's tyrosine kinase.

- **A Phase Ib/II, Open-Label Study Evaluating the Safety and Pharmacokinetics of GDC-0199 (ABT-199) in Combination with Rituximab (R) or Obinutuzumab (G) Plus Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (CHOP) in Patients with B-cell Non-Hodgkin's Lymphoma (NHL) and DLBCL**

  IRB #: 14-130; PI: Andrew Zelenetz, Co-PI: John Gerecitano

  Diffuse large B cell lymphoma is the most common form of lymphoma seen around the world. Rituximab and CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) is the most commonly used treatment for this disease but at least 35% of patients will recur. Venetoclax (GCD-0199/ABT-199) is a small molecule inhibitor of BCL2 which acts to promote enhance cell death by the chemotherapy. This trial is evaluating whether addition of venetoclax to R-CHOP will improve the outcome of patients with DLBCL. We are the lead center for this international trial and all of the patients have been accrued to this study. We expect preliminary results in late 2017.

HEMATOLOGY

- **A Open Label Phase II Study for Chemotherapy Induced Thrombocytopenia**

  IRB #: 13-132; PI: Gerald Soff, Co-PI: Rekha Parameswaran

  This is a clinical trial testing the use of romiplostim for the treatment of Chemotherapy Induced Thrombocytopenia. We have now reached our primary and secondary endpoints, demonstrating that romiplostim can safely correct the CIT in over 90% of patients, without evidence of adverse events.

- **Efficacy and Safety of Rivaroxaban Prophylaxis Compared with Placebo in Ambulatory Cancer Patients Initiating Systemic Cancer Therapy and at High Risk for Venous Thromboembolism (BAY59-7939/39039039STM4001/18262)**

  IRB #: 16-375; PI: Gerald Soff, Co-PIs: Simon Mantha, Jodi Mones, Rekha Parameswaran

  Cancer patients are at high risk of developing thrombosis. This is an ongoing clinical trial to determine is prophylactic treatment of high risk cancer patients with rivaroxaban can significantly reduce the rate of thrombosis, compared with the thrombosis rate observed in a placebo controlled arm.

MYELOMA

- **Ixazomib (MLN9708) and Dexamethasone in High Risk Smoldering Multiple Myeloma: A Clinical and Correlative Pilot Study**

  IRB #: 15-294; PI: Sham Mailankody, Co-PI: Ola Landgren

  The standard management of patients with smoldering myeloma is clinical surveillance with treatment only if progression to multiple myeloma. This is a pilot study of early treatment with ixazomib and dexamethasone for individuals with high-risk myeloma to assess the efficacy of this treatment to lower disease burden and delay progression to myeloma.

- **Carfilzomib, Lenalidomide, and Dexamethasone in Newly-Diagnosed Multiple Myeloma: A Clinical and Correlative Phase I/II Dose Escalation Study**

  IRB #: 15-326; PI: Neha Korde, Co-PI: Ola Landgren

  This is a phase I/II study to assess the safety and efficacy of maximum of up to 12 cycles of combinational therapy with dexamethasone, lenalidomide, and higher doses of carfilzomib in newly diagnosed MM patients. The primary objective of the phase II study is to assess the rate of MRD negativity after completion of the combination therapy, and the total number of cycles delivered will be determined by the patient's individual response rate.

- **An Investigator-Initiated Phase I Study of Selinexor (KPT-330), Ixazomib, and Low Dose Dexamethasone in Patients with Relapsed and/or Refractory Multiple Myeloma**

  IRB #: 15-310; PI: Nikoletta Lendvai, Co-PI: Ola Landgren

  This is an investigator initiated, single institution study of a combination therapy that includes ixazomib (the first FDA approved oral proteasome inhibitor), dexamethasone and selinexor. Selinexor is the first member of a novel class of drugs referred to as SINE (selective inhibitor of nuclear export). The combination of these 3 oral drugs is being evaluated in patients whose myeloma has come back after initial therapy.

- **TTI-621-01: A Phase 1a/1b Dose Escalation and Expansion Trial of TTI-621, a Novel Biologic Targeting CD47, in Subjects with Relapsed or Refractory Hematologic Malignancies (Version date 29-AUG-2016 and 27-SEP-2016)**

  IRB #: 16-1347; PI: Alexander Lesokhin, Co-PI: Michael Postow

  At the end of their life cycle blood cells are normally engulfed by macrophages, a type of cell specialized in eating debris and other cells. Younger healthier cells prevent this engulfment by displaying the "do not eat me" signal CD47. Many cancer cells upregulate CD47 to hide from macrophages. This study is designed to identify a safe dose of TTI-621, a drug designed to block CD47, and to evaluate for preliminary signs of efficacy in myeloma, lymphoma, and leukemia. ■

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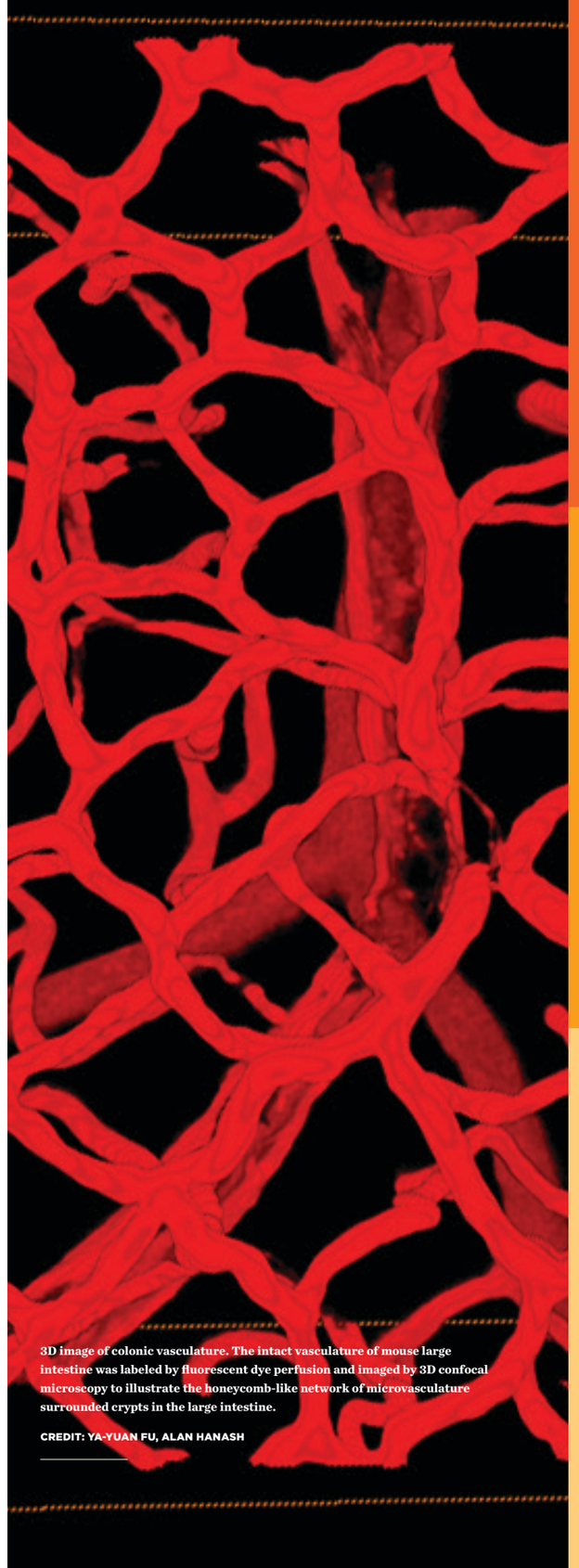
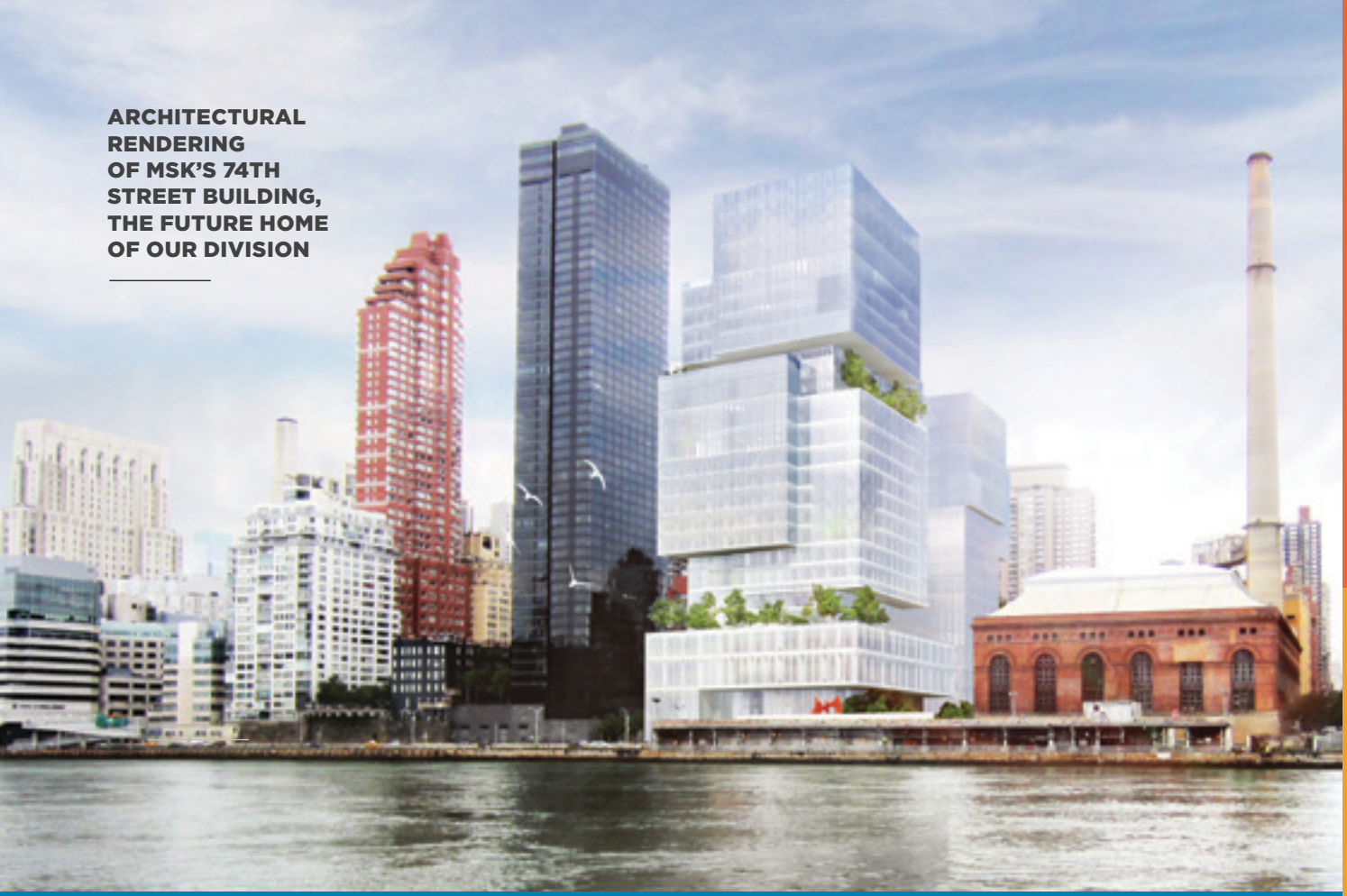


3D image of colonic vasculature. The intact vasculature of mouse large intestine was labeled by fluorescent dye perfusion and imaged by 3D confocal microscopy to illustrate the honeycomb-like network of microvasculature surrounded crypts in the large intestine.

CREDIT: YA-YUAN FU, ALAN HANASH



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