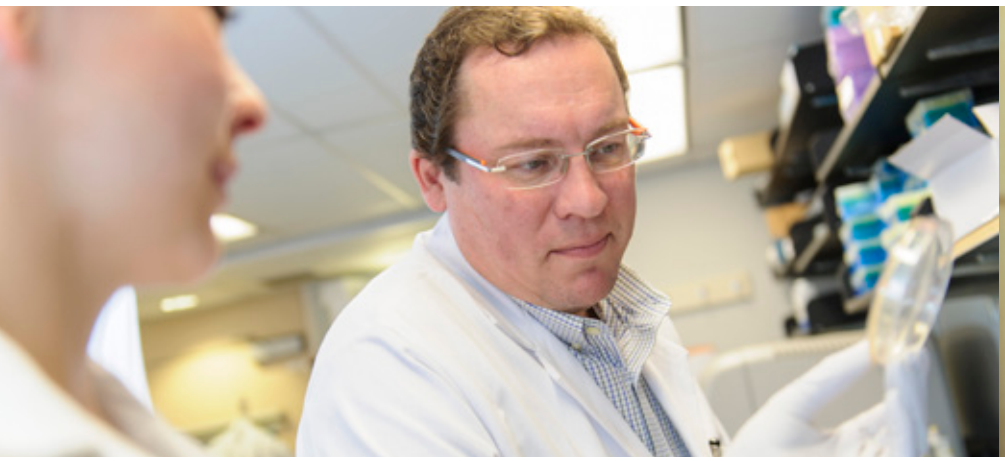
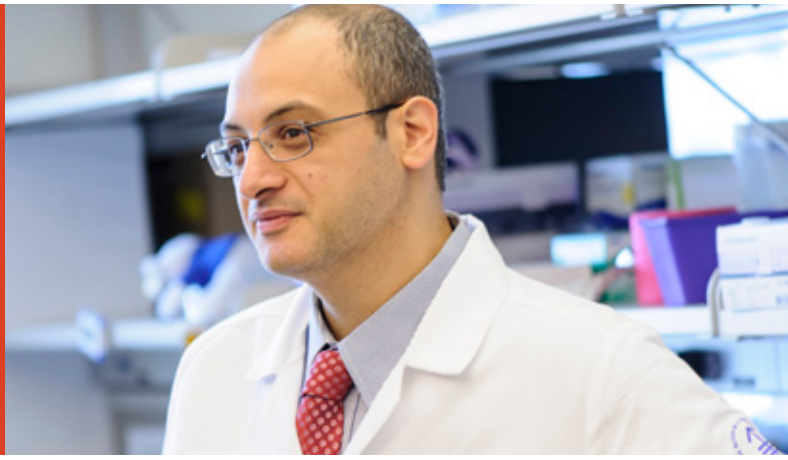


HEMATOLOGIC ONCOLOGY 2013 ANNUAL REPORT



Memorial Sloan Kettering Cancer Center

TABLE OF CONTENTS

On the cover:
Top row: Renier Brentjens, Juliet Barker
Middle Row: Omar Abdel-Wahab
Bottom Row: Minal Patel and Yuliya Yavich

MESSAGE FROM THE DIVISION HEAD

In 2013, the Division of Hematologic Oncology continued its growth in all aspects of clinical care, education and clinical, translational and basic research.

The Division consists of 5 services: Adult Bone Marrow Transplantation, Hematology, Leukemia, Lymphoma and Myeloma and has grown to 61 faculty members. We recruited nine new faculty members in 2013, including Dr. Anas Younes, Chief Attending of the Lymphoma Service.

One of Memorial Sloan Kettering's greatest strengths is the close collaboration between our physicians and scientists, which allows us to provide patients with top-quality clinical care while we develop groundbreaking therapies to prevent, control and ultimately cure cancer.

Our exceptional laboratory-based research resulted in several breakthroughs in 2013 including CAR T-cell therapy for Acute Lymphoblastic Leukemia and FoundationOne™ Heme, a commercially available genomic profile assay for hematologic cancers developed in collaboration with Foundation Medicine in Cambridge, Massachusetts.

In the 3rd edition of our Annual Report, we have highlighted a few of our accomplishments.

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

HEMATOLOGIC ONCOLOGY FACULTY

ADULT BONE MARROW TRANSPLANTATION


Juliet Barker


Hugo Castro-Malaspina


David Chung


Parastoo Dahi


Sergio Giralt
Chief Attending


Boglarka Gyurkocza


Alan Hanash


Katharine Hsu


Ann Jakubowski

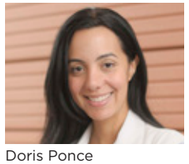

Robert Jenq


Guenther Koehne

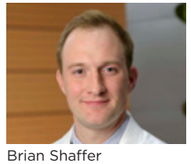

Heather Landau


Esperanza Papadopoulos


Miguel Perales


Doris Ponce


Craig Sauter


Brian Shaffer


Roni Tamari

HEMATOLOGY


Marcel van den Brink
Division Head


James Young


Simon Mantha


Rekha Parameswaran


Lilian Reich


Gerald Soff
Chief Attending

LEUKEMIA

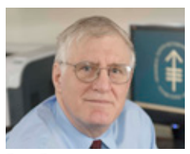

Omar Abdel-Wahab


Ellin Berman


Renier Brentjens


Stephen Chung


Bayard Clarkson


Dan Douer


Faye Feller


Virginia Klimek

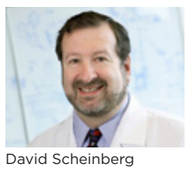

Ross Levine


Peter Maslak


Michael Mauro


Jae Park


Raajit Rampal


David Scheinberg


Alan Shih


Eytan Stein

Martin Tallman
Chief Attending

LYMPHOMA

Helen Chung

John Gerecitano

Paul Hamlin

Steven Horwitz

Anita Kumar*

Matthew Matasar

Alison Moskowitz

Craig Moskowitz
Clinical Director

Ariela Noy

Lia Palomba

Carol Portlock

David Straus

MYELOMA

Anas Younes*
Chief Attending

Andrew Zelenetz

Hani Hassoun

Neha Korde*

Ola Landgren*
Chief Attending

Nikoletta Lendvai

REGIONAL NETWORK

Alexander Lesokhin

Philip C. Caron

Pamela R. Drullinsky

Audrey M. Hamilton

*Not pictured: Elina Tsyvkin, Lymphoma Service**

**Joined faculty in 2014*

COLLABORATING TEAMS

- Cardiology Service
- Case Management
- Colorectal Service
- Critical Care Medicine Service
- Dental Service
- Dermatology Service
- Endocrinology Service
- Gastroenterology and Nutrition Service
- Gastric and Mixed Tumor Service
- General Internal Medicine Service
- Geriatrics Service
- Gynecology Service
- Head and 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 and Palliative Care Service
- Pathology
- Diagnostic Molecular Pathology
- Hematopathology
- Pathology Diagnostic Services, Cytology
- Surgical Pathology Diagnostic Services
  - Bone and Soft Tissue Pathology
  - Dermatopathology
  - Gastrointestinal Pathology
- Physical Therapy
- Plastic and 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

Foundation Medicine Launches FoundationOne™ Heme, Developed in Collaboration with Memorial Sloan Kettering

On December 7, 2013, Foundation Medicine announced the launch of its second clinical product, FoundationOne™ Heme, a fully informative genomic profile for hematologic cancers (leukemia, lymphoma and myeloma), as well as many sarcomas and pediatric cancers. The test was developed in collaboration with Memorial Sloan Kettering and was designed to provide physicians with clinically actionable information to guide treatment options for patients based on the genomic profile of their cancer.

"By introducing our second clinical product, FoundationOne Heme, in only our second year of commercialization, we are demonstrating our commitment to ongoing product innovation to make molecular information broadly available to the hematology and oncology communities at academic medical centers and community hospitals worldwide," said Michael J. Pellini, MD, president and chief executive officer of Foundation Medicine. "Consistent with FoundationOne, our first clinical product for solid tumors, this new test is designed to fit within routine clinical practice and provide a physician with all of the relevant genomic information needed to make an informed treatment decision, which may include a targeted therapy or clinical trial. Our shared goal in developing FoundationOne Heme with Memorial Sloan Kettering is to enable precision medicine and to advance treatment options for more patients living with cancer."

FoundationOne Heme uses comprehensive, clinical next-generation sequencing (NGS) to assess routine cancer specimens for all genes that are currently known to be somatically altered and unambiguous drivers of oncogenesis

Ahmet Dogan, Chief of the Hematopathology Service, has included the FoundationOne Heme test in the evaluation of patients with hematological malignancies.

in hematologic malignancies, as well as many sarcomas and pediatric cancers. Utilizing NGS, FoundationOne Heme simultaneously detects all classes of genomic alterations, including base pair substitutions, insertions and deletions, copy number alterations and select gene rearrangements in 405 cancer-related genes. In addition to DNA sequencing, FoundationOne Heme employs RNA sequencing across 265 genes to capture a broad range of gene fusions, a type of alteration that is a common driver of hematologic cancers, sarcomas and pediatric cancers. FoundationOne Heme fits easily into the clinical workflow of the ordering physician, and test results are provided in an easy-to-interpret report supported by a comprehensive review of published literature.

"Our vision is to make cancer genomic testing available in routine care to enable more precise and informed treatment decisions for patients with a broad range of cancers," added Craig B. Thompson, MD, president and chief executive officer of Memorial Sloan Kettering. "We look forward to continuing our efforts with Foundation Medicine to advance the ongoing development of this best-in-class test and to further define its clinical utility in patients with hematologic cancers."

New data from ten studies demonstrating the utility of FoundationOne Heme in hematologic malignancies was presented during the 2013 American Society of Hematology Annual Meeting, which took place December 7-10 in New Orleans. FoundationOne Heme was developed using technology, methods and computational algorithms developed by Foundation Medicine, combined with Memorial Sloan Kettering's deep and vast expertise in clinical and laboratory research into hematologic malignancies. Over the seven-month development process, researchers from Memorial Sloan Kettering analyzed more than 400 patient samples to demonstrate the accuracy and performance of FoundationOne Heme in validation studies. Data demonstrating that comprehensive genomic profiling with FoundationOne Heme may expand treatment options for patients was presented in an oral presentation by Ross L. Levine, MD, medical oncologist and member of the Human Oncology and Pathogenesis Program at Memorial Sloan Kettering, on Monday, December 9, 2013 (titled Identification Of Actionable Genomic Alterations In Hematologic Malignancies By a Clinical Next Generation Sequencing-Based Assay, abstract number 230). Foundation Medicine will commercialize FoundationOne Heme in the United States and internationally. For more information or to order FoundationOne Heme, please visit www.FoundationOne.com.

ABOUT FOUNDATIONONE™ HEME

FoundationOne Heme is a fully informative genomic profile for hematologic cancers (leukemia, lymphoma and myeloma), as well as many sarcomas and pediatric cancers, designed to provide physicians

Ross Levine, Scott Armstrong, and Marcel van den Brink

with clinically actionable information to guide treatment options for patients based on the genomic profile of their cancer. It is Foundation Medicine's second commercially available targeted sequencing assay and was developed in collaboration with Memorial Sloan Kettering. Using next-generation sequencing in routine cancer specimens, FoundationOne Heme interrogates all genes somatically altered in these cancers that are validated targets for therapy or unambiguous drivers of oncogenesis based on current knowledge. The test employs RNA sequencing in addition to DNA sequencing to simultaneously detect all classes of genomic alterations, including base pair substitutions, insertions and deletions, copy number alterations and rearrangements, and gene fusions (a type of alteration that is a common driver of hematologic malignancies. sarcomas and pediatric cancers). FoundationOne Heme fits easily into the clinical workflow of the ordering physician, and test results are provided in an easy-to-interpret report supported by a comprehensive review of published literature. FoundationOne Heme is a laboratory-developed test performed at Foundation Medicine's CLIA-certified lab.

ABOUT MEMORIAL SLOAN KETTERING

Memorial Sloan Kettering is the world's oldest and largest private cancer center with more than 125 years devoted to exceptional patient care, innovative research, and outstanding educational programs. Memorial Sloan Kettering is one of 41 National Cancer Institute–designated Comprehensive Cancer Centers, with state-of-the-art science flourishing side by side with clinical studies and treatment.

The close collaboration between physicians and scientists enables Memorial Sloan Kettering to provide patients with the best care available as they work to discover more-effective strategies to prevent, control, and ultimately cure cancer in the future. Memorial Sloan Kettering's education programs train future physicians and scientists, and the knowledge and experience they gain at Memorial Sloan Kettering has an impact on cancer treatment and biomedical research around the world.

ABOUT FOUNDATION MEDICINE

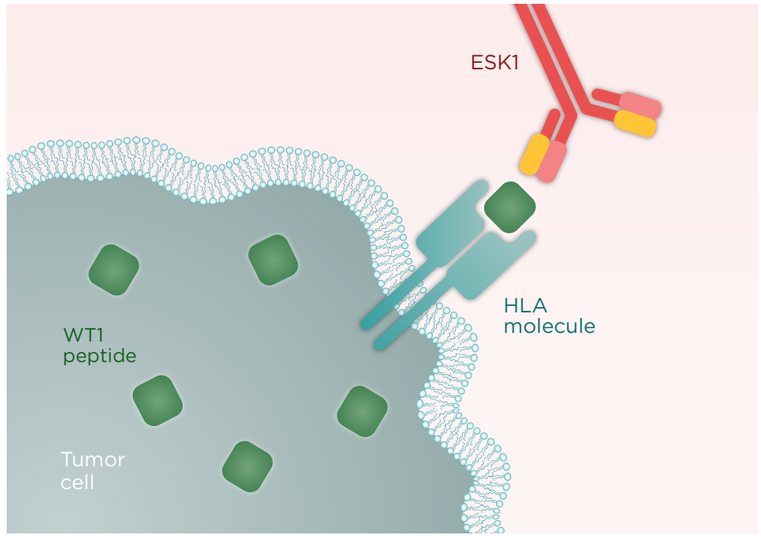
Foundation Medicine® (NASDAQ: FMI) is a molecular information company dedicated to a transformation in cancer care in which treatment is informed by a deep understanding of the genomic changes that contribute to each patient's unique cancer. The company's clinical assays, FoundationOne™ for solid tumors and FoundationOne™ Heme for hematologic malignancies, each provide a fully informative genomic profile to identify a patient's individual molecular alterations and match them with relevant targeted therapies and clinical trials. Foundation Medicine's molecular information platform aims to improve day-to-day care for patients by serving the needs of clinicians, academic researchers and drug developers to help advance the science of molecular medicine in cancer.

NEW MOLECULE TARGETS PROTEINS INSIDE CANCER CELLS

Scientists from Memorial Sloan Kettering have discovered a unique monoclonal antibody that appears to be very effective at targeting and destroying several types of cancer cells. The research was done in collaboration with the California-based biotechnology company Eureka Therapeutics and was reported March 13 in Science Translational Medicine.

Monoclonal antibodies are molecules that can be engineered to target specific proteins on cancer cells. A number of them are already available to treat a variety of different cancers. The new monoclonal antibody, called ESK1, targets a protein that is associated with many types of cancer and is of great interest to cancer researchers.

Because of their large size, monoclonal antibodies can target only proteins located on the outside of cancer cells. But ESK1 is different because it is capable of recognizing the presence of a protein that resides within the cell. This is a long-sought goal for this important class of anticancer agents, since most proteins that cause cancer or are associated with the disease are buried inside cancer cells.



The ESK1 monoclonal antibody was engineered to recognize WT1 peptides brought to the surface of cancer cells.

AN IMPORTANT CANCER TARGET

"This is a new approach for attacking an important cancer target with an antibody therapy. This is something that was previously not possible," says David A. Scheinberg, Chair of the Sloan Kettering Institute's Molecular Pharmacology and Chemistry Program and an inventor of the antibody. "Our research shows that you can use a monoclonal antibody to recognize a cancer-associated protein inside a cell, and it will destroy the cancer cell."

ESK1 targets a protein called WT1, which is overexpressed in a range of leukemias and other cancers including myeloma, mesothelioma, breast cancer, ovarian cancer, and colorectal cancer.

WT1 is a critically important target for cancer drugs because it is an oncogenic protein, meaning that it supports the formation of cancer. In addition, it is found in very few healthy cells, so there are less likely to be side effects from drugs that target it.

MIMICKING THE IMMUNE SYSTEM

ESK1 was engineered to mimic the function of T cells, white blood cells that are key components of the immune system. T cells have a receptor system that is designed to recognize proteins that are inside the cell.

> "This is a new approach for attacking an important cancer target with an antibody therapy. This is something that was previously not possible."
>
> — David A. Scheinberg

As proteins inside the cell get broken down as part of regular cellular processes, molecules known as HLA molecules carry fragments of those proteins — known as peptides — to the surface. When T cells recognize certain peptides on the surface of cells as abnormal, the T cells kill the diseased cells.

In the current study, the investigators showed that ESK1 was able to recognize the WT1 peptide even though the antibody itself did not enter the cells. ESK1 killed cancer cells in a test tube and also in mouse models for two different types of human leukemia.

"We were surprised that the antibody worked so well on its own," says Dr. Scheinberg, senior author of the paper. "We had originally expected that we might need to use the antibody as a carrier to deliver a drug or a radioactive therapy to kill the cancer cells, but this was not necessary."

ADVANCING TO CLINICAL STUDIES

Additional studies must be done in the laboratory before ESK1 is ready to be used in clinical trials for patients. The monoclonal antibody was engineered to be completely human, which should shorten the time it takes to move the drug into the clinic. Researchers expect that the first clinical trials, for leukemia, could begin in about a year.

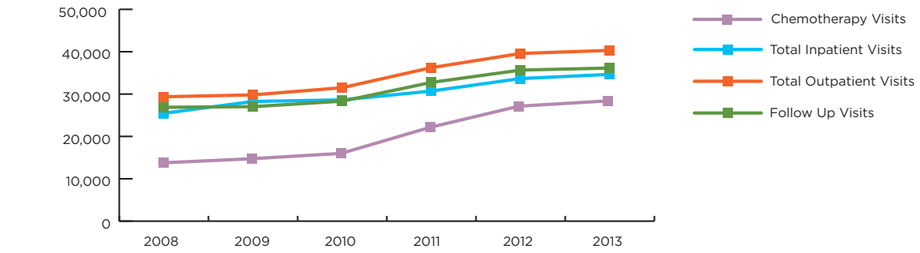
The antibody was developed under a collaborative effort between Memorial Sloan Kettering and Eureka Therapeutics, which have jointly filed for patent protection.

Research is also under way to target WT1 with vaccines and engineered T cells. These therapeutic approaches are currently in clinical trials at Memorial Sloan Kettering for leukemia, multiple myeloma, ovarian cancer, and mesothelioma.

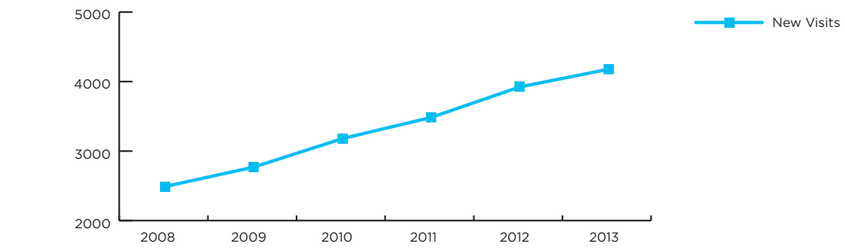
David A. Scheinberg, MD, PhD
Vincent Astor Chair;
Chairman, Molecular Pharmacology & Chemistry Program and Experimental Therapeutic Center;
Member, Leukemia Service

This work was supported by grants from the Leukemia and Lymphoma Society, the National Cancer Institute (under award numbers CA23766 and CA55349), the Sloan Kettering Institute's Experimental Therapeutics Center and its Technology Development Fund, the Commonwealth Foundation for Cancer Research, the Tudor and Glades Foundations, the Merker Fund, the Lymphoma Foundation, and the Mesothelioma Applied Research Foundation.

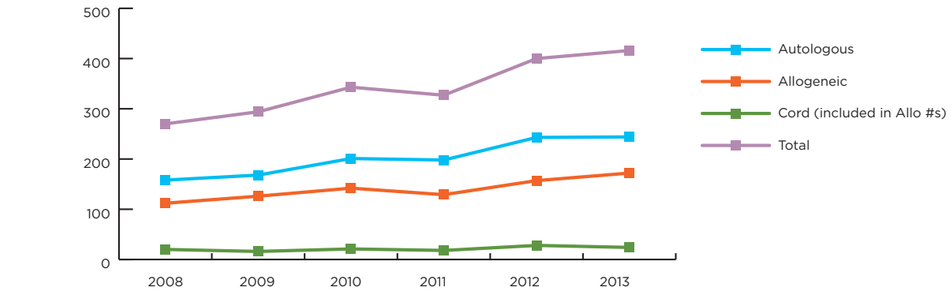
Hematologic Oncology Visits



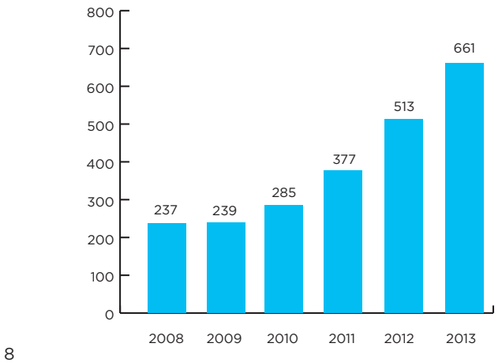
Hematologic Oncology New Visits



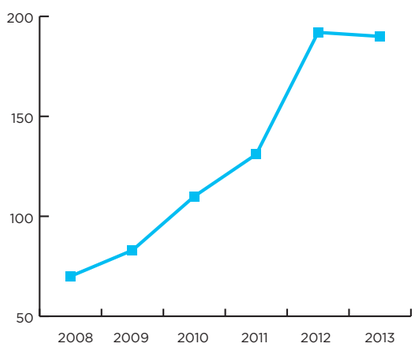
Bone Marrow Transplant Facts and Figures



Clinical Trial Accruals



Publications



REGIONAL NETWORK

"Our commitment to expand our Regional Care Network and newly formed MSK Cancer Alliance means that more patients — including those living outside the New York City area — will now have access to the most-advanced, evidence-based care, including Memorial Sloan Kettering clinical trials."

José Baselga, MD, PhD, Memorial Sloan Kettering's Physician-in-Chief

MSK's regional network currently consists of seven suburban outpatient treatment centers. The new Memorial Sloan Kettering West Harrison site, which opened in October 2014, is a state-of-the-art, 114,000 square foot outpatient facility serving the needs of patients from the Bronx, Hudson Valley and Fairfield County regions.

In 2013, Richard Barakat MD, FACS was appointed Deputy Physician-in-Chief for the Memorial Sloan Kettering Regional Care Network and Alliances. Under his leadership, the network will continue to expand its presence throughout the New York metro area while also building relationships and forming alliances with medical institutions outside the region. In addition, Ephraim S. Casper, MD, Head of the Division of Network Medicine Services in the Department of Medicine is dedicated to ensuring consistency of care at our regional campuses and is leading the effort to expand the clinical trials infrastructure to facilitate participation throughout the Regional Network.

MSK West Harrison opened October 6, 2014

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

MSK Commack
650 Commack Road
Commack NY 11725

MSK Hauppauge
800 Veterans Memorial Highway, 2nd Floor
Hauppauge, NY 11788

MSK West Harrison
500 Westchester Avenue
Harrison, NY 106043

Memorial Sloan Kettering Cancer Center
1275 York Avenue
New York, NY 10065

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

MSK Sleepy Hollow
777 North Broadway
Sleepy Hollow, NY 10591

FUTURE SITE
MSK Monmouth

LONG-TERM ISOLATION POSES SPECIAL CHALLENGES AFTER STEM CELL TRANSPLANTATION

"The thing I remember most about the weeks after the transplant was that everyone who came in to see me was wearing a mask. I didn't have to wear one, but they did. Day after day, week after week, all I saw of the people I loved was the little rectangle of their faces — eyes and forehead — that the mask did not cover. Everyone who touched me was wearing gloves, and I grew to miss that, too, the feel of holding (my partner's) hand, the touch of my sisters' and friends' lips on my cheek."

Robin Roberts with Sergio Giralt, Chief of the Adult Bone Marrow Transplant Service.

In this quote from her 2014 memoir, Everybody's Got Something, morning news show veteran Robin Roberts crystallized the sense of disconnection ubiquitous among stem cell and bone marrow transplant, or BMT, patients. Ms. Roberts — who anchors ABC's Good Morning America — received a stem cell transplant at Memorial Sloan Kettering in the fall of 2012 to treat the life-threatening bone marrow disorder myelodysplastic syndrome (MDS).

For the hundreds of adults who undergo stem cell or bone marrow transplants each year at MSK, mostly for blood cancers, Ms. Roberts' book relates a familiar experience. Beyond the physical difficulties of the treatment itself, this type of transplantation requires prolonged isolation from everyday life, adding emotional challenges to an already steep recovery.

"With any diagnosis that threatens your life, even for patients with the greatest amount of support, there may be a sense of aloneness at different points in the illness and treatment experience," says MSK social worker Margery Davis, who works with patients on the Adult Bone Marrow Transplant Service. "For transplant patients, there's also a physical isolation and restrictive lifestyle imposed by the treatment that's very different from other experiences."

CREATING COMFORT DURING THE HOSPITAL STAY

During hospitalization, which frequently ranges from two to six weeks, it's paramount to keep bacteria, viruses, and fungi from infecting BMT patients — particularly for those receiving a donor-derived, or allogeneic, transplant, whose immune systems are being entirely rebuilt as these "foreign" cells engraft in their bone marrow. That's why all visitors, along with medical staff, bear the rectangular visage of masks and don gloves, as Ms. Roberts poignantly describes. It's only after patients' blood counts begin to rise again that they're even allowed out of their hospital room to walk the halls.

This isolation doesn't have to equal solitary confinement, since a small circle of family and friends can spend time with BMT patients both in the hospital and at home in the first months after discharge. Instead, the separation stems from being deprived of normal sights, sounds, smells, tastes, and touches along with regular patterns of socializing, working, shopping, and moving about.

"People generally feel well taken care of here, so I wouldn't say the isolation is only because of the environment and the masks and gloves," Ms. Davis says. "I think the room isolation contributes to feeling disconnected at times. It's hard to cope being in a room that represents their illness and treatment 24-7."

To compensate, some patients outfit their space for the long haul with homey touches such as comforters, photographs, and simple wall hangings, says Ann Jakubowski, a physician on MSK's Adult Bone Marrow Transplantation Outpatient Unit. They can also shun hospital gowns and wear their own leisure clothes during much of their stay.

MAKING ADJUSTMENTS AT HOME

Psychologically, a far more vulnerable time for most BMT patients is the 100 or so days after they leave the hospital, according to Dr. Jakubowski and Ms. Davis. At home, a multitude of adjustments await, all to minimize germs: Dirt and dust are enemies. Many foods are discouraged. No taking mass transit, no eating out, no venturing into crowds. Visitors must be limited and screened to make sure they're not sick. Even the family pet — because it may carry bacteria or other infectious organisms — might have to temporarily live elsewhere.

"For some people, their dog is like their baby, especially for those who don't have kids," Dr. Jakubowski says. "It's really hard on them. There are a lot of rules and recommendations they are given while their immune system is suppressed...all trying to protect them."

Unless they're able to work from home, many patients must also leave their jobs for at least three months, which can add to the mounting financial strain of treatment. Some people also experience the long separation from work as a blow to their identity. Creating structure around these home-based months — when patients are encouraged to limit outside activities to only frequent follow-up medical visits — is key. Quiet routines that include bathing, exercise, reading, and light household chores such as folding laundry can help focus patients during seemingly endless days.

"I think the slow recovery is very hard for people to sit with," Ms. Davis says. "People need to get back to work for financial reasons, but also for purpose and meaning in their life. They need to create a structure for themselves without being able to work."

Beyond the physical difficulties of the treatment itself, this type of transplantation requires prolonged isolation from everyday life, adding emotional challenges to an already steep recovery.

STRATEGIES FOR RECOVERY

To smooth recovery psychologically and physically during isolation, Dr. Jakubowski and Ms. Davis offer the following advice. These tips may be helpful not only to patients who have undergone BMTs but also to those whose immune systems may be compromised due to chemotherapy or other cancer treatments.

KEEP ACTIVE.

Yes, your energy is limited, and you can't hit the gym. But while you're hospitalized, get out of bed at least twice a day, if possible, and do the exercises hospital staff members recommend, which reduce the risk of infection and help maintain muscle tone. At home, short treks outside (away from crowds) help build endurance, and wisely selected video fitness games such as tennis, basketball, or bowling offer a surprisingly effective workout. "It's about keeping a positive perspective and moving forward as opposed to being in a sick mode," Dr. Jakubowski says.

STAY CONNECTED.

Virtual connections — through email, Skype, and social media outlets such as Facebook — can fill the void while face-to-face contact is scarce. MSK offers the online community Connections (http://www.mskcc.org/cancer-care/counseling-support/connections-online-community) for patients and caregivers to give and receive support. Just be careful about chat rooms and websites operating without oversight from a major health organization, Dr. Jakubowski says, since information may be misleading or wrong.

"With the Internet, it's easier to keep some connection with other people," she says. "You can see and hear them in ways that wouldn't have been possible ten or 15 years ago. And in terms of being able to talk to your kids while you're in the hospital, or talk to your friends, being able to use Skype is huge."

Our Patient-to-Patient Support Program (http://www.mskcc.org/cancer-care/counseling-support/patient-patient-support) can also put you in touch with a cancer survivor or caregiver who has been through the experiences of treatment and is willing to listen to any concerns or anxieties you may have. These conversations may take place over the phone or via e-mail.

TAKE A TASTE.

The chemotherapy and radiation typical before stem cell transplantation, as well as some of the medications needed to protect the transplant patient, temporarily affect many patients' sense of smell and taste, lowering appetite and causing varying degrees of weight loss. Despite your aversion, "keep trying tastes of everything — salty, sweet, and different textures — to see what works right now," Dr. Jakubowski suggests.

FOCUS ON THE END GAME.

Set small, short-term goals such as attending a social event (with your doctor's blessing) so you have something to look forward to. "It's a relief to go even to the grocery store," Ms. Davis says. "It's a sign you're moving toward recovery, toward normal life."

But don't do too much, too soon, even if you're feeling stronger, Dr. Jakubowski warns. "Some patients live by the rules... and others feel very cheated that things aren't normal. It's maybe a year of your life, but if it's what it takes to save your life, try to hang in there."

SET EXPECTATIONS.

Appoint a "spokesperson" who can keep others in the loop about your transplant and recovery. This person can also help set expectations for your at-home healing period. "Patients say that everyone expects them to do everything they did before, but just because you're home doesn't mean you're back to normal," Ms. Davis says. "It's a very high-risk phase, and I think a sense of isolation comes when people have a different schedule for you to get back to normal than the real schedule."

CELL-BASED IMMUNE THERAPY SHOWS PROMISE IN LEUKEMIA PATIENTS

For decades, doctors have dreamed of attacking cancer by harnessing one of the most powerful and precise weapons in the therapeutic arsenal — a person's own immune system. Now Memorial Sloan Kettering investigators report a potential breakthrough using genetically modified immune cells to treat a severe form of leukemia.

The patients being treated had B cell acute lymphoblastic leukemia (ALL), a rapidly progressing disease that often returns, or relapses, after initial treatment with chemotherapy. All five of the patients who have received the new therapy — known as targeted immunotherapy — have gone into complete remission, with no detectable cancer cells.

"This is a very exciting finding for patients with B cell ALL and a major achievement in the field of targeted immunotherapy," says Michel Sadelain, Director of MSK's Center for Cell Engineering, who led the study along with medical oncologist Renier J. Brentjens.

ENGINEERING PRECISE WEAPONS

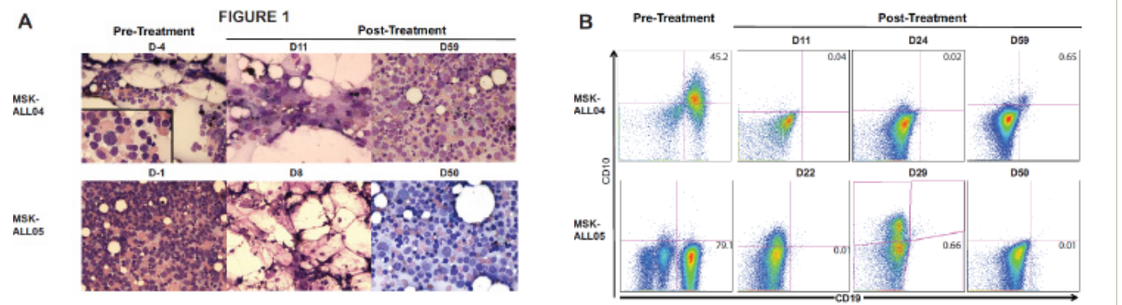
Targeted immunotherapy is aimed at instructing the immune system to recognize and attack tumor cells. Over the past decade, Drs. Sadelain and Brentjens, and other MSK researchers — including Isabelle Rivière, Director of Memorial Sloan Kettering's Cell Therapy and Cell Engineering Facility, and physician-scientist Marco L. Davila — have investigated an approach that involves removing white blood cells called T cells from patients and introducing a new gene into the cells using an engineered viral vector.

Viral vectors are disabled viruses that cannot replicate but efficiently shuttle their genetic cargo into cells — in this case a gene coding for a chimeric antigen receptor (CAR) that directs the T cells to attack the cancer. After the gene is transferred and expressed, the T cells are infused back into the patient, where they multiply and cause a variety of immune responses aimed at attacking the cancer cells. The gene used in the targeted immunotherapy for ALL codes for the creation of a CAR that enables T cells to recognize the CD19 protein, which is present in B cell ALL tumor cells.

Much of the early research into this approach was supported by MSK's Experimental Therapeutics Center and benefactors of the Center for Cell Engineering.

"We have been a leading center in developing this technology, including the CAR design, the proof-of-principle efficacy studies, and the T cell manufacturing process, and we were the first center to bring this CD19-targeted approach to the clinic," Dr. Sadelain explains.

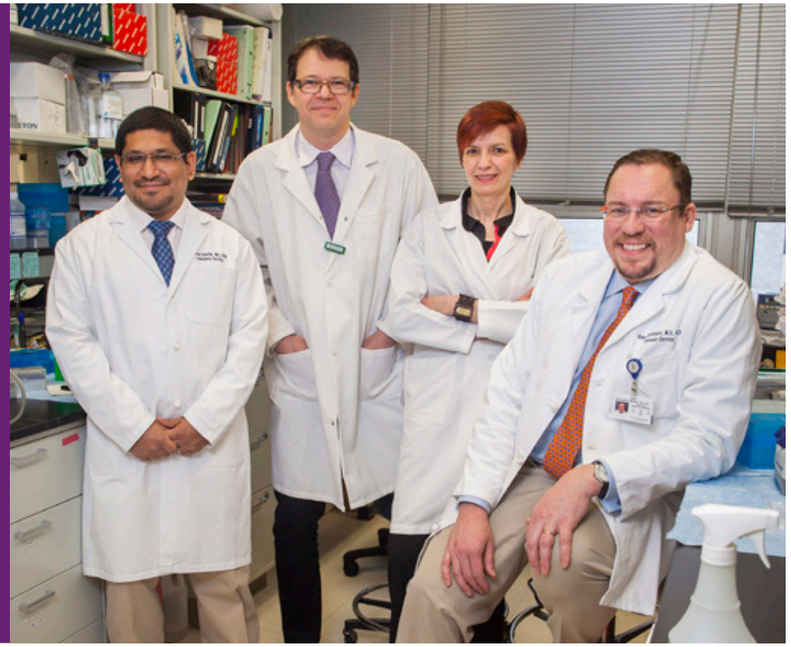
In the phase I clinical trial, five patients with relapsed B cell ALL had cancer that was detectable at varying levels in the blood and bone marrow. After receiving the genetically modified T cells, all five patients achieved complete remission, and even highly sensitive molecular analyses found no cancer cells remaining. The results of this ongoing clinical trial were reported online on March 20 in the journal Science Translational Medicine.



A. BM aspirates pre- and post-treatment with 19-28z T cells in 2 patients with morphologic chemotherapy-refractory B-ALL. Cyclophosphamide was given at Day -1 and CD19 CAR-targeted T cells were infused on Days 1 and 2. Left panels. BM prior to CAR modified T cell therapy demonstrated predominant blast cells with an absence of normal BM precursors. For MSK-ALL04 the left panel includes an inset with 100x magnification. Middle panels are BM aspirates done shortly after 19-28z T cell infusion and is hypocellular with normal stromal elements, histiocytes, and no evidence of blasts. Right panels. By 1 to 2 months after CAR modified T cell therapy there is BM recovery with normal hematopoiesis and no evidence of abnormal blasts.

B. Flow cytometry for CD19 and CD10 expression in BM pre- and post-treatment. Cells were gated on CD45+7AAD- cells.

Figure 1. Rapid leukemia eradication in patients with relapsed ALL. Brentjens, Davila, Rivière et al, Science Transl Med, 2013



Marco Davila, Michel Sadelain, Isabelle Rivière, and Renier Brentjens

A BRIDGE TO STEM CELL TRANSPLANTATION

"Patients with relapsed B cell ALL resistant to chemotherapy have a particularly poor prognosis," says Dr. Brentjens. "The ability of our approach to achieve complete remissions in all of these very sick patients is what makes these findings so remarkable and this novel therapy so promising."

Four of the five patients subsequently received additional therapy in the form of a bone marrow transplant, the standard of care for those patients who successfully achieve complete cancer remissions after treatment for relapsed disease.

"By serving as a bridge to a stem cell transplant, this therapy could potentially help cure adult patients with B cell ALL that has relapsed and who are chemotherapy resistant. Otherwise, these patients have a virtually incurable disease," Dr. Brentjens says. "We need to examine the effectiveness of this targeted immunotherapy in additional patients before it could potentially become a standard treatment for patients with relapsed B cell ALL."

Further clinical trials, including a phase II study, have already been planned to test whether B cell ALL patients would benefit from receiving this targeted immunotherapy along with chemotherapy earlier in the disease stage, either as part of the initial frontline treatment or after remission has been achieved to help prevent relapse.

"We have been a leading center in developing this technology, including the CAR design, the proof-of-principle efficacy studies, and the T cell manufacturing process, and we were the first center to bring this CD19-targeted approach to the clinic."

— Michel Sadelain

GERALD A. SOFF

CHIEF, HEMATOLOGY SERVICE

Hematologic disorders occurring in cancer patients — such as low blood counts, hemorrhages or blood clots — can sometimes be as dangerous to a patient's health as the malignancy itself. This issue is always top of mind for Gerald A. Soff, who was appointed chief of Memorial Sloan Kettering's Hematology Service in 2010.

A hematologist who specializes in benign hematology disorders, Dr. Soff's research focuses heavily on the interaction of the coagulation system and cancer. He has published numerous clinical and basic science studies in the field.

In this interview, Dr. Soff discusses his department's mission, research successes and future goals.

As chief of the hematology service, what priorities guide your leadership?

We recognize that our mission, to a large degree, is to allow everyone else here to do their jobs optimally. We try to remove the limitations on what medical oncologists, surgeons and radiation oncologists can do to treat cancer. Our first clinical target is thrombocytopenia, or low platelet counts, associated with chemotherapy. Thrombocytopenia can lead to excessive bleeding. It's well-known that patients getting chemotherapy experience a suppression of blood counts, including red and white blood cells and platelets. We can transfuse blood to support red cell counts and offer a growth factor to support white blood cells. But a common and significant problem for cancer patients has been to prevent and treat thrombocytopenia following chemotherapy. The platelet counts drop and recover too slowly for the oncologist to continue treating the patient with chemotherapy on the intended dose and schedule.

What advances in thrombocytopenia therapies epitomize the improvements in hematology treatments compared to even a decade ago?

Historically, there was simply nothing available to treat chemotherapy-induced thrombocytopenia. But for the past several years, we've been exploring the use of a drug that boosts platelet production called romiplostim, known commercially as Nplat®. We recently published a study in the journal Supportive Care in Cancer showing that of 20 patients treated, all 20 experienced a benefit. Their platelet counts came up, they were able to resume full-dose chemotherapy, and the oncologist was then able to optimally treat the cancer.

Now we have an open clinical trial to validate this in a prospective study. We'll have a total of 60 patients, 40 of whom will be on romiplostim and 20 who will be observed. But any of the patients in the observation arm who don't spontaneously correct their platelet counts will be eligible for romiplostim after three weeks. This way, we'll be able to obtain scientific and statistically valid numbers to demonstrate what we're doing is working. We're uniquely situated to have a major impact on this particular problem.

What other current hematology research seems especially compelling?

Another major area of our clinical research is to help develop new strategies to treat thrombosis, or blood clots in cancer. Besides dying of cancer itself, the second biggest cause of death is from thrombosis. Standard practice over the last dozen years has been to use an injectable anticoagulant, which is very painful and expensive. Patients need the shots twice a day, and if they don't have insurance coverage, it's prohibitively expensive. But this was the best available treatment to us, and there had been no advance in treatment of cancer-associated thrombosis for over a decade.

We're now opening a quality improvement initiative to use one of the new oral anticoagulants, rivaroxaban, known commercially as Xarelto®, to treat this. Rivaroxaban is FDA-approved for treatment of thrombosis, but there's inadequate experience published on how rivaroxaban can be used in cancer patients. We've been using it here for one and a half years, and because our experience has been so favorable, we're now expanding this and making it our first-choice drug. It's our expectation that bleeding and thrombosis rates will be as good or better than those observed with low molecular weight heparin. Again, we're taking an already available drug and utilizing it in a relatively new way that can dramatically improve quality of life and possibly extend the lives of our cancer patients. When they switch to the oral anticoagulant, they want to hug me. They tell me that I've spared them from the brutal pain of those injections.

What enthuses you about your research?

What excites me right now is the fact that we're addressing very practical questions. We're looking at scenarios where a successful outcome could impact countless patients in very real time. If our strategy in treating thrombocytopenia does well, it has the potential of doing for chemotherapy-induced thrombocytopenia what G-CSF has done for white blood cell counts after chemotherapy. We have the possibility of reproducing that kind of success and the opportunity to have cancer patients across the world be treated more effectively. And we're not talking about five or ten years down the road – we're talking one or two years.

Which aspects of hematology still need more research?

We're trying to move more into translational science. One of the projects we're just beginning is developing biomarkers telling us which patients are at risk for thrombosis. Right now, we use factors such as age, cancer type and surgery as our crude tools to indicate this risk, but we're trying to look at levels of certain factors in the blood that serve as a warning that a patient is at high risk, such as clotting factor activity, platelet activity and vascular injury. Just like we know that one chemotherapy regimen doesn't fit all cancers, it's my belief that one strategy for preventing and treating thrombosis doesn't fit all patients. We may have to tailor prevention and treatment based on measurable biomarkers, but first these have to be characterized.

JULIET N. BARKER

DIRECTOR, CORD BLOOD TRANSPLANTATION PROGRAM

As head of Memorial Sloan Kettering's Cord Blood Transplantation Program since 2005, Juliet Barker has helped create one of the leading programs in this type of transplantation in the world. Dr. Barker and her team have overseen more than 200 cord blood transplants during her tenure, representing more than 20 percent of such transplants at MSK for patients with cancers of the blood and bone marrow requiring a donor transplant but without a suitable matched sibling donor.

Collected from the umbilical cords and placentas of healthy newborns and held in public banks, cord blood contains blood-forming stem cells that help rebuild a healthy bone marrow and immune system after transplant. Cord blood transplantation has become a valuable addition to traditional stem cell transplants obtained from matched sibling or unrelated adult donors, and Dr. Barker's clinical research has focused on new ways of using this therapy and improving patient outcomes.

In this interview, Dr. Barker discusses her research priorities, successes, and some of the remaining obstacles in cord blood transplantation.

Why are cord blood transplants an important treatment option?

For patients with cancers of the blood and bone marrow, many of those with high-risk or relapsed disease will fail non-transplant treatment options and ultimately die of their disease. Transplanting such patients with blood-forming stem cells from a donor offers them a potential cure and can work when other treatments haven't. However, only about 25 percent of patients will have a suitably matched and healthy brother or sister to act as a donor, so 75 percent of patients will need another type of donor to proceed to transplant.

The standard approach in this situation is to search for a matched adult volunteer donor through international registries. However, some European patients — those from the South of Europe, for example — and the majority of patients with non-European ancestry are poorly represented in the volunteer registries and many have complex tissue typing. Such patients may not find a suitably matched unrelated donor. Plus, some volunteer donations occur too slowly, especially for those patients with aggressive cancers of the blood and bone marrow who require urgent transplants. In both scenarios, cord blood is an attractive alternate stem cell source. It's cryopreserved in cord blood banks, so it's readily available, and it's less important to find a perfect match than when using an adult donor.

What excites you about your research?

Cord blood has shown an extraordinary capacity to extend transplantation to those who otherwise wouldn't have a suitable donor stem cell source. Greater than 50 percent of the 200-plus cord blood transplant recipients at Memorial Sloan Kettering to date have had non-European or part non-European ancestry and have included patients of Hispanic, Asian and African backgrounds. There's no doubt that in this area, we're a leader in the field, and we're particularly invested in this endeavor because of the diverse patient population we have in New York City.

Secondly, in patients with acute leukemia, we've recently demonstrated that the disease-free survival after cord blood transplant is comparable to that of stem cell transplants from adult volunteer donors. It's thrilling that we can extend access to transplantation to patients of racial and ethnic minority populations and achieve comparable disease-free survival to the gold standard in transplant therapy.

What clinical trials are underway that you find especially compelling?

We're researching how to identify the best cord blood donors for our patients, and this is contributing to progressively improving transplant outcomes. We've developed a new chemotherapy-radiation regimen that is given in the week prior to the cord blood transplant to improve how well the transplant is tolerated but maintain its effectiveness. This regimen has also contributed to improved results in our patients. Another trial is investigating new strategies to enhance the recovery of the patient's blood counts after transplant, which is improving the tolerability and toxic side-effects of transplantation and should ultimately shorten hospitalization times and improve outcomes.

Which areas of cord blood transplantation still need more research emphasis?

While we have had many successes in treating adults with acute leukemia, the cure rates for cord blood transplants in such patients is approximately 65 percent, meaning one in three patients will not have a successful transplant. We're constantly striving to pursue a variety of approaches to further improve these results. There has been spectacular progress in the last decade – but we're not done optimizing these results.

What are some of the challenges remaining in cord blood transplantation?

There are many. Even with the size of the current global inventory of cord blood units, there are some patients – particularly those of African ancestry, who have the most diverse tissue typing – for whom we can't identify suitable donors, including cord blood. Some patients with significant pre-existing conditions before transplant face great medical challenges when undergoing transplant therapy, and we're striving to be able to more safely perform the transplant in those patients and avoid life-threatening complications. In addition, cord blood transplant patients are at risk for both infections and graft-versus-host disease (GVHD), where the donor's immune system recognizes the patient's tissues as foreign. There is still much work to be done to prevent such complications and this is also a major focus of our program.

ANDREW D. ZELENETZ

ATTENDING PHYSICIAN, LYMPHOMA SERVICE
VICE CHAIR, MEDICAL INFORMATICS

Andrew D. Zelenetz has spent his career developing new ways to treat Hodgkin and non-Hodgkin lymphomas. Joining Memorial Sloan Kettering in 1991 after an internship, residency and fellowship at Stanford, Dr. Zelenetz has worked as part of a multidisciplinary team to evaluate many combinations of lymphoma drugs through clinical trials. He has published more than 100 papers on lymphoma research in journals such as Blood, Journal of Clinical Oncology, and Clinical Cancer Research.

In this interview, Dr. Zelenetz discusses his path toward oncology as well as his professional high points and future goals.

What factors guided your decision to go into oncology?

Even back in high school, I had a strong interest in the biology of growth. In college, I worked with others to examine the regulation of glutamine metabolism in bacteria and how that influenced growth. When I moved on for my PhD, I focused on understanding the components necessary to transform cells. We studied Rous Sarcoma Virus, which can cause tumors in chickens, and cloned the SRC gene and showed it had a powerful ability to transform cells, making it an oncogene. We went on to clone the normal version of this gene and identified the differences between the virally derived gene and its normal counterpart. The molecular biology of cancer just fascinated me.

What brought you to Memorial Sloan Kettering?

A good job. I did an abbreviated internship and residency at Stanford after medical school, only two years, and directly tracked into medical oncology, where I was specifically interested in how slow-growing lymphomas transform into aggressive lymphomas. During my post-doctoral fellowship at Stanford, I worked in the lab of Ronald Levy studying this process of how follicular lymphoma transforms. This is an all-too-common problem in patients with follicular lymphoma, and understanding the basis for transformation held the promise to identify novel treatment approaches. When it came time to find a permanent position, I was looking for someplace that would be able to support my clinical and lab interests, and Memorial Sloan Kettering was the place.

How has lymphoma research at Sloan Kettering evolved during your tenure here?

Early on, our research was really focused on lab investigation. We were trying to understand how lymphomas develop by identifying genes that got activated by chromosomal breakpoints. One of the features of many lymphomas and leukemias is that the chromosome in the tumor cell breaks and rejoins in ways that have a profound impact on the cellular biology. Identification of the gene or genes that are activated as a consequence of the chromosomal translocations contributes to our understanding of the pathology of the lymphoma. We identified that activation of MUC1 can contribute to aggressive behavior of some cases of aggressive large cell lymphoma.

We also developed a tool to track minimal amounts of disease in patients. When the B cells develop, a unique DNA sequence is created as a consequence of the rearrangement of immunoglobulin genes. Thus, each B-cell lymphoma has a unique 'clonotypic' sequence than can be used to track the tumor clone by the polymerase chain reaction (PCR). Because of the tremendous sensitivity of the PCR technique to identify rare tumor cells, we can identify a single tumor cell out of 100,000 cells.

Our drug development program has contributed a number of drugs to the armamentarium for lymphoma treatment, including bexarotene for cutaneous T-cell lymphoma; pralatrexate for peripheral T-cell lymphoma; iodine-131 tositumomab, and bortezomib in mantle cell lymphoma. All became FDA-approved drugs, in no small measure due to our work here at MSK.

Which research in lymphoma therapies do you feel has made the biggest impact on patient outcome?

In 1994, when I became chief of the Lymphoma Service, one of my major responsibilities was to reinvigorate the clinical trial efforts and we have had a lot of success. One of the first things we did was develop a regimen called ICE specifically for patients with recurrent lymphoma that was named after the initials of the drugs used: ifosfamide, carboplatin and etoposide. It was a very effective regimen and has become one of the standard regimens around the world for relapsed and refractory lymphoma. For some patients, we added the monoclonal antibody rituximab, which added to the efficacy.

The ICE treatment is so effective that we have also integrated it into the up-front treatment of patients with large cell lymphoma. Compared to historical controls, patients treated with sequential rituximab and CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) followed by ICE have a substantial improvement in outcome compared to R-CHOP chemotherapy alone. Our work with ICE chemotherapy has been quite seminal and has really changed the way many people treat lymphoma.

Which aspects of lymphoma have seen the most research in recent years?

The biggest recent accomplishment has been coming to understand the molecular pathways that are critical in the process of lymphoma. This work has really illuminated new potential targets for therapy, and a lot of our work is building on that new knowledge. We know certain molecular pathways are the Achilles' heel of the disease, and we try to attack those pathways, hoping to take advantage of the tumor's weakness.

One promising new drug is called ibrutinib, which is the first drug designed to target a protein critical to the growth of B-cells — which are affected in most cases of non-Hodgkin lymphoma — but leave healthy T-cells in the immune system largely unaffected. We have two exciting new trials with this drug in mantle cell and large cell lymphoma comparing ibrutinib to standard treatment.

How is lymphoma research at MSK set apart from other institutions both nationally and internationally?

We have a very tight, dedicated group of clinicians, pathologists, radiation oncologists and others who work very closely to conduct both clinical trials and translational research. The effort at MSK is large and well coordinated. Most centers might have one or two faculty members who study lymphoma, but we have 12 medical oncologists alone in the field. The depth of our faculty provides tremendous expertise to our patients that simply is not readily available elsewhere.

What obstacles confront you in your research?

One of the big challenges — and this is a universal challenge in oncology — is the difficulty we often have in getting patients engaged in the clinical trial process. All patients want to benefit from the best new discoveries, but without their help and support new discoveries can't be made. They don't want to be a 'guinea pig.' That's despite the fact that there's tremendous oversight, control and care in conducting a clinical trial, but many patients are uncertain and uncomfortable about being in a trial.

What do you hope to accomplish next?

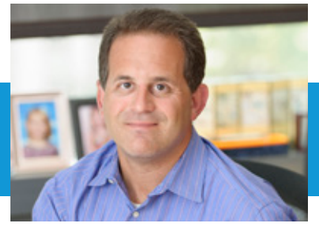
We'd like to prescreen patients to understand their molecular lesions and potentially treat them on this basis, which might be the same in two different lymphomas. This concept of treating patients based on molecular findings, rather than how tumors look under the microscope, is the next direction in lymphoma.

Also, I have recently taken on new challenges in my role as Vice Chair for Medical Informatics in the Department of Medicine. MSK is an institution that was an early adopter of computerized medical records. With the passage of the HiTECH act providing Federal mandates for 'meaningful use' of electronic health information systems, however, MSK is facing new challenges as how to meet the new requirements. In my new position, I have the challenge of helping MSK update and improve technology integration at the Center.

Scientific data being presented at a weekly Lymphoma Service faculty meeting

ROSS L. LEVINE

LAURENCE JOSEPH DINEEN CHAIR IN LEUKEMIA RESEARCH



Meet Ross L. Levine, a physician-scientist whose leading-edge research into the genetic basis of myeloproliferative neoplasms (MPNs) has led to targeted therapies for these blood cancers and unprecedented insight into their causes. Inspired to work in science from a young age, Dr. Levine holds a joint appointment on the Leukemia Service, where seeing patients in the clinical program facilitates his laboratory research.

In seminal research with colleagues, Dr. Levine discovered that in two-thirds of patients with MPNs, their cancer cells contained a single mutation in the gene for the signaling molecule JAK2, suggesting the JAK2 pathway was involved in several types of blood cancer. Further research revealed that leukemia cells can use other means of maintaining the function of the JAK2 kinase — even when exposed to JAK2 inhibitors — and opened paths to new targeted treatments.

Here, Dr. Levine discusses the blend of patient care and research at MSK that continues to improve outcomes in leukemia.

How does your work with patients inform your research efforts?

For us, the studies we've done in patient samples are the cornerstone of everything we do. By identifying what mutations or other genetic abnormalities are present in individual patients, it allows us to focus on specific genetic events that occur at a high frequency in patients and are associated with poor outcome. Those insights underscore what we've done in the lab. It's really critical to focus on questions that matter most in the clinic.

What energizes you most about your research?

I think the constant series of challenges is exciting. The development of genomic technologies is allowing us an unprecedented look into the genetic events occurring in patients' leukemia cells, a view we didn't have before, and helps us understand the players involved in leukemia development in much greater detail. We can develop better models of leukemia in the lab and identify new drug targets, which is ultimately the goal.

How is leukemia research at Memorial Sloan Kettering set apart from other institutions nationally and internationally?

We have two strengths that are really quite special. First, we have a tremendous group of investigators with diverse backgrounds and interests who work very well together, so we're really a collaborative team. We leverage our skills in ways I haven't seen in other places I've worked. We have great strengths in both the lab and the clinic, which allows a synergistic aspect of working together towards translational goals. It's really a seamless integration here.

Which aspects of leukemia have seen the most research in recent years?

It's a rapidly changing area. Historically we as a field have known a lot about certain leukemias, including AML (acute myeloid leukemia) and CML (chronic myeloid leukemia). But with the development of new genomics, we're beginning to see insights leading to biologic studies and new therapeutic concepts for virtually every type of leukemia. It's a great time to have the collaborative team MSK has assembled because we're tackling all types of leukemia — they're all up for grabs.

Which facets still need more focus?

There are always challenges we still need to address. One important area is AML, and other leukemias, in older adults. Older patients present with leukemias that are more genetically complex than those in younger adults and they don't tolerate leukemia treatments as well. We need to find less toxic, more effective treatments for those who can't withstand current treatments, so that we have more efficacious therapies for older adults with refractory disease that doesn't respond to current treatments.

We also see many patients with leukemia who, because they were treated previously for other cancers, develop secondary leukemias. We understand far less about the causes of these leukemias and we have few effective treatments. We need to figure out how to better prevent and treat those leukemias because they're very different from primary leukemias. Are there shared features between treatment-induced leukemias and other leukemias, or do we need to consider them a completely distinct entity? It's a fundamental question we don't fully understand.

What are some of the challenges remaining in leukemia research?

One of things we're all very hopeful we'll address collaboratively in next few years is how we take the great insights being made in leukemia biology and therapy and apply them as part of an integrated approach; including chemotherapy, radiation, immunotherapy and treatments targeting molecular pathways. How do we best mix and match those in a multi-modality therapy? I'm looking forward to seeing how we can tap into all these approaches, and how hitting leukemia from different angles may be better than a single type of treatment.

How have patient outcomes improved over the last decade?

We see two trajectories. For most leukemias, the improvement we've seen is real, but it's definitely a continued process. We're seeing survival rates improve, and still like to build on that. But what's really notable is that in a number of leukemias, important discoveries have been made that have made them much more treatable and curable based on new genetic studies and on the development of innovative treatment approaches. It hasn't happened for leukemia as a whole but rather for one subtype at a time. The question is how we march toward greater success for all as we continue to markedly improve things for specific subtypes, to bend the curve and change the paradigm, dramatically changing things for one group at a time.

What do you hope to accomplish next?

Our view of leukemia has evolved a lot in just the past few years, and we know it's a much more genetically complicated disease than we appreciated just a few years ago. But our ability to understand that in the lab and to leverage that in the clinic is just beginning. How do we understand the basis of that complexity, how it contributes to leukemia, and integrate that into new treatments? This is why multi-modality treatment is so important. We need to be smart and highly collaborative while we work together to hit leukemia from multiple angles.

HEMATOLOGIC ONCOLOGY TISSUE BANK

In 2010, the Division of Hematologic Oncology established the Hematologic Oncology Tissue Bank (HOTB) to support the many different research projects of Memorial Hospital and Sloan Kettering Institute investigators.

When the bank was created in 2010, about 150 samples were processed each month. Sample processing has since increased to more than 600 per month. The HOTB currently has an inventory of more than 70,000 aliquots, including pheripheral blood components (plasma, serum, granulocyte pellets and mononuclear cells), buccal swabs for DNA, bone marrow mononuclear cells, skin, and lymphoid tissue.

Kristina Knapp, Translational Research Manager

James Young, Director of the HOTB

The bank is 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.

THE SUSAN AND PETER SOLOMON DIVISIONAL GENOMICS PROGRAM

Through the support of the Peter and Susan Solomon Family Foundation, Memorial Sloan Kettering has implemented a state of the art genomics platform to look for genetic mutations in the tumor samples of patients with a variety of blood cancers. Our initial efforts have led to rapid, cost-effective mutational studies for MSK patients with acute myeloid leukemia (AML), myelodysplastic syndromes, and myeloproliferative neoplasms. We have developed research-based genomic tests for all patients with hematologic malignancies and in collaboration with Foundation Medicine, we developed a state-of-the-art DNA/RNA sequencing test, which can be used to comprehensively profile samples from leukemia, lymphoma and myeloma samples (see pages 4-5). This test is now being offered nation-wide, and has allowed our investigators to lead the field by bringing genomic testing to the clinical setting.

Susan and Peter Solomon

The Solomon program has also invested in new technologies that are aimed to innovate discovery and translational research in hematologic malignancies, including DNA/RNA sequencing and proteomic approaches to study blood cancers.

ANAS YOUNES, Chief of the Lymphoma Service

As Chief of Memorial Sloan Kettering's Lymphoma Service, medical oncologist Anas Younes is spearheading an intensified effort to identify new disease biomarkers that help predict which patients might benefit from new targeted therapies. These lymphoma treatments will be tested in highly focused clinical trials for the many different subtypes of the disease, trials that Dr. Younes will advocate with his non-medical secret weapon — social media.

My connection to Memorial Sloan Kettering and New York goes back more than two decades. After completing my residency in internal medicine at SUNY Downstate College of Medicine in Brooklyn, I did a hematology-oncology fellowship at Memorial Sloan Kettering. I then moved to Houston in 1992 to serve on the faculty at M. D. Anderson Cancer Center. Twenty years later, earlier this year, I came back!

I was drawn back to Memorial Sloan Kettering for two main reasons. First, the outstanding collective clinical expertise in diagnosing and managing patients with lymphoma is unmatched anywhere in the world. Our 12 clinical faculty members on the Lymphoma Service have a combined experience that exceeds 100 years, and each of us has managed even the rarest and most complex forms of lymphoma. There's also a long tradition of close interaction with our outstanding pathologists, radiologists, radiation oncologists, and surgeons. I was very honored to be asked to rejoin the Memorial Sloan Kettering community and lead the Lymphoma Service.

Second, and equally important, is the opportunity to collaborate with world-class scientific leaders who have made numerous discoveries that enhanced our understanding of cancer and lymphoma biology, immunology, and genetics. This environment, which brings together clinical and basic science faculty in close physical proximity, is unique in the cancer world, positioning Memorial Sloan Kettering to drive the lymphoma field forward.

"We have already started implementing novel trial designs to match patients with specific treatments based on their tumor biology"

Finally, as much as we enjoyed living in Texas, my wife and I always felt and lived like New Yorkers. It was natural for us to return.

A FOCUS ON NEW DRUGS

Lymphoma was one of the first human cancers to become curable with multi-agent chemotherapy. Today, 40 years later, we still use the same drugs. They have cured many patients but remain rather nonspecific for lymphoma. Nevertheless, we give these treatments to a variety of patients hoping we can cure some of them. Working with 40-year-old drugs is like trying to sequence the human genome using your old Macintosh computer. We need to develop treatments that are more effective and safer based on recent advances in our knowledge of tumor biology.

How do we accomplish this? The answer lies in our ability to rapidly translate the latest scientific discoveries into smarter, more rationally designed, mechanism-based clinical trials.

The old way of selecting patients for testing of new drugs was based primarily on the histologic type of their cancer — how the cells look under the microscope. But we have recently learned that lymphoma cells that look the same under the microscope may differ in their genetic composition and in their response to any given therapy. The current treatment approach is not only slow and inefficient, it also exposes a large number of patients to toxic effects from which they may not benefit.

A 'DIVIDE AND CONQUER' APPROACH

Instead, we've begun taking a "divide and conquer" approach, separating lymphomas into groups based on newly identified genetic and biologic alterations in the cancer cells, and irrespective of the underlying histology. We are actively screening lymphoma tumors for new biomarkers and possible new therapeutic targets. This strategy allows us to select patients for specific therapies that are likely to be more successful. Trials conducted in this way will require fewer numbers of patients to participate so we may complete these studies and learn the results in a shorter period of time.

We have already started implementing these novel trial designs to match patients with specific treatments based on their tumor biology. Our lymphoma group is collaborating with several laboratories, including Foundation Medicine, a commercial laboratory that is a leader in genetic sequencing, to develop a molecular diagnostic test that will simultaneously evaluate the status of hundreds of genes in a variety of lymphomas. Using this genomic panel, we may soon be able to offer more patients the opportunity to participate in clinical trials testing novel agents more tailored for their specific lymphoma tumors.

TARGETING RESISTANCE

The Lymphoma Service holds weekly clinical research meetings to discuss current and future strategies and plan new collaborations and clinical trials.

Despite this progress, many tumor cells quickly learn how to outsmart a particular drug, no matter how active its effect. We are designing new combination regimens based on our understanding of the mechanisms that lead to tumor cell resistance.

To improve this understanding, it is important to obtain fresh tumor cells from patients both prior to therapy and then at the point of tumor progression. Data from such sequential biopsies can benefit not only the patient, as they may guide the selection of subsequent treatment, but also the lymphoma community in general.

SPREADING THE WORD

To accelerate our progress, it is essential to find ways to reach out to patients, caregivers, and referring physicians to make them aware .

AMERICAN SOCIETY OF HEMOTOLOGY MEETING 2013 New Orleans, LA

Our faculty was well represented at the 2013 annual meeting of the American Society of Hematology (ASH) in New Orleans, Louisiana with over 110 abstracts, 41 of which were selected for oral presentation.

Marco Davila presented exciting results using infusion of T cells modified to express a chimeric antigen receptor (CAR) targeting the cell surface molecule CD19 for patients with relapsed/refractory acute lymphoblastic leukemia (ALL). Although the primary goal of this study was to evaluate safety, he observed a complete response rate of 88% in these patients with a dismal prognosis, who were now eligible to undergo a potentially life-saving bone marrow transplant. These results in combination with similar results from groups at NCI and Pennsylvania University have generated tremendous excitement and hope that CAR T cells will soon be approved as therapy for ALL. CAR T cell therapy (and other cancer immunotherapies) was selected by the journal Science as the breakthrough of the year 2013.

Anas Younes (MSK) demonstrated that combination therapy of the new BTK inhibitor Ibrutinib with RCHOP (the current standard of care) for newly diagnosed patients with B cell lymphoma is relatively safe and produced a 100% response rate. Based on these promising data MSK investigators are leading an international randomized trial comparing standard RCHOP with Ibrutinib + RCHOP in patients with newly diagnosed non-germinal center type of diffuse large B cell lymphoma. In addition, Steve Treon (Dana Farber Cancer Institute), Lia Palomba (MSK) and others reported remarkable response rates for patients with relapsed or refractory Waldenstrom's macroglobulinemia with Ibrutinib.

Parastoo Dahi, Juliet Barker (both MSK) and colleagues analyzed donor availability in 708 patients and demonstrated that cord blood transplantation is of critical importance to provide access to transplant for minorities.

ABOVE:
Jenna Goldberg, Doris Ponce, Ewelina Morawa

RIGHT:
Christiane Querfeld, James Young, Melody Smith, Connie Batlevi, and Alison Moskowitz

HEMATOLOGIC ONCOLOGY NURSING AND PHYSICIAN ASSISTANT HIGHLIGHTS AND ACCOMPLISHMENTS

AWARDS

2013 Samuel and May Rudin Awards for Excellence in Nursing

- Excellence in Nursing Leadership: Karen Collum, MSN, RN
- Excellence in Nursing Practice: Virginia Morales

The Pearl Moore Frontline Care "Making a Difference" Award presented by ONS

- Virginia Morales

HEMATOLOGIC ONCOLOGY NURSES REPRESENT MSK AT NATIONAL MEETINGS

Nurses and Physician Assistants in the Division of Hematologic Oncology made presentations at several meetings around the country in 2013, including:

ASBMT 2013 Tandem Meetings

- "Implementation of an Electronic Form for Hematopoietic Stem Cell Transplant (HSCT) Infusions Improves Documentation Compliance" Karen Collum, RN, MSN (podium presentation)
- "Transforming Change of Shift Handoff: Implementing Walking Rounds in Adult Bone Marrow Transplant" — Pamela Grant-Navarro, RN BSN OCN, Marianne Holly Wallace, RN, BSN, MPH, CNML, Kathy Choo, RN, MSN, OCN, Jennifer Feustel, RN (poster presentation)

Association of Physician Assistants in Oncology's 16th Annual Meeting

- Abby Staible, MMS, PA-C presented "BMT Survivorship"

Scripps 10th Annual Advanced Practice Oncology Providers Symposium

- Heather Hylton, MS, PA-C presented "The ABCs of BMT and SCT"

HIGHLIGHTS

- M12 Inpatient Practice Council members Tara Diaz, CN III & Kristen Battiato, CNIV proposed yellow slipper socks for our high risk patients to enhance our current fall program initiatives. Ms. Diaz & Ms. Battiato presented to the council and the initiative was approved for our patients identified as high risk for falls.
- Heather Hylton, MS, PA-C served as President of the Association of Physician Assistants in Oncology for 2012-2013, was appointed to ASCO's Government Relations Committee and the ASCO University Editorial Board in 2013, and was elected as a Director at Large for the Association of Physician Assistants in Oncology for 2014-2015.
- Apryl Sarabia, MS, PA-C served as the Scholarship Chair for the Association of Physician Assistants in Oncology in 2013 and 2014.

AWARD RECIPIENTS (left to right)

Excellence in Nursing Leadership
Karen Collum, MSN, RN, Division of Hematologic Oncology

Excellence in Nursing Practice
Fred Haro-Zuniga, RN

Excellence in Patient Care Support*
Katherine Gamble

Excellence in Nursing Education
Janine Kennedy, MSN, RN

Excellence in Nursing Practice
Virginia Morales, MSN, RN, Division of Hematologic Oncology

Excellence in Advanced Nursing Practice
Joseph B. Narus, DNP, APRN, NP-BC

**Supported by the Department of Nursing*

Samuel and May Rudin Awards Recognize Nursing Excellence

MSK nurses and their colleagues gathered on May 8, 2013 in the Rockefeller Research Laboratories Auditorium for a ceremony honoring five nurses and one support staff member, recipients of the 2013 Samuel and May Rudin Awards for Excellence in Nursing. "Your steadfast commitment to delivering the highest-quality care while recognizing the humanity of everyone you serve — whether patients, families, or caregivers — is irreplaceable," said MSK President and CEO Craig B. Thompson. The annual awards, which recognize excellence in nursing practice, advanced nursing practice, nursing leadership, nursing research, nursing education, and patient care support, are sponsored by the Rudin Family Foundation.

THE MORTIMER J. LACHER FELLOWS CONFERENCE

The Division held its annual Mortimer J. Lacher Fellows Conference on May 17, 2013. The event honors Dr. Lacher, a longtime member of MSK's Lymphoma Service and the Sloan Kettering Institute. Dr. Lacher joined the Lymphoma Service at Memorial Hospital in 1960 and served as a member of the Sloan Kettering Institute from 1960 until 1990. With John R. Durant, he published a seminal report in 1965 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. Every year, the Lymphoma Foundation provides funding for Medical Oncology/Hematology fellows at MSK and specific projects in the laboratories of MSK physician scientists. Dr. Lacher is now a Consultant in MSKC's Department of Medicine.

Dr. Marcel van den Brink, Head of the Division of Hematologic Oncology, delivered the Fourth Annual Mortimer J. Lacher Lecture titled, "Allogeneic Bone Marrow Transplantation: the original immunotherapy of cancer."

Dr. Mortimer J. Lacher, M.D., FACP
President, the Lymphoma Foundation
Consultant, Department of Medicine
Memorial Sloan Kettering

The 2013 Lacher Fellows are listed below along with their abstracts:

Amanda Olson, MD (Mentor: Sergio Giralt)
"Frequent Human Herpesvirus-6 (HHV-6) Viremia but Low Incidence of Encephalitis in Double-Unit Cord Blood Recipients Transplanted Without ATG"

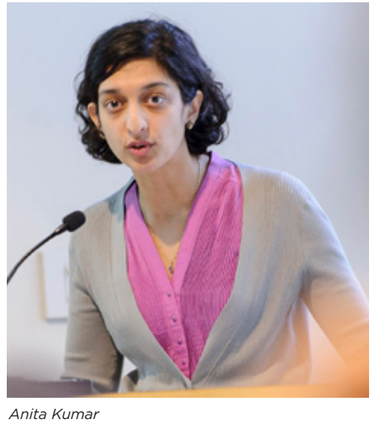
Raajit Rampal, MD, PhD (Mentor: Ross Levine)
"Development and Characterization of a Murine Model of Leukemic Transformation of Myeloproliferative Neoplasms for Preclinical Therapeutic Studies"

Anita Kumar, MD (Mentor: Andrew Zelenetz)
"Early Stage Hodgkin Lymphoma: Prognostic Markers and Novel Therapeutics"

Matthew Lunning, DO (Mentor: Steven Horwitz)
"Remission Duration ≤ 12 Months for Early Relapsed and Refractory Follicular Lymphoma is Predictive of Early Failures Post-High Dose Therapy and Autologous Stem Cell Rescue"

Sewit Teckie, MD (Mentor: Joachim Yahalom)
"Characteristics, Treatment and Long-Term Outcome of 360 Patients with Marginal Zone Lymphoma"

Raajit Rampal



Anita Kumar

A CELEBRATION OF STEM CELL TRANSPLANT SURVIVORS

On October 16, 2013, MSK's 18th Annual Stem Cell Transplant Survivorship Celebration drew more than 550 guests and allowed transplant patients to meet one another and reunite with doctors, nurses, and other staff, and to share memories about how the procedure restored their health and changed their lives.

Among the attendees was Good Morning America co-host Robin Roberts. Ms. Roberts received a stem cell transplant at Memorial Sloan Kettering in the fall of 2012 for the treatment of myelodysplastic syndrome (MDS), a disease that arises in the bone marrow due to a disorder of hematopoietic stem cells, the immature cells from which all blood cells develop. She was hospitalized for several weeks and was closely monitored and cared for as an outpatient by a team of doctors, nurses, and staff under the direction of Dr. Giralt.

"We meet to celebrate the success you've had in this journey and to acknowledge all the people who helped you to have that success," Sergio A. Giralt, Chief of the Adult Bone Marrow Transplant Service, told those gathered. "We also meet to thank you, because all of you here don't know how invigorating it is to all the staff at Memorial to see you. It really is heartwarming to see that we were able to be part of the reconstruction of your lives."

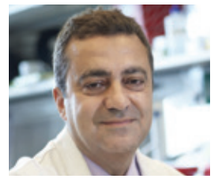
Robin Roberts with her transplant physician, Sergio Giralt, and nurses who helped with her care. (Left to right) Sheila Kenny, NP, Julie Kleber, RN, Dr. Giralt, Robin Roberts, Jenny Tran, RN, Gloria Coffey, NP, Lorraine Jackson, NP

SENATOR SCHUMER VISITS MSK

MSK leadership and Board members gathered on May 1 for a reception honoring US Senator Charles Schumer for his advocacy on behalf of New York's healthcare and biomedical research sector. Craig B. Thompson, MSK President and CEO, highlighted the Senator's efforts to secure emergency funds in the wake of Superstorm Sandy. Dr. Thompson also noted the work that Senator Schumer and his staff have done to help identify solutions to longer-term problems, including adequate funding for the National Institutes of Health, immigration reform, and Medicare reimbursement.

Isabelle C. Rivière, Director of MSK's Cell Therapy and Cell Engineering Facility, describes to Senator Schumer (far right) the new cell engineering laboratory under development in the Zuckerman Research Center. With Dr. Rivière are medical oncologist Renier J. Brentjens (far left) and Marcel R. M. van den Brink, head of the Division of Hematologic Oncology.

ANAS YOUNES IS CHIEF OF THE LYMPHOMA SERVICE



Anas Younes has joined Memorial Sloan Kettering as Chief of the Lymphoma Service in the Division of Hematologic Oncology. He succeeds Andrew D. Zelenetz, who had led the service since 1994 and is now Vice Chair for Medical Informatics in the Department of Medicine.

Dr. Younes is a medical oncologist with clinical and research interests in the field of Hodgkin and non-Hodgkin lymphoma. He brings to Memorial Sloan Kettering more than 20 years' experience in the management of patients with lymphoma. He has extensive experience in clinical and translational research focused on the development of novel target therapy and the identification of biomarkers to match patients with the most effective but least toxic therapy.

After receiving his MD degree from the University of Damascus School of Medicine, in Syria, Dr. Younes completed residencies at the Medical College of Ohio and SUNY Downstate Medical Center, and subsequently was a hematology/oncology fellow at Memorial Sloan Kettering. Before joining MSK, he had served on the faculty of the University of Texas M. D. Anderson Cancer Center for more than two decades.

MICHAEL J. MAURO JOINED LEUKEMIA SERVICE

Michael J. Mauro has joined MSK's Leukemia Service and will lead the myeloproliferative diseases program. He is a board-certified hema-tologist who is an expert in chronic myeloid leu-kemia (CML) as well as other myeloproliferative diseases (MPDs) such as myelofibrosis and polycythemia. Dr. Mauro received his MD degree from Dartmouth Medical School and completed his residency and fellow-ship training at NewYork-Presbyterian Hospital/Weill Cornell Medical Center. He comes to MSK after 13 years at Oregon Health and Sciences University Hos-pital, in Portland, Oregon, where he oversaw the clinical research program in CML and MPDs, including the clinical development of currently available tyrosine kinase inhibitors for CML.

ANDREW D. ZELENETZ APPOINTED VICE CHAIR FOR MEDICAL INFORMATICS

Medical oncologist Andrew D. Zelenetz served as Chief of the Lymphoma Service from 1994 until 2012 when he was appointed Vice Chair for Medical Informatics in the Department of Medicine. In this role he is harnessing data from cancer patients in various departments at MSK in order to improve decisions about treat-ment and to find ways to make the care of cancer patients more efficient. In addition to these new responsibilities, he con-tinues his active clinical and translational research program in lymphoma. Dr. Zelenetz received his MD and PhD degrees from Harvard University. He was a resident at Stanford University Medical Center, where he also held research and clinical fellowships. He joined the MSK faculty in 1991.

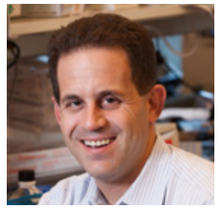
STEVEN M. HORWITZ PROMOTED TO ASSOCIATE MEMBER

Steven M. Horwitz is a medical oncologist whose clinical and research efforts have focused on improving outcomes for patients with T cell and cutaneous lymphomas. His work has led to the develop-ment of the only two approved agents for the treatment of T cell lymphomas and has paved the way for MSK to become an international leader in these diseases. Dr. Horwitz earned his MD degree from Case Western Reserve University. He did his residency training at University of Rochester Medical School and held a fellowship at Stanford University Medical Center. He joined the MSK faculty in 2001. He is board certified in internal medicine and medical oncology.

MIGUEL PERALES PROMOTED TO ASSOCIATE MEMBER

Miguel Perales is a medical oncologist and an expert in donor-derived hematopoietic (blood-forming) stem cell transplantation, a procedure that can cure many patients who have diseases of the blood and bone marrow, including leukemias and lymphomas. He leads translational research efforts focused on immune reconstitution after stem cell transplantation. Dr. Perales received his MD degree from the Free University of Brussels, in Belgium, and did his residency training at New England Medical Center, in Boston. He came to MSK as a fellow in 1998 and joined the faculty in 2001. He currently serves as Deputy Chief of the Adult Bone Marrow Transplant Service and as Director of the Adult Stem Cell Transplantation Fellowship Program.

AWARDS AND RECOGNITION



ROSS LEVINE

Physician-scientist Ross Levine has been named the incumbent of the newly established Laurence Joseph Dineen Chair in Leukemia Research. Dr. Levine is a member of the Human Oncology and Pathogenesis Program whose research explores the molecular underpinnings of myeloproliferative neoplasms and acute myeloid leukemia. The Dineen Chair places special emphasis on leukemia in children and young adults. It was established with support from Kathryn Dineen Wriston in honor of her brother, who died of leukemia at age 7.

MICHEL SADELAIN

In October, Memorial Sloan Kettering's Michel Sadelain was a recipient of the 2012 William B. Coley Award for Distinguished Research in Tumor Immunology. Dr. Sadelain was recognized for his "groundbreaking work on the development of chimeric antigen receptor T cell therapy for cancer, a highly promising new approach to strengthening a patient's immune response to cancer." At the ceremony, MSK physician-scientist Jedd D. Wolchok presented Dr. Sadelain with the award.

BAYARD CLARKSON

The American Association for Cancer Research (AACR) has named chemical biologist Bayard Clarkson to the inaugural class of Fellows of the AACR Academy. The AACR Academy honors distinguished scientists whose major contributions have propelled significant innovation and progress against cancer.

MARCEL R. M. VAN DEN BRINK

Physician-scientist Marcel R. M. van den Brink was elected member of the Association of American Physicians.

AHMET DOGAN

Ahmet Dogan was named Chief of the new Hematopathology Service established within the Departments of Pathology and Laboratory Medicine. His current research interests include lymphoma, plasma cell disorders, and diagnostic techniques for hematopathology such as cytogenetic analysis, genomics, and proteomics. His previous work has contributed much to the understanding of the histogenesis of lymphomas, MALT lymphomas, and T cell lymphomas in particular. As service chief, Dr. Dogan will orchestrate the integration of diagnostic results across multiple laboratories and helps foster increased primary and collaborative research related to hematologic malignancies at Memorial Sloan Kettering.

CLINICAL TRAINING AND EDUCATION

Programs Train the Leaders of the Future

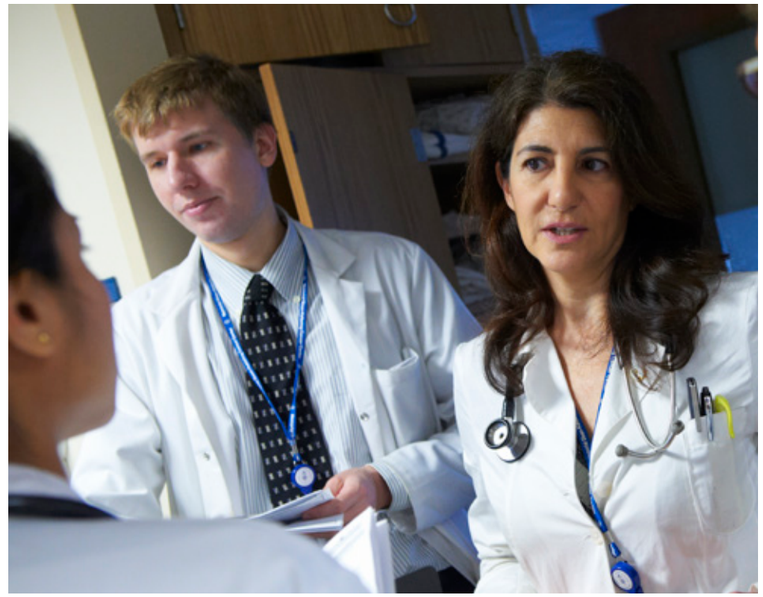
Memorial Sloan Kettering attracts applicants from all over the world for two distinguished fellowships in Medical Oncology/Hematology and Bone Marrow Transplantation. Education in benign hematology is also provided by the Hematology Service to international medical students, internal medicine residents, 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 some 450 applicants each year for just 15 coveted spots. In addition to being outstanding physicians, fellows must have interests 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.



Medical Oncology/Hematology Fellow Patrick Burke and Lia Palomba, Assistant Attending on the Lymphoma service during inpatient rounds

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 is 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 will also have opportunities to participate in ongoing research projects or to initiate an independent project. This process will be helped by the assigning of a mentor throughout the fellowship, who will ensure 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.

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

SWIM ACROSS AMERICA

Swim Across America, Inc., (SAA) is an organization that raises funds for cancer research, prevention and treatment through swimming-related events. Over 5,000 swimmers, ranging in ages from 4 to 78 and in ability from recreational swimmers to former Olympians, participate nationally on an annual basis. There are typically 600-700 swimmers for the Long Island Sound event alone. To date, SAA has raised over $45 million for cancer research, prevention and treatment.

Memorial Sloan Kettering is one of SAA's major beneficiaries. Dr. James Young, Attending Physician on the Adult BMT Service and an avid distance swimmer, began swimming the Long Island Sound Open Water event in 2006. Three years later, a patient who is also a distance swimmer and who had successfully recovered from an allogeneic transplant for acute leukemia, proposed that they start an actual team dedicated to supporting the Adult BMT program at MSK. Since 2009, Team Transplant has raised over $100,000 for the much needed support of 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. Team Transplant swam for its fifth year on July 27th, 2013, participating in the Long Island Sound Open Water Swim, and raised nearly $35,000.

TEAM TRANSPLANT, SWIM ACROSS AMERICA LONG ISLAND SOUND OPEN WATER SWIM 2013 BACK ROW: KAYAKERS: *Carol Ipsen, Erik Ipsen, Abigail Young;* SWIMMERS: *Jeff Bodenmann, Jim Young, Nicole Magaldi, Chris Eddy, Dick Endris, Jeb Singer.* FRONT ROW: *Shannon and Carmine Petruzello*

SWIM ACROSS AMERICA
www.swimacrossamerica.org

SWIM ACROSS AMERICA
★ MAKING WAVES TO FIGHT CANCER ★

FRED'S TEAM

Fred's Team is Memorial Sloan Kettering's athletic fundraising program that enables athletes of all abilities to fundraise directly for MSK by competing in marathons, half-marathons, triathlons, cycling races and other endurance events worldwide. In 2013, members raised more than $4.1 million.

On November 3, 2013, 875 Fred's Team members — including 34 Memorial Sloan Kettering staff members — ran the 26.2-mile 2013 ING NYC Marathon, taking them through all five New York City boroughs to raise funds for the institution's lifesaving mission.

In 2013, the Division of Hematologic Oncology received nearly $253,000 from Fred's Team participants. Since 1995, Fred's Team has raised over $56 million.

Left to right: Archie Kumar, Marcel van den Brink, Katya Ahr, Stephanie Benardis

FRED'S TEAM MEMBERS FROM THE DIVISION OF HEMATOLOGIC ONCOLOGY

Katya Ahr
Nancy Albistequi-Amaya
Stephanie Benardis
Stephen Chung
Megan Heavey
Michael Mauro
Marcel van den Brink
Alexandra Vincenti

CYCLE FOR SURVIVAL

Cycle for Survival is a national indoor team cycling event that raises money for research on rare cancers at Memorial Sloan Kettering. It became an official MSK event in 2009, after being founded by the late Jennifer Goodman Linn and her husband David Linn in 2007, two years after Jennifer was diagnosed with sarcoma.

In 2013, nearly 12,000 indoor cyclists participated to raise $14 million at events at Equinox clubs in 10 cities: Boston; Chicago; Greenwich, Connecticut; Long Island; Los Angeles; Miami; Summit, New Jersey; New York City; San Francisco; and Washington, DC. 100% of Cycle for Survival funds go directly to research initiatives at Memorial Sloan Kettering within six months of the events.

To date, Cycle for Survival has raised $51.5 million and participation nearly doubles every year.

Participants from the Division included:

Miguel Perales

Ashley Helmes, Chelsea Brooklyn, Ayaz Alam

TEAM BMT

Miguel Perales
Apryl Sarabia
Arnab Ghosh
Ashley Helmes
Ayaz Alam
Carmine Petruzello
Chelsea Brooklyn
Craig Sauter
Emily Lauer
Hetal Shah
Kathryn Jose
Martin Toulouse
Mary Griffin
Michelle Lange
Nisa Amoils
Shannon Durand
Shannon Petruzello
Sheelah Hyland
Tiffany Watson

TEAM T CELL RACERS

Steven Horwitz
Shani Miller
Audrey Rodriguez
Caren Pinto
Daniel Layon
Janelle Walkley
Josie Hubschman
Kelly Tharp
Lauren Hogan
Leslie Cheteyan
Patrycja Mysliwiec
Stephen Randolph
Sumi Nair
Susan Mccall

TEAM INFUSION (VAN DEN BRINK LAB)

Katya Ahr
Megan Solberg
Fabiana Kreines
Margaret O'Connor
Emily Levy
Kelly Piersanti
Anna Mertelsmann

Fred's Team group picture in Times Square at 6am before the NYC Marathon on November 3, 2013

PUBLICATIONS

These are a few articles out of the 190 total articles published by the Division of Hematology Oncology faculty in 2013.

ADULT BONE MARROW TRANSPLANTATION

Ponce DM et al. A novel reduced-intensity conditioning regimen induces a high incidence of sustained donor-derived neutrophil and platelet engraftment after double-unit cord blood transplantation. Biol Blood Marrow Transplant. 2013; 19(5):799-803.

Double-unit cord blood transplantation (CBT) has been a successful treatment for high-risk hematologic malignancies in adults and extends transplant access to minority patients. However, high-dose myeloablative conditioning is associated with a significant risk of transplant-related mortality. While non-myeloablative conditioning could be a potential alternative, it is limited by the risk of graft rejection and disease relapse, especially in patients with acute leukemia. Therefore, we investigated the safety and efficacy of a novel intermediate intensity (reduced intensity but myeloablative) preparative regimen using the combination of cyclophosphamide, fludarabine, thiotepa and 400 cGy total body irradiation followed by CBT. This regimen has demonstrated a high incidence of sustained donor-derived neutrophil and platelet engraftment with promising disease-free survival despite the median age of the patients in this study being in the mid fifties. We conclude that this therapy is highly effective in older patients who are otherwise reasonably fit. Consequently, it has become a routine alternative in adults with otherwise lethal cancers of the blood and bone marrow at Memorial Sloan Kettering.

Goldberg JD et al. T cell-depleted stem cell transplantation for adults with high-risk acute lymphoblastic leukemia: long-term survival for patients in first complete remission with a decreased risk of graft-versus-host disease. Biol Blood Marrow Transplant. 2013; 19(2):208-13.

We describe the long-term follow-up of 56 adult patients with ALL in complete remission who underwent T cell depleted allogeneic hematopoietic stem cell transplantation from related or unrelated donors following myeloablative cytoreduction. Baseline cytogenetics were classified as poor risk (n = 24, including Ph+ = 17), standard risk (n = 25), good risk (n = 3) or non-evaluable (n = 4). The 2-year and 5-year OS were 0.39 (95% CI: 0.26-0.52) and 0.32 (95% CI: 0.19-0.44), respectively. The 2-year and 5-year DFS were 0.38 (95% CI: 0.25-0.50) and 0.32 (95% CI: 0.20-0.44). The cumulative incidence of grade II-IV acute GVHD at one year was 0.20 (95% CI: 0.10-0.31), and no patients developed grade IV acute GVHD. The cumulative incidence of chronic GVHD at 1 year was 0.12 (95% CI: 0.02-0.22), and of extensive chronic GVHD at one year was 0.05 (95% CI: 0-0.12). We demonstrate OS and DFS rates that compare favorably to unmodified allo-HSCT with lower rates of GVHD.

Doubrovina E et al. Adoptive immunotherapy with unselected or EBV-specific T cells for biopsy-proven EBV+ lymphomas after allogeneic hematopoietic cell transplantation. Blood. 2013;119(11):2644-56.

This paper reports MSK experience of efficient and safe use of EBV specific T cells inducing durable remissions without any risk of GVHD in patients with biopsy-proven EBV-associated lymphoproliferative disease emerging after allogeneic HCT. The authors analysed factors (i.e. disease characteristics, its prior treatment and the T cells used for adoptive therapy) contributing to tumor response or continued progression and revelaled that failures are ascribable to impaired T-cell recognition of tumor-associated viral antigens or their presenting HLA alleles.

Davila ML et al. Efficacy and toxicity management of 19-28z CAR T cell therapy in B cell acute lymphoblastic leukemia. Sci Transl Med. 2014;6(224):224ra25.

This is a seminal paper describing the responses and the management of toxicities of the novel chimeric antigen receptor T cells developed at MSK by Dr Sadelain, Brentjens, Riviere and colleagues. These engineered T cells have shown potent antileukemia activity and have been successful bridges to transplant for many patients.

Bayraktar UD, de Lima M, Saliba RM, Maloy M, Castro-Malaspina HR, Chen J, Rondon G, Chiattone A, Jakubowski AA, Boulad F, Kernan NA, O'Reilly RJ, Champlin RE, Giralt S, Andersson BS, Papadopoulos EB. Ex vivo T cell-depleted versus unmodified allografts in patients with acute myeloid leukemia in first complete remission. Biol Blood Marrow Transplant. 2013; 19(6):898-903.

This paper is a report of a retrospective comparative analysis in transplant outcomes in patients with first remission acute myeloid leukemia undergoing allogeneic stem cell transplantation at MSK and MDACC over a 10 year period. GvHD prophylaxis consisted of T cell depletion only in the MSK patients while in the MDACC group standard drug prophylaxis was used. While there was no statistical difference between the two groups with respect to overall survival, disease free survival, relapse, or non-relapse mortality at 3 yrs, there was a statistically significant reduction in both acute and chronic graft-vs host disease in the patients transplanted at MSK with T cell depleted transplants. These and other reports from our group utilizing T cell depletion as a method of GvHD prophylaxis have led to an upcoming BMT Clinical Trials Network study that will prospectively randomize patients undergoing allogeneic transplants to one of 3 different GvHD prophylaxis strategies, one of which is the T cell depletion strategy used in our patients at MSK.

Hsu, KC et al. HLA-C-dependent prevention of leukemia relapse by donor activating KIR2DS1. N Engl J Med. 2012;367: 805-816.

The major discovery in this study demonstrated that an additional type of gene known as KIR might influence the long-term effectiveness of transplants in patients with AML. The investigators performed a retrospective study of 1,277 cases in which AML patients had received a bone marrow transplant from an HLA-matched donor. The findings indicate that some people are less likely to redevelop their disease after a transplant if their donor carries certain genetic traits.

LEUKEMIA

Shah, S. et al. A recurrent germline PAX5 mutation confers susceptibility to pre-B cell acute lymphoblastic leukemia. Nat Genet. 2013; 45(10): 1226-1231.

Ken Offit and colleagues demonstrated in two families with a high incidence of B cell acute lymphoblastic leukemia (B-ALL) the presence of an inherited mutation in a transcription factor termed PAX5 (or BSAP). This study provides new insights in the pathogenesis of and susceptibility to B-ALL.

Brentjens, R. J. et al. CD19-targeted T cells rapidly induce molecular remissions in adults with chemotherapy-refractory acute lymphoblastic leukemia. Sci Transl Med. 2013; 5(177): 177ra38.

Renier Brentjens and colleagues treated five patients with relapsed B-ALL with T cells expressing a CD19-specific chimeric antigen receptor (CAR) termed 19-28z. All patients responded and achieved complete remissions as assessed by deep sequencing polymerase chain reaction. The therapy was well tolerated, although some patients had symptoms due to increased cytokine levels requiring steroid therapy. These results demonstrate the marked antitumor efficacy of 19-28z CAR-modified T cells in patients with relapsed/refractory B-ALL and the reliability of this therapy to induce profound molecular remissions, forming a highly effective bridge to potentially curative therapy with subsequent allogeneic hematopoietic stem cell transplantation.

Shih, A. H. et al. Mutational analysis of therapy-related myelodysplastic syndromes and acute myelogenous leukemia. Haematologica. 2013; 98(6): 908-912.

This study provides evidence that therapy-related MDS and AML (t-MDS/AML) has a distinct molecular profile compared to de novo MDS/AML. While the genetic lesions and cytogenetic abnormalities may be similar, the mutation frequencies are different in classically mutated genes, such as TP53, and in the epigenetic modifiers and splicing genes. As cancer survivorship improves, the incidence of t-MDS/AML will likely increase. We anticipate that a better understanding of the molecular underpinnings of t-MDS/AML will provide hints into the pathogenesis of t-MDS/AML and guide the future development of t-MDS/AML-targeted therapies.

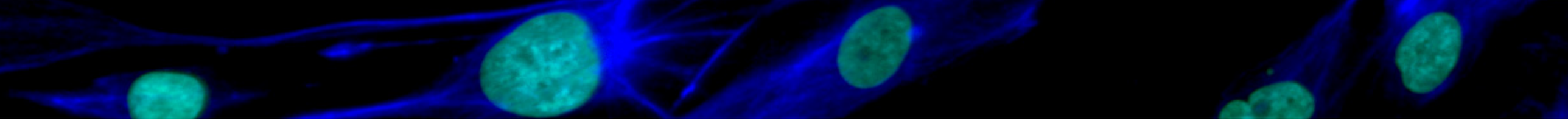
Abdel-Wahab, O, et al., Efficacy of intermittent combined RAF and MEK inhibition in a patient with concurrent BRAF- and NRAS-mutant malignancies. Cancer Discov. 2014; 4(5): 538-545.

Vemurafenib, a RAF inhibitor, extends survival in patients with BRAFV600–mutant melanoma but activates extracellular signal–regulated kinase (ERK) signaling in RAS-mutant cells. In a patient with a BRAFV600K-mutant melanoma responding to vemurafenib, we observed accelerated progression of a previously unrecognized NRAS-mutant leukemia and identified that intermittent combined RAF and MEK inhibitor therapy prevented RAF inhibitor-induced activation of the RAS-mutant leukemia.

Dao, T. et al., Targeting the intracellular WT1 oncogene product with a therapeutic human antibody. Sci Transl Med. 2013; 5(176): 176ra33

Anticancer antibody-based drugs have largely targeted proteins on the surface of cancer cells. But, arguably the most important, tumor-specific proteins are on the inside — safely tucked away within the cell. Wilms tumor 1 (WT1) is one of these intracellular oncoproteins. Despite its insider status, degraded WT1 fragments are presented on the surface of leukemia cells and many other cancer tissues, including ovarian. To kill leukemia, Dao and colleagues hypothesized that intracellular WT1 was the perfect target.

Dao et al. engineered a monoclonal antibody, named "ESK1," that recognizes a peptide fragment of WT1, called RMF, complexed with human leukocyte antigen (HLA) –A0201. After demonstrating that ESK1 bound to several WT1+ cell lines in vitro and leukemia patient cells ex vivo, the authors tested their new antibody in two mouse models of human acute lymphoblastic leukemia. They delivered ESK1 alone or along with human "effector" cells (peripheral blood natural killer cells) and saw that the combination therapy killed nearly all leukemia in comparison to control groups, allowing all of the treated mice to have prolonged or even leukemia-free survival. Treating animals with cancers that lacked either HLA-A0201 or WT1 had no effect.



With a defined mechanism and no toxicity in mice, this ESK1 antibody is poised for testing in human trials. The authors point out that more than 1 million patients in the world may have a WT1 + cancer, with many of these being HLA-A02 +. In this case, ESK1 — with its ability to target a cancer protein inside the cell — could help treat many patients that have not responded to antibody-based therapies focused on the cell surface.

LYMPHOMA

Matasar, M. J, et al. Ofatumumab in combination with ICE or DHAP chemotherapy in relapsed or refractory intermediate grade B-cell lymphoma. Blood. 2013; 122(4):499-506.

Relapsed aggressive B-cell lymphoma is life threatening, but standard treatments are often unable to control the disease. We led a multi-center trial using a next-generation anti-CD20 antibody, ofatumumab, instead of rituximab, in combination with standard chemotherapies; results were promising, even in the highest-risk patients, and our findings motivated the design of an international randomized clinical trial testing this approach.

Moskowitz, A. J, et al. Phase II study of bendamustine in relapsed and refractory Hodgkin lymphoma. J Clin Oncol. 201; 31(4):456-60.

This was a phase II study evaluating the activity of bendamustine in relapsed and refractory Hodgkin lymphoma. This was the first study to establish the role for bendamustine in Hodgkin lymphoma and has led to multiple studies evaluating bendamustine combinations in this disease.

Vijai, J. et al. Susceptibility Loci Associated with Specific and Shared Subtypes of Lymphoid Malignancies. PLoS Genet. 2013; 9(1): e1003220.

Ken Offit and colleagues studied in 944 patients with lymphoma whether genetic changes in the DNA of their non-cancerous cells were associated with their disease. They identified several novel susceptibility regions and heterogeneity, which points to the existence of pathways of susceptibility to both shared as well as specific subtypes of lymphoid malignancy.

Younes A, et al. Brentuximab vedotin combined with ABVD or AVD for patients with newly diagnosed Hodgkin's lymphoma: a phase 1, open-label, dose-escalation study. Lancet Oncol. 2013; 14(13):1348-56.

This study for the first time combined brentuximab vedotin with standard ABVD chemotherapy regimen in patients with newly diagnosed classical Hodgkin lymphoma.

Based on the safety of the regimen and promising clinical activity, this study provided a rationale for an ongoing international randomized study comparing standard ABVD regimen with Brentuximab + AVD arm.

Younes A, et al. Combination of ibrutinib with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) for treatment-naive patients with CD20-positive B-cell non-Hodgkin lymphoma: a non-randomised, phase 1b study. Lancet Oncol. 2014; 15(9):1019-26.

This study for the first time combined Ibrutinib with standard RCHOP chemotherapy regimen in patients with newly diagnosed B-cell non-Hodgkin lymphoma. Based on the safety of the regimen and promising clinical activity, this study provided a rationale for an ongoing international randomized study comparing standard RCHOP regimen with Ibrutinib + RCHOP in patients with newly diagnosed diffuse large B cell lymphoma of the non-GCB subtype.

HEMATOLOGY

Gucalp A, Parameswaran R, Lacouture M, Abou-Alfa G, Soff G. Skin Necrosis Induced By Generic Enoxaparin. Am. J. Hemat. 2013; 88(4):339.

The FDA approved generic enoxaparin, as a "biological equivalent" to the prior brand named Lovenox ®, without requiring human testing. At our institution, we observed four cases of enoxaparin-induced skin necrosis in the initial 18-months since switching to generic enoxaparin, compared with no known cases in at least prior 3 years with Lovenox. This observation raises concern that the generic equivalent may have unforeseen side effects or toxicities, not observed with Lovenox.

Mantha S. Target-specific oral anticoagulants in atrial fibrillation: results of phase III trials and comments on sub-analyses. J Thromb Thrombolysis. 2013; 36(2):155-162.

Review of target-specific oral anticoagulants for atrial fibrillation (dabigatran, rivaroxaban and apixaban), focusing on efficacy and safety outcomes. The major trials in the field are discussed.

Zwicker JI, Liebman HA, Bauer KA, Caughey T, Campigotto F, Rosovsky R, Mantha S, Kessler CM, Eneman J, Raghavan V, Lenz HJ, Bullock A, Buchbinder E, Neuberg D, Furie B. Prediction and prevention of thromboembolic events with enoxaparin in cancer patients with elevated tissue factor-bearing microparticles: a randomized-controlled phase II trial (the Microtec study). B J Haematol. 2013; 160(4):530-537.

Patients with cancer were assessed for tissue factor microparticle levels. Those with high levels were randomized to VTE prophylaxis with enoxaparin or observation. There was a trend towards a lower incidence of VTE in the treatment arm, at 5.6% vs 27.3% (p=0.06).

Mantha S, et al. New avenues for anticoagulation in atrial fibrillation. Clin Pharmacol Ther. 2013;93(1):68-77.

Review of target-specific oral anticoagulants for atrial fibrillation (dabigatran, rivaroxaban and apixaban), discussing pharmacokinetics, efficacy and safety.

Aron JL1, Gosselin R, Moll S, Arkin CF, Mantha S. Effects of recombinant factor VIIa on thrombin generation and thromboelastography in a patient with dabigatran-associated intracranial hemorrhage. J Thromb Thrombolysis. 2014; 37(2):76-79.

Case report of a patient who sustained an intracranial hemorrhage associated with the new anticoagulant dabigatran and use of an antidote with resulting laboratory and clinical findings.

MYELOMA

Lendvai N, et al. A phase 2 single-center study of carfilzomib 56 mg/m2 with or without low-dose dexamethasone in relapsed multiple myeloma. Blood. 2014;124(6):899-906.

Patients with relapsed/refractory multiple myeloma (MM) have few good options for treatment. Carfilzomib, a novel proteasome inhibitor, is now approved for MM that has relapsed or is refractory to treatment with at least two prior therapies including bortezomib and an immunomodulatory agent. The current study was an investigator-initiated, single center study conducted at Memorial Sloan Kettering. Our results suggest that carfilzomib 56 mg/m2 ± dexamethasone may provide added benefit with respect to depth of response and duration of response compared with the currently approved 20/27 mg/m2 dose of single-agent carfilzomib. Importantly, adding low-dose dexamethasone to carfilzomib may allow patients to prolong treatment, which is clinically meaningful in the advanced MM setting where salvage treatment options are limited. Based on small numbers, an increased incidence of grade 3/4 HTN and heart failure was noted. Almost all patients who had Grade 3/4 HTN had pre-existing HTN, therefore, close monitoring of blood pressure and tight control of pre-existing HTN is an important component of the care of these patients.

Zamarin D, Giralt S, Landau H, Lendvai N, Lesokhin A, Chung D, Koehne G, Chimento D, Devlin SM, Riedel E, Bhutani M, Babu D, Hassoun H. Patterns of relapse and progression in multiple myeloma patients after auto-SCT: implications for patients' monitoring after transplantation. Bone Marrow Transplant. 2013 Mar;48(3):419-24.

Precise knowledge of the patterns of disease progression after transplant in multiple myeloma patients has been limited. In this paper, we have examined the patterns of disease progression in 273 patients after transplant. These observations have allowed us to develop informed recommendations for appropriate monitoring of patients after transplant.

Zamarin, D., S. M. Devlin, M. E. Arcila, H. Landau, A. Lesokhin, N. Lendvai, D. J. Chung, D. Chimento, J. Weltz, D. Babu, S. Giralt, and H. Hassoun. 2013. Polyclonal immune activation and marrow plasmacytosis in multiple myeloma patients receiving long-term lenalidomide therapy: incidence and prognostic significance. Leukemia. 27(12):2422-4

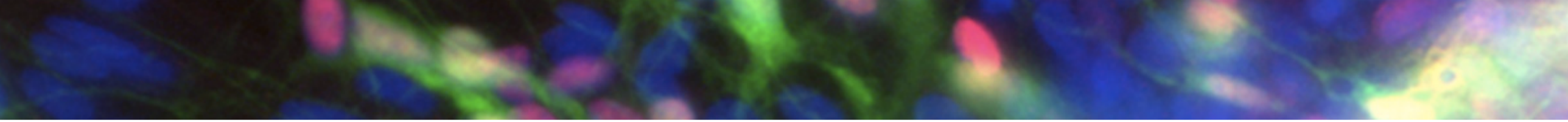
In this paper we report and characterize a novel observation consisting of polyclonal immune activation (including polyclonal hypergammaglobulinemia and a striking polyclonal plasmacytosis in the bone marrow), which occurs with a relatively high frequency (20%), in patients with multiple myeloma treated with extended courses of lenalidomide. The findings raise an important cautionary warning when interpreting bone marrow biopsies since this little known phenomenon must not be confused with disease progression.

Landau H, et al. Bortezomib and dexamethasone consolidation following risk-adapted melphalan and stem cell transplantation for patients with newly diagnosed light-chain amyloidosis. Leukemia. 2013;27(4):823-8.

This phase II trial included 40 patients with newly diagnosed light chain (AL) amyloidosis who underwent risk-adapted melphalan and stem cell transplantation (SCT) followed by bortezomib and dexamethasone (BD) consolidation in order to minimize toxicity and improve efficacy of SCT. We showed that BD following SCT was safe and rapidly improves responses resulting in high complete response rates, maintained organ improvement and promising overall survival (82% at 2 years post SCT).

Pozotrigo M, Adel N, Landau H, Lesokhin A, Lendvai N, Chung DJ, Chimento D, Riedel E, Chen X, Reich L, Comenzo R, Giralt S, Hassoun H. Factors impacting stem cell mobilization failure rate and efficiency in multiple myeloma in the era of novel therapies: experience at Memorial Sloan Kettering. Bone Marrow Transplant. 2013 Aug;48(8):1033-9. PMID: 23334269

The purpose of this retrospective review was to re-evaluate the risk factors that impact stem cell mobilization, especially exposure to novel induction regimens, since there have been concerns about novel agents negatively affecting stem cell yield. Among 317 patients, we found, by multivariate analysis, that older age (P=0.04), lower platelet count (P=0.002), and use of single-agent G-CSF for mobilization (P<0.0001), were independent risk factors and we were not able to show a negative impact associated with novel agents in this population mobilized mostly with cyclophosphamide and G-CSF.



CLINICAL TRIALS

These are a few highlighted clinical trials out of the 147 currently active clinical trials in the Division of Hematologic Oncology. For more information, please visit **http://www.mskcc.org/cancer-care/clinical-trials**

ADULT BONE MARROW TRANSPLANTATION

Myeloablative Unrelated Donor Cord Blood Transplantation with T-Cell Depleted Haplo-identical Peripheral Blood Stem Cells for Patients with High Risk Hematological Malignancies

IRB # 12-153, PI: Juliet Barker

This protocol explores the use of CD34 selected cells provided by a mismatched related donor as a bridge to cord blood transplant engraftment. With over 60 patients treated we have shown that we can reduce the time to white blood cell recovery by almost 10 days in a fraction of patients undergoing double cord blood transplants, and reduced the average length of stay in these patients.

Randomized Phase II Trial of Bulk Versus Fractionated Stem Cell Infusions in Patients with Hematologic Malignancies Undergoing Stem Cell Transplantation

IRB # 12-016, PI: Sergio Giralt

Enhancing immune recovery after donor stem cell transplantation is a major research emphasis for the Adult BMT Service at MSK. We currently have two studies looking at strategies that in animal models have resulted in more rapid immune recovery. One of the strategies is to infuse the stem cell over many days (fractionated) versus infusing them all in one day (bulk). The hypothesis is that a blood stem cell has a better chance of finding a spot to live and grow in (a niche) if the cells are given over multiple days. This study is almost concluding and we should have results next year.

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

High-dose chemotherapy followed by autologous stem cell transplantation (HDT-ASCT) is the established standard of care for patients with relapsed or refractory diffuse large B-cell lymphoma, the most common non-Hodgkin lymphoma (NHL). Despite this, in the modern era, cure is achieved in only ~50-60% with this modality at best. At MSK we've opened a clinical trial consolidating patients following HDT-ASCT with immunotherapy via chimeric antigen receptor modified autologous T cells directed against B-cell NHL antigen CD19 with early encouraging results.

LEUKEMIA

A Phase II Study of the BRAF Inhibitor, Vemurafenib, in Patients with Relapsed or Refractory Hairy Cell Leukemia

IRB # 12-200, PI: Jae Park

Although treatment with purine analogs is associated with a high response rate, hairy cell leukemia (HCL) remains incurable with 30-40% relapse rate. For these patients and those intolerant to purine analogs, novel therapies are needed. The major finding that BRAFV600E mutation occurs in 98% of HCL suggests BRAF as a promising therapeutic target. Protocol 12-200 is exploring the clinical efficacy of the BRAF inhibitor vemurafenib in patients with relapsed or refractory HCL, and biologic determinants of response and resistance to vemurafenib in HCL.

A Phase 1, Open-Label, Dose Escalation and Expanded Cohort, Continuous Intravenous Infusion, Multicenter Study of the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of EPZ-5676 in Treatment Relapsed/Refractory Patients with Leukemias Involving Translocations of the MLL Gene at 11q23 or Advanced Hematologic Malignancies

IRB # 12-181, PI: Martin Tallman

Acute leukemias with rearrangements of the MLL gene are particularly challenging to treat. Researchers at MSK discovered that DOT1L is a protein that is intimately involved in the development of these leukemias. Protocol 12-181 is exploring the safety, tolerability, and initial clinical activity other DOT1L inhibitor, EPZ-5676.

A Phase 1, Multicenter, Open-Label, Dose-Escalation, Safety, Pharmacokinetic, Pharmacodynamic, and Clinical Activity Study of Orally Administered AG-221 in Subjects with Advanced Hematologic Malignancies with an IDH2 Mutation

IRB # 13-154, PI: Eytan Stein

Researchers at MSK and others have discovered that mutations in the IDH-2 gene, leads to acute myeloid leukemia by blocking the ability of immature blasts to develop into normal, healthy, infection fighting neutrophils. AG-221, is a small molecule that inhibits the mutant IDH-2 protein and aims to cure leukemia by reprogramming leukemic cells to mature into normal neutrophils. Protocol 13-154 is exploring the safety, tolerability and initial clinical activity of AG-221.

A Phase I Trial of Precursor B Cell Acute Lymphoblastic Leukemia (B-ALL) Treated with Autologous T Cells Genetically Targeted to the B Cell Specific Antigen CD19(CAR)

IRB # 09-114, PI: Jae Park

Relapsed adult acute lymphoblastic leukemia (ALL) is associated with high reinduction mortality, chemotherapy resistance and dismal prognosis. Adoptive immunotherapy using patient's own T cells genetically modified to express chimeric antigen receptor (CAR) targeting CD19 antigen expressed in most B-cell ALL has been shown to induce high response rates in patients with relapsed ALL and CLL. Protocol 09-114 is exploring the safety and clinical efficacy of autologous CD19-targeted CAR modified T cells in adult patients with relapsed or refractory B-ALL.

A Phase II Study of the HSP90 Inhibitor, AUY922, in Patients with Primary Myelofibrosis (PMF), Post-Polycythemia Vera Myelofibrosis (Post-PV MF), Post-Essential Thrombocythemia Myelofibrosis (Post-ET MF), and Refractory PV/ET

IRB # 12-076, PI: Raajit Rampal

This is phase II trial of the heat-shock protein 90 (HSP90) inhibitor AUY922, which produces JAK2 degradation. This is a novel approach to inhibiting the JAK-STAT pathway in patients with MPNs (ET,PV,MF) who are refractory to, or ineligible for, conventional therapies.

LYMPHOMA

A Phase 1 Study Evaluating the Safety and Pharmacokinetics of ABT-199 in Subjects with Relapsed or Refractory Chronic Lymphocytic Leukemia and Non-Hodgkin Lymphoma

IRB # 11-152, PI: John Gerecitano

A phase I study of ABT-199 in patients with relapsed or refractory chronic lymphocytic leukemia or non-Hodgkin lymphoma.

Phase I Open Label, Multi-center, Dose-escalation Study to Assess the Safety, Tolerability and Pharmacokinetics of Orally Administered CUDC-907, a PI3K and HDAC Inhibitor, in Subjects with Refractory or Relapsed Lymphoma or Multiple Myeloma

IRB # 13-045, PI: Anas Younes

A phase I study of CUDC-907 in patients with relapsed or refractory lymphoma or multiple myeloma.

A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study of Brentuximab Vedotin and CHP (A+CHP) Versus CHOP in the Frontline Treatment of Patients with CD30-positive Mature T-cell Lymphomas

IRB # 13-055, PI: Steven Horwitz

A phase III study of brentuximab vedotin plus CHP versus CHOP therapy for patients with previously untreated CD30-positive peripheral T-Cell lymphoma.

Brentuximab Vedotin (SGN-35) in Transplant Eligible Patients With Relapsed or Refractory Hodgkin Lymphoma

IRB # 11-142, PI: Alison Moskowitz

Brentuximab (SGN-35) in transplant-eligible patients with relapsed or refractory Hodgkin lymphoma.

A Randomized, Double-blind, Placebo-controlled Phase 3 Study of the Bruton's Tyrosine Kinase (BTK) Inhibitor, PCI-32765 (Ibrutinib), in Combination with Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (R-CHOP) in Subjects With Newly Diagnosed Non-Germinal Center B-Cell Subtype of Diffuse Large B-Cell Lymphoma

IRB # 13-146, PI: Anas Younes

A phase III study of Ibrutinib (PCI-32765) plus R-CHOP chemotherapy in patients newly diagnosed with diffuse large B-Cell lymphoma (DLBCL).

A Phase 1 Study of CPI-0610, a Small Molecule Inhibitor of BET Proteins, in Patients with Progressive Lymphoma

IRB # 13-259; PI: Anas Younes

A phase I study evaluating CPI-0610 in patients with progressive lymphoma.

A Phase Ib Multi-Cohort Trial of MK-3475 in Subjects with Hematologic Malignancies

IRB #: 13-220, PI: Craig Moskowitz

A trial of MK-3475 in participants with blood cancers (MK-3475-013).

HEMATOLOGY

A Randomized Open Label Phase II Study of Romiplostim Versus Observation for Chemotherapy Induced Thrombocytopenia

IRB # 13-132, PI: Gerald Soff

Rivaroxaban (Xarelto ®) for Cancer-Associated Venous Thromboembolic Disease: Investigator Initiated Quality Improvement Initiative

IRB # , PI:

MYELOMA

A Randomized Phase III Study Comparing Conventional Dose Treatment Using a Combination of Lenalidomide, Bortezomib and Dexamethasone (RVD) to High-Dose Treatment with Peripheral Stem Cell Transplant in the Initial Management of Myeloma in Patients Up to 65 Years of Age

IRB # 12-018, PI: Hani Hassoun

Timing of high dose therapy for myeloma patients is a major question with the advent of more effective therapies. Should ALL patients receive high dose chemotherapy and autologous stem cell transplant as part of their initial therapy or should this procedure can be delayed and utilized only in those patients in which initial chemo did not work. MSK is a major participant in the DETERMINATION Trial which is being run by the ALLIANCE and the Blood and Marrow Transplant Clinical Trials Network and aims to answer that question.

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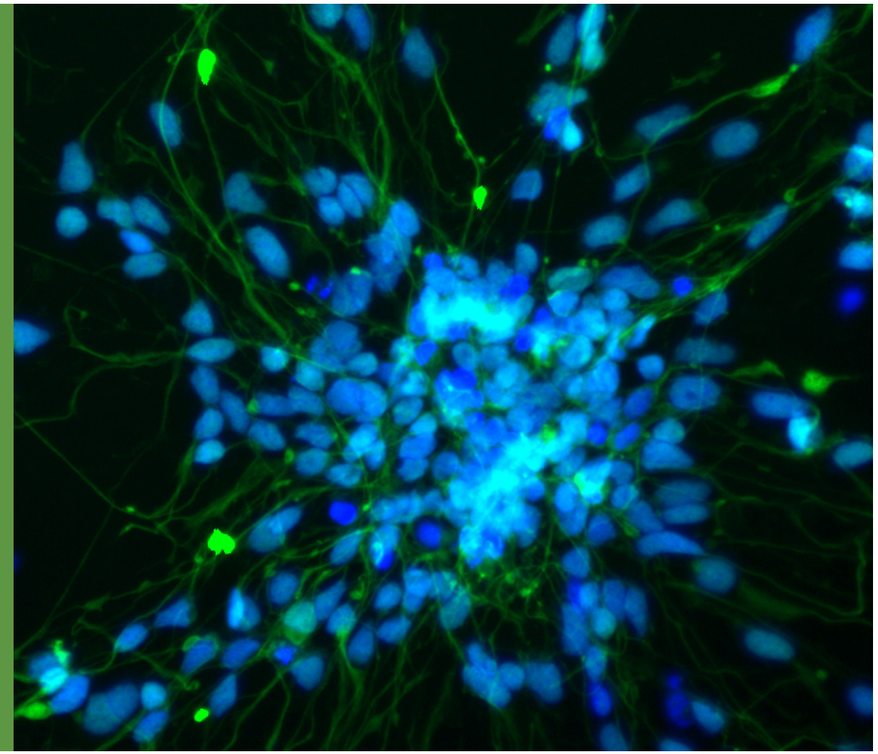
Neural cells derived from induced pluripotent stem cells expressing SP5 (green) with nuclear counterstain (blue). Mark Tomishima, SKI Stem Cell Research Facility.



Special thanks to Mark Tomishima, PhD, Associate Laboratory Member, SKI Stem Cell Research Facility Manager for his contribution of the scientific images used throughout the Division of Hematologic Oncology's 2013 Annual Report.

Architectural rendering of MSK's 74th Street building, the future home of our Division.

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