

Hematologic Oncology

2012 ANNUAL REPORT



Memorial Sloan-Kettering
Cancer Center

Contents

Letter from the Division Head	1	Events	
Hematologic Oncology Team	2	American Society of Hematology Annual Meeting.	11
Patient Care		The Mortimer J. Lacher Fellows Conference.	11
Making Cell-Based Therapies Safer and More Effective	4	Hematologic Oncology Nurses Represent MSK at National Meetings.	12
Five Facts about Stem Cell Transplantation and How to Become a Donor	5	Stem Cell Transplant Survivors Celebration	12
Patient Story: A Team Approach to Tackling a Rare Cancer	6	Appointments and Promotions	13
Overview of Centers and Programs.	7	Clinical Training and Education	14
Expanding Our Program.	7	Fundraising	
Interview with Martin S. Tallman	8	Swim Across America.	15
Research		Stand Up to Cancer Dream Team.	15
Investigators Discover Why Some Leukemia Drugs Are Not Sufficiently Effective	9	Fred's Team	16
Helping the Thymus Bounce Back	10	Cycle for Survival	16
		Publications	17
		Philanthropic Donors	19
		You Can Help	19

ON THE COVER

[LEFT] DR. REKHA PARAMESWARAN, MD
ASSOCIATE ATTENDING, HEMATOLOGY SERVICE

[RIGHT] DR. ROSS LEVINE, MD
ASSOCIATE ATTENDING, LEUKEMIA SERVICE





Letter from the Division Head

The Division of Hematologic Oncology is one of the largest programs in the United States dedicated to caring for people with hematologic cancers. We are also home to the nation's largest fellowship program for Medical Hematology/Oncology. In 2012, we expanded our clinical program (Table I). We recruited three new faculty members and established a new service devoted to Multiple Myeloma. Our clinical research continues to grow and our outstanding laboratory-based research has resulted in novel approaches, including an improved classification of Acute Myeloid Leukemia and a breakthrough therapy with genetically modified T cells for Acute Lymphoblastic Leukemia. In this Annual Report, we have highlighted a few of our accomplishments.

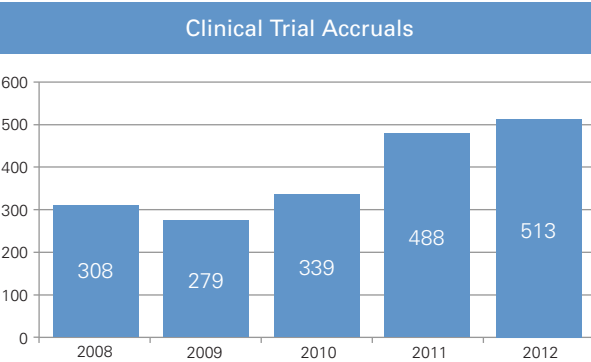


Marcel R.M. van den Brink, MD, PhD
 Alan Houghton Chair in Immunology
 Head, Division of Hematologic Oncology

2012 Hematologic Oncology Facts and Figures

	New Visits/ Initial Encounters	Follow-Ups	Total
Outpatient	3,923	35,662	39,585
Inpatient	1,957	31,300	33,257

Adult Bone Marrow Transplants	
Allogeneic	157
Autologous	243
Total	400



Hematologic Oncology Team

ADULT BONE MARROW TRANSPLANTATION



Juliet Barker



Hugo Castro-Malaspina



David Chung



Parastoo Dahi*



Sergio Giralt



Jenna Goldberg



Alan Hanash



Katharine Hsu



Ann Jakubowski



Robert Jenq



Guenther Koehne



Heather Landau



Esperanza Papadopoulos



Miguel Perales

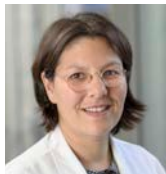
HEMATOLOGY



Doris Ponce



Craig Sauter



Roni Tamari*



Marcel van den Brink



James Young



Simon Mantha



Rekha Parameswaran

LEUKEMIA



Lilian Reich



Gerald Soff



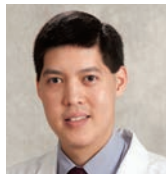
Omar Abdel-Wahab



Ellin Berman



Renier Brentjens



Stephen Chung



Bayard Clarkson



Marco Davila



Dan Douer



Faye Feller*



Virginia Klimek



Ross Levine



Peter Maslak



Michael Mauro*



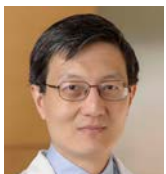
Jae Park



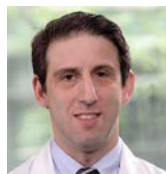
Raajit Rampal*



David Scheinberg



Alan Shih*

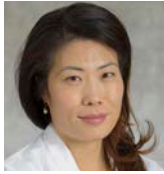


Eytan Stein*



Martin Tallman

LYMPHOMA



Helen
Chung



John
Gerecitano



Paul
Hamlin



Steven
Horwitz



Matthew
Matasar



Alison
Moskowitz



Craig
Moskowitz



Ariela
Noy



Lia
Palomba



Carol
Portlock



David
Straus



Andrew
Zelenetz

MYELOMA



Anas
Younes*



Hani
Hassoun



Nikoleta
Lendvai



Alexander
Lesokhin

REGIONAL NETWORK



Philip C.
Caron



Pamela R.
Drullinsky



Audrey M.
Hamilton

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

* Joined faculty in 2013

Making Cell-Based Therapies Safer and More Effective

Cell-based therapies are highly personalized approaches which harness the power of each patient’s immune system to attack and kill cancer cells. As targeted as they are, however, they may also cause side effects by harming normal cells. Memorial Sloan Kettering investigators developed a new technique to generate more specific cell-based immune therapies for cancer that may be safer and more effective.

Cell-based therapies make use of patients’ own immune cells that have been enhanced in the laboratory. They have shown early success for treating blood cancers, including certain types of leukemia. One challenge, however, has remained: It has been difficult for investigators to train immune cells to attack cancer cells without damaging normal, healthy cells in the body with some of the same features. “We are getting better at working with patients’ immune cells and enhancing them to achieve a powerful immunological response against cancer,” says Michel Sadelain, Director of Memorial Sloan Kettering’s Center for Cell Engineering, who led the research. “Our goal now is to avoid potentially harmful side effects.”

Investigators use adoptive cell transfer (ACT) to engineer white blood cells, called T cells, to recognize a certain antigen on the surface of a cancer cell and mount an immune response. These T cells are removed from the patient; a gene is added in the laboratory to allow them to recognize the antigen; the modified T cells are grown



DR. MICHEL SADELAIN AND DR. RENIER BRENTJENS

in the laboratory; and then the enhanced T cells are given back to the patient to seek out and attack cancer cells.

Cancer cells overproduce certain antigens, which can help T cells to recognize them, but those same antigens are often found in lower levels on healthy cells. “There are very few antigens, if any, that are found only on cancer cells,” Dr. Sadelain explains. “This means that T cells engineered to recognize a certain antigen could attack normal cells that have that same antigen as well.”

Through the latest approach, scientists at MSK have learned to modify a patient’s T cells to recognize two antigens. “We can create T cells that recognize two different antigens found on the tumor cell — a signature unique to that type of cancer — and only attack cells with both antigens, sparing the normal cells that express either antigen alone,” Dr. Sadelain adds.

The new technique makes use of two kinds of receptors: chimeric antigen receptors (CARs), which allow T cells to target antigens on the surface of a tumor cell, and chimeric costimulatory receptors (CCRs), which allow T cells to recognize a second antigen. CAR and CCR work together through a process known as “balanced signaling,” in which the presence of either antigen on its own is not enough to trigger the immune response. As a result, only tumor cells that carry both antigens will be targeted.

New Hope for a Challenging Leukemia

Researchers on the Leukemia Service, led by Renier Brentjens and Marco Davila, reported in *Science Translational Medicine* the first results of a cell-based therapy evaluated in a clinical trial of adults with relapsed B-cell acute lymphoblastic leukemia (B-ALL), a disease that carries a dismal prognosis. Using a disabled virus, the scientists introduced new genetic material into T cells removed from the patients, reprogramming them to recognize and destroy cells expressing the CD19 protein on B-ALL cells. Remarkably, all five patients described in the report achieved a remission, with no molecular evidence of leukemia. Four of the patients were then able to go on to a potentially curative bone marrow transplant. The Leukemia Service is continuing to enroll patients from around the country in this groundbreaking clinical trial.

In a study published online December 16, 2012 in *Nature Biotechnology*, the team reported creating T cells that carried receptors for two antigens in prostate cancer cells: a CAR for an antigen called PSMA and a CCR for an antigen called PSCA. The investigators then generated mouse models of prostate cancer and infused the mice with the engineered cells. They found that the T cells attacked only tumors that carried both antigens.

“We are the first to evaluate this concept and show that it works,” Dr. Sadelain concludes. “We plan to develop clinical trials based on this approach. Ultimately, our goal is to create targeted immunotherapies that are both potent and safe for patients.”

Five Facts about Stem Cell Transplantation And How to Become a Donor

Over the course of three decades, Memorial Sloan Kettering physicians have performed more than 4,000 bone marrow transplants — nearly 400 annually in recent years.

In 1973, Memorial Sloan Kettering doctors performed the world's first successful transplant between a patient and an unrelated donor. Many of the transplant and supportive care approaches widely used today were pioneered at Memorial Sloan Kettering.

This procedure, also known as a stem cell transplant, is used to replenish bone marrow and hematopoietic stem cells destroyed due to a variety of reasons, such as certain types of cancer, cancer treatments, blood diseases, or immune disorders. Hematopoietic, or blood-forming, stem cells are produced in the bone marrow. Here are some key facts about stem cell transplantation:

There are two types: autologous and allogeneic. In an autologous transplant, a patient's own stem cells are collected and then transplanted back. In an allogeneic transplant, the stem cells are obtained from another person or from donated umbilical cord blood and then given to the patient.

In both cases, the patient receives high doses of chemotherapy or a combination of chemotherapy and radiation therapy to kill any cancerous cells and hematopoietic



DR. SERGIO GIRALT, DR. MARCEL VAN DEN BRINK, DR. JULIET BARKER, DR. GUENTHER KOEHNE

stem cells in their bone marrow. Healthy blood stem cells are then transplanted into the bloodstream through an intravenous catheter, in a process similar to a blood transfusion. The stem cells travel to the bone marrow to develop into new blood cells.

Recipients must be carefully selected. Transplantation can be extremely challenging for a patient and his or her family. The high-dose regimens used before the transplant are toxic, and the patient's immune system must be suppressed for an extended period of time after the procedure to prevent a rejection of the transplanted cells. So doctors take meticulous steps to determine if a patient is a candidate for transplantation.

During recovery, great care is taken to prevent complications. Most patients remain in the hospital for several weeks to receive medical support. To protect against infection, everyone who enters the patient's room must wear gloves, masks, and sometimes disposable gowns, and wash their hands with antiseptic soap. The first year after the transplant is critically important because it's the period when complications — such as infection or rejection — are most likely to develop. Patients are typically able to get back to their regular activities after a year,

with a lower risk of developing an infection.

Stem cell transplants can be curative. Despite the risks, outcomes have dramatically improved over the past decades, and stem cell transplants can often cure a person's disease. A recent study conducted by the National Marrow Donor Program found that 75 percent of patients undergoing allogeneic transplantation at MSK survived through the first year, exceeding the predicted rate of 62 percent.

What are the reasons for this success? Because patients are at such a high risk of infection, we use very sensitive tests to detect viral infections early. Richard O'Reilly, Chief of Memorial Sloan Kettering's Pediatric Bone Marrow Transplant Service, has pioneered research that uses donor-specific immune-fighting cells against viruses. This is a new way of treating viral infections in patients who are severely immune-compromised. We've also pioneered an approach called T-cell depletion therapy, a powerful way of preventing graft-versus-host disease (GVHD). We know that T cells, a type of white blood cell in the donor graft, can cause GVHD. By removing those T cells from the donor's cells before a patient receives the transplant, we can significantly reduce the risk of GVHD.

Donors must be carefully selected. Finding an appropriate donor is critical to the success of an allogeneic transplant.

More information:

National Marrow Donor Program and the "Be The Match" Registry (bethematch.org)
Delete Blood Cancer DKMS (<http://www.deletebloodcancer.org>)

Because the immune system can identify and destroy any cells perceived as foreign, a donor's tissue type should match the patient's as closely as possible. The process of tissue typing is based on analyzing proteins called human leukocyte antigens (HLA), which are found on the surfaces of white blood cells and tissues.

We work closely with our patients to find a bone marrow match. The ideal donor is often a sibling who has inherited the same HLA. Most patients do not have a brother or sister who is a match, so we look for other family members who may be a partial match. Because family size is getting smaller in North America, however, it is becoming more challenging to find appropriate family member donors, and we need to expand our search to volunteer donor registries, such as the National Marrow Donor Program.

In some cases, we consider using umbilical cord blood stored in public banks, such as through the National Cord Blood Program. Juliet Barker, a cord blood transplantation expert at MSK, has developed a number of new approaches. Through clinical trials, we can often offer unique stem cell transplantation techniques for patients who do not have a donor in their family or in volunteer registries.

You can register to become a donor. Everyone who is medically able should consider becoming part of a marrow registry. It can be especially difficult to find stem cells from people of mixed ethnic or minority backgrounds through these registries, so we encourage more people to consider becoming a donor. You can join the Be The Match Registry or Delete Blood Cancer DKMS. Learn more about who can donate, donor requirements, and medical guidelines from the National Marrow Donor Program.

PATIENT CARE

A Team Approach to Tackling a Rare Cancer: A Patient Story

When John* was diagnosed with upper tract urothelial carcinoma, a rare form of bladder cancer that grows in the kidney, it was immediately clear that the 71-year-old faced a daunting set of obstacles.

Not only had the aggressive malignancy already spread to a lymph node, but it was too large to remove surgically. Moreover, the chemotherapy that might shrink his tumor was off-limits to John because of a prior condition causing low platelets. These seemingly intractable roadblocks, however, became puzzle pieces smartly coordinated in tandem among leaders from three departments at Memorial Sloan Kettering. John's cancer was successfully treated, enabling him to resume a high-profile career. "No single doctor, no matter how great, could have solved this problem," says Gerald Soff, Chief of the Hematology Service. "Memorial Sloan Kettering has that power, that team approach that is lacking in so many other places."

Dr. Soff's expertise was instrumental in significantly boosting John's platelets so he could receive chemotherapy. Dr. Soff was pleased and relieved to find that the platelet-producing drug romiplostim (Nplate®) quickly raised John's platelet counts to the normal range. "Nplate isn't indicated for John's type of low platelet count and has never been used to prop up platelet counts to give chemotherapy, so that's really novel," explains medical oncologist Dean Bajorin, who specializes in genitourinary tumors and also collaborated on John's care.

Dr. Bajorin oversaw John's chemotherapy treatments for several months. A two-drug regimen normally used for ovarian cancer was chosen for its kidney- and platelet-protecting properties, as well



DR. GERALD SOFF

as its effectiveness against urothelial malignancies. The chemotherapy shrank John's tumor to half its original size and caused few side effects aside from fatigue. "The chemotherapy regimen reduced John's disease sufficiently so we could do the operation and leave him in good condition for surgery," Dr. Bajorin recalls. "He just sailed through."

The surgery itself, performed in July 2012 by urologic surgeon Jonathan Coleman, was done robotically through three incisions in John's back, removing his left kidney and ureter as well as lymph nodes from the area. Within a few days of the operation, John suffered a common complication known as a lymphatic leak, which required inserting drains to empty extra fluid from the site. "When a patient requires multiple therapies, the risks for complications are higher," Dr. Coleman says. "This case really demonstrates Memorial Sloan Kettering at its best, with open communication from every member of the team."

John's case has led to other ambitious efforts to help more patients facing similar issues. Combining John's off-label success with Nplate with the experiences of about 50 other Memorial Sloan Kettering patients whose low platelet counts would ordinarily prevent chemotherapy, Dr. Soff plans to lead a larger clinical research effort based on the results. "We're a world leader in developing this therapeutic approach," Dr. Soff says. "So far, more than 90 percent of the patients we've managed have had their platelet counts improve sufficiently to allow for ongoing chemotherapy."

Concludes John, "There's no question that Memorial Sloan Kettering has the best people and was the best place to receive my care."

**Patient's full name is being withheld at his request to protect anonymity.*

Overview of Centers and Programs

LUCILLE CASTORI CENTER FOR MICROBES, INFLAMMATION, AND CANCER

The Lucille Castori Center for Microbes, Inflammation, and Cancer, directed by Eric Pamer, was created to shed light on the role that microbes and the body's inflammatory and immunological responses to them play in the development of cancer. It unites researchers from a range of specialties to develop technologies to examine the causes of infections in patients, characterize infections associated with cancer treatment and hospitalization, study how inflammation can promote the development of cancer, and study the relationships between specific microbes and the development or progression of cancer.

With support from the Castori Center, members of the Division are studying how bone marrow transplantation can affect the makeup of the intestinal microbiota (the ecosystem of microorganisms that live in the intestine). By studying mouse models in the laboratory as well as patients in clinic, the investigators found strong evidence that graft-versus-host disease can have a significant impact on the composition of intestinal bacteria. They have also found evidence that the risk for developing graft-versus-host disease can be reduced by targeting intestinal bacteria.

THE SUSAN AND PETER SOLOMON DIVISIONAL GENOMICS PROGRAM

Through the support of the Peter J. 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. This testing platform allows for rapid, cost-effective mutational studies for Memorial Sloan-Kettering patients with acute myeloid leukemia (AML), myelodysplastic syndromes, and myeloproliferative neoplasms.

This program has helped us to perform detailed mutational analysis of the largest clinical trial group of patients with AML, allowing us to define a mutational signature associated with high risk of relapse. Being able to recognize this signature enables us to identify patients who need more aggressive therapies or who may benefit from clinical trials of investigational agents.

CENTER FOR STEM CELL BIOLOGY

The Center for Stem Cell Biology was established in 2010 to serve as a hub for existing stem cell efforts at MSKCC, support recruitment of stem cell faculty, and provide resources for stem cell research such as core facilities and training programs. MSKCC has been at the forefront of various aspects of stem cells in the treatment of hematopoietic malignancies, the use of umbilical cord blood as a source of stem cells suitable for transplantation, and the isolation of embryonic and adult stem cells.

CORD BLOOD TRANSPLANTATION PROGRAM

MSKCC has one of the leading programs

for the transplantation of cord blood in patients with hematologic malignancies. Cord blood is collected from the umbilical cords and placentas of healthy newborn babies and held in public banks. It contains blood-forming stem cells that have unique properties that are helpful for rebuilding a healthy blood and immune system. These transplants are a growing alternative for people who are unable to find traditional matches, but are still relatively uncommon. MSKCC has been a leading research center in establishing new protocols that make use of this technique.

A team led by Juliet N. Barker, head of the Cord Blood Transplantation Program, has proven that cord blood transplantation can extend transplant access to patients from racial and ethnic minorities who lack other suitable donors. Cord blood transplantation yields survival rates comparable to those of transplantation using adult donors.

TRI STATE TRANSPLANT CONSORTIUM

The Tri-State Transplant Consortium was initiated by Sergio Giralt and includes members of stem cell transplant programs in New York, New Jersey, and Connecticut. The consortium's mission is to collaborate in the design, implementation, and analysis of clinical trials addressing important issues in hematopoietic stem cell transplantation as it relates to patients and the institutions that deliver these therapies to them. The group has one active clinical trial; other research activities include correlative research and retrospective study analysis.

Expanding Our Program

NEW MYELOMA SERVICE ESTABLISHED

In 2012, the Myeloma Service was officially established as a distinct service in the Division of Hematologic Oncology, under the leadership of Sergio Giralt, an expert in the use of stem cell transplantation for

multiple myeloma and other hematologic malignancies. The team includes four transplant physicians and three non-transplant physicians focused on the care of patients with multiple myeloma. They collaborate with a team of nurses, pharmacists, social workers, and support

staff to provide optimal care for patients. Together with a multidisciplinary group of radiology, pathology, renal, rehabilitation, radiation oncology, and neuroradiology specialists, the staff forms a core group of physicians involved in all aspects of care for

CONTINUED ON PAGE 8

myeloma patients.

Under Dr. Giralt's leadership, the service has significantly expanded its portfolio of clinical trials. The service has special expertise in the application of immune-based therapies, including immunomodulatory antibodies, vaccines, and T-cell therapies. The ultimate goal is to be able to offer a clinical trial for every stage of malignant disease of plasma cell origin.

HEMATOLOGIC ONCOLOGY EXPANDS AT NETWORK SITES

The Division of Hematologic Oncology further strengthened its relationship with

the Division of Network Medicine Services in 2012 by expanding its presence at the regional care network sites. MSK programs in Basking Ridge, New Jersey; Commack and Rockville Centre, on Long Island; and Sleepy Hollow, in Westchester County, New York, now each include a physician who is a member of the Division of Hematologic Oncology. These talented faculty members focus on patients with hematologic malignancies and assure a uniform approach to the care of patients with these cancers across MSK.

An expanding list of clinical trials for patients with hematologic malignancies is available within the network. Patients seen

at these sites are increasingly identified as candidates for the Division's research programs which require the resources of MSK's Manhattan facilities. A bi-weekly interactive videoconference for network-based hematologic oncologists has been extremely successful as a venue for case presentations, the exchange of the latest research data, and the development of protocols. Lead by the Division's Manhattan-based faculty, this videoconference helps to link patients who have hematologic malignancies with Memorial Sloan Kettering's expertise and developing research programs, regardless of where they seek MSK's renowned care.

INTERVIEW

Martin S. Tallman

Meet Martin S. Tallman, an internationally recognized expert who has been at the forefront of several key clinical trials that have led to new standards of care for patients with acute and chronic leukemias. He came to Memorial Sloan Kettering in 2010 to become Chief of the Leukemia Service in the Department of Medicine, following a 21-year career at Northwestern University.

As Chief of the Leukemia Service, what priorities have guided your leadership?

I had a specific vision of what I thought it would take to develop the finest leukemia service in the world. Recruitment has been one of my top priorities, and we have added nine junior and senior faculty members since 2010. Adding more clinical trials was

my second priority. There has never been such an explosion in our understanding of the pathogenesis of both acute and chronic leukemia, the number of novel agents with unique mechanisms of action, and other new strategies, including immunologic approaches.

A third priority was to foster interactions between laboratory scientists and clinical investigators. I thought that if we could accomplish these goals, we would further distinguish this already very prestigious institution and make important contributions.

How do you hope to build on Memorial Sloan Kettering's rich history of developing effective leukemia therapies?

Since 2010, we have opened many clinical trials — all with important correlative laboratory science studies. The number of exciting new targeted molecules and therapies now available is unprecedented. I have wanted to see our laboratory efforts increase to learn more about how these therapies work and to see them applied in well-designed, meaningful clinical trials. I think that's the responsibility of our institution — not just to deliver pristine patient care, which we do, but also to develop new treatments which change the standards of care and



improve the lives of patients.

There has been an explosion of knowledge addressing the molecular genetics of acute and chronic leukemias. How is this area progressing, and how is it impacting patient care?

Our group has been at the forefront of identifying what has become so important now, which are the genetic abnormalities in a given leukemia cell and the relationship of the various genetic abnormalities to each other. It has begun to influence our treatment decisions. For example, physician-scientists Ross Levine, Omar Abdel-Wahab, and their colleagues identified gene mutations in acute myeloid leukemia, or AML, and demonstrated the importance of the interactions of these genes in a large group of patients.

It was extremely important because certain gene relationships confer a very favorable prognosis — meaning we can decrease the intensity of a patient's treatment and avoid unnecessary treatment — while others are associated with an unfavorable prognosis, indicating we should use new and hopefully more effective strategies. Other investigators here are working to harness the ability of T cells to eradicate leukemia, and have shown very encouraging results in patients with acute lymphoblastic leukemia.

What are the biggest challenges remaining in leukemia research?

The real challenge for the future is to develop a nimble infrastructure for the development and activation of clinical trials to evaluate new agents and other therapeutic strategies. It is a challenge to make important trials attractive and easier to conduct for patients and their treating physicians. While we still need more insight into what drives a leukemia cell and what turns a benign cell into a malignant one, a number of the major challenges aren't so much scientific as logistical.

What philosophy guides your care of patients?

I've long said that I like to imagine that every patient is a member of my own family and to treat them accordingly. You find yourself thinking, if this were my spouse or my brother or my child, would I really recommend a given therapy? The patient may not respond to a certain treatment, but no healthcare professional makes anything but the best decisions for his or her own family. This way of thinking connects a doctor to a patient.

What treatment advance drives home the improvement in treating leukemias today compared to just a decade or two ago?

Acute promyelocytic leukemia has emerged as the most highly curable subtype of AML. It's very exciting — we can now cure about 85 to 90 percent of all patients. Historically, we have treated patients with this subtype of AML as we have all others, with induction chemotherapy and consolidation chemotherapy. Two decades ago, we began treating all patients with a vitamin A derivative called ATRA (all-trans-retinoic acid) plus chemotherapy. In the last decade, we've also witnessed the development of a new formulation of the old drug arsenic trioxide. New studies show that treating patients with ATRA and arsenic trioxide,

with minimal to no chemotherapy, has produced spectacular results. The cure rate is high, and we can also spare the patient from the side effects of chemotherapy.

What do you hope to accomplish next?

My broad goals are to recruit more patients to well-designed clinical trials and to continue to link clinical trials with important correlative studies in the laboratory to elucidate the mechanisms by which effective treatments work. I sincerely hope that soon almost every patient will be on a clinical trial, and that we will be treating very few patients off-study.

Ultimately, we want to change the standard of care and to contribute to the cure of more patients with leukemia. We have initiated efforts to move consolidation therapy in AML completely to the outpatient setting. Furthermore, given the new, more potent antibiotics available, growth factor support, and comprehensive home care, we are developing a protocol to move induction therapy after initial chemotherapy to the outpatient setting. We've made tremendous progress treating several subtypes of leukemia, but for most patients with acute myeloid leukemia and acute lymphoblastic leukemia, we still have much work left to do.

RESEARCH

Investigators Discover Why Some Leukemia Drugs Are Not Sufficiently Effective

Memorial Sloan Kettering researchers have discovered why a class of drugs called JAK2 inhibitors has not been sufficiently effective for treating blood cancers known as myeloproliferative neoplasms (MPNs).

They showed that these drugs could successfully treat such blood diseases if they are combined with a different type of therapy. The findings, reported in the September 6, 2012 issue of *Nature* by medical oncologist Ross Levine and his colleagues, are guiding researchers as they plan clinical trials to improve therapies for patients with these types of leukemias, which affect more than 200,000 people at any given time in the United States.

MPNs are diseases in which several types

of blood cells are excessively produced by the bone marrow. Earlier research by Dr. Levine and others found that cancer cells in many people with MPNs have a mutation in a gene called JAK2, which governs the production of the JAK2 kinase — a protein that helps regulate a number of basic cell functions.

Identifying the JAK2 mutation offered a potential target for therapeutic drugs. However, clinical trials assessing therapies that inhibit the mutated form of JAK2 have

CONTINUED ON PAGE 10

been less successful in patients than targeted therapies for other blood cancers — most notably imatinib (Gleevec®), which is very effective against a blood cancer called chronic myelogenous leukemia. Although disease-related symptoms are alleviated — for example, swollen spleens get smaller and patients report feeling better — cancerous cells remain in the blood.

“It isn’t a case of patients becoming resistant to the drug over time. There is a lack of a response from the beginning,” Dr. Levine says. “Something is allowing the cancer cells to endure despite ongoing treatment. It’s a case of persistence rather than resistance.”

In the *Nature* study, he and his team discovered that the cancer cells can use other means of maintaining the function of the mutated JAK2 kinase, even when the cells are exposed to JAK2 inhibitors. When the mutated JAK2 protein comes into contact with an inhibitor, the protein enters an altered state that allows it to remain activated by other JAK kinases. “Exposure to the JAK2 inhibitor causes mutated JAK2 to rely on this alternative activation mechanism to avoid the drug’s effects and stay active, enabling cancer cells to continue to live and proliferate,” Dr. Levine explains. “The cancer cell’s persistent reliance on JAK2, however, tells us that it is still the best target. We just need to find a better way to inhibit it.”

He and his colleagues previously showed that the JAK2 protein could be targeted indirectly by inhibiting another protein, HSP90, which helps keep JAK2 stable. When HSP90 is inactivated, JAK2 becomes degraded inside the cell. In the new study, the researchers reported that combining HSP90 inhibitors with JAK2 inhibitors can kill MPN cells in the laboratory.

“Understanding why the disease persists provides a potential new avenue to achieve better responses,” Dr. Levine concludes. “New therapies are in late-stage preclinical testing, and we hope to move into the clinic soon. This approach could have a significant impact on these diseases.”

Helping the Thymus Bounce Back

T lymphocytes are white blood cells that play an important role in arming the immune system against pathogens (such as viruses) and cancer. The thymus is a fundamental immune organ responsible for generating and selecting the diverse array of T cells needed for an effective immune response against invaders.

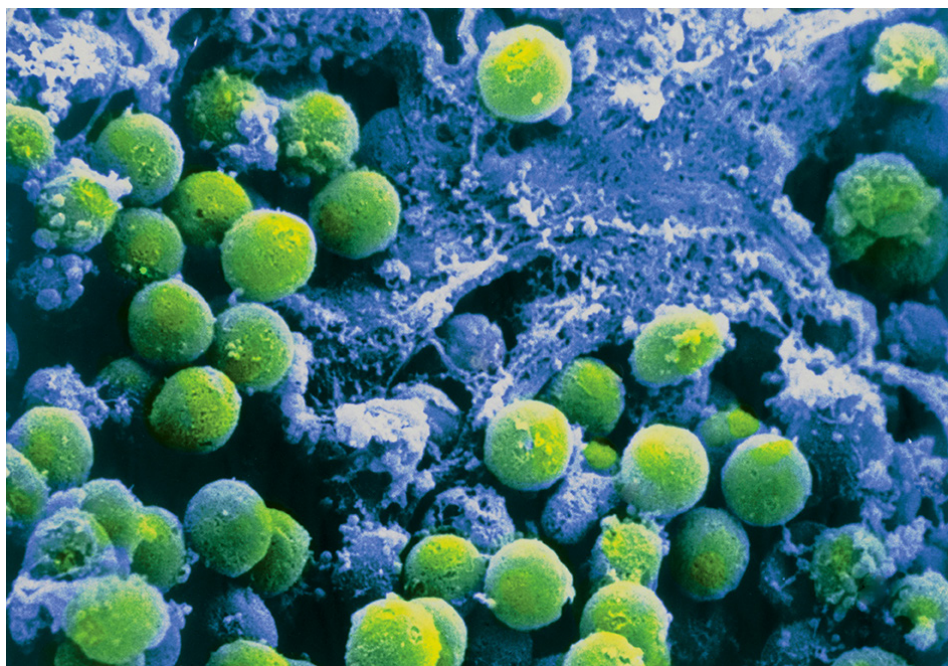
Despite being exquisitely sensitive to injury, the thymus is remarkably resilient in young healthy animals. However, in many patients, the ability of the thymus to recover after injury or insult is poor, due to age, chronic infection, or repeated treatments such as chemotherapy or radiation therapy.

Compromised thymus function can raise the risk of infections and cancer. Rapid regeneration of the immune system, particularly the thymus, and a better

understanding of how this process occurs could help clinicians overcome the clinical barriers to repairing the immune systems of patients with diminished immune function.

Little has been known, however, about how the thymus regenerates. Memorial Sloan Kettering investigators shed light on this process in a paper published in April 2012 in the journal *Science*, in which they identified a natural cellular network underlying how the thymus can repair itself following injury. In a study of mice, they described a framework of natural repair of the thymus which involves a population of cells called innate lymphoid cells, as well as a protein they produce called interleukin-22 (IL-22).

Most importantly, their findings demonstrated that IL-22 could potentially be used as a treatment to stimulate growth of the thymus after the immune system has been distressed. The findings offer hope for people with less robust immune systems, such as recipients of bone marrow transplants and individuals with T-cell deficiencies due to aging, autoimmune diseases, infectious disease (such as HIV/AIDS), shock, chemotherapy, and radiation exposure.



American Society of Hematology Annual Meeting

At the 2012 annual meeting of the American Society of Hematology in Atlanta, Georgia, our faculty was well represented with over 100 abstracts, 28 of which were selected for oral presentation.

The following are a few examples:

Dr. Robert Jenq presented research in mouse and man regarding the role of intestinal microbiota and graft-versus-host disease after allogeneic bone marrow transplantation. Dr. Craig Moskowitz presented a novel strategy for risk adapted therapy of advanced stage Diffuse Large B Cell Lymphoma using PET imaging. Dr. Steven Horwitz demonstrated the feasibility of the inclusion of a novel agent (Brentuximab Vedotin) as frontline therapy for T cell Lymphoma. Dr. Stephen Chung reported on a novel cell surface protein, CD99, which can be used for the detection of leukemic stem cells. Finally, Dr. Omar Abdel-Wahab demonstrated the importance of ASXL1 deletion in the pathogenesis of myelodysplastic syndrome.

Dr. Marcel van den Brink organized in collaboration with Dr. Ned Waller a winter workshop devoted to Hematopoietic Stem Cell Transplantation held at the Winship Cancer Institute of Emory University. This workshop consisted of short presentations regarding unpublished recent research and was attended by 131 physicians and scientists.

In addition, the MSKCC Alumni Society and the Division of Hematologic Oncology held its fifth annual reception at the Atlanta Marriott Marquis hotel, which was attended by MSKCC alumni, current faculty, fellows, and colleagues from other institutions as well as invited guests of the MSKCC Hematology department.



DR. GUENTHER KOEHNE, DANIELLE CHIMENTO (FORMER RSA),
ELEANOR TYLER

The Mortimer J. Lacher Fellows Conference



On May 18, 2012, the Division held its annual Mortimer J. Lacher Fellows Conference.

The event honors Dr. Lacher, a longtime member of MSK's Lymphoma Service and the Sloan-Kettering Institute. In 2012, the Third Annual Mortimer J. Lacher Lecture was given by Brian Druker, Director of the Oregon Health & Science University Knight Cancer Institute, JELD-WEN Chair of Leukemia Research at OHSU, and a Howard Hughes Medical Institute Investigator. Dr. Druker has won many awards (including the 2009 Lasker-DeBakey Clinical Medical Research Award) for his groundbreaking research which resulted in the development of imatinib as a treatment for patients with chronic myeloid leukemia.



DR. MATTHEW LUNNING

Five fellows presented their work at the 2012 Lacher Fellows Conference:

- Richard Bakst (mentor: Joachim Yahalom)
- Zachary Hector-Word (mentor: Paul Hamlin)
- Matthew Lunning (mentor: Steven Horwitz)
- Alan Shih (mentor: Ross Levine)
- Eytan Stein (mentor: Daniel Douer)

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 MSK's Department of Medicine, and delivered personal remarks at the conference after the fellows' presentations.

Hematologic Oncology Nurses Represent MSK at National Meetings

Nurses in the Division of Hematologic Oncology made presentations at several professional meetings around the country in 2012, including:

Oncology Nursing Society

- “The Oncology Nurse–Patient Relationship at the Center of Care: Implementation of Primary Nursing” — Mary Dowling, MSN, RN, CENP, OCN; Donna Miale-Mayer, MSN, RN; Diane Llerandi, MA, RN, AOCNS; Donna Braccia BSN, RN; Katherine Ruan, BSN, RN; Lauren Aho, BSN, RN
- “Getting A Head Start: Achieving Meaningful Use with Early Morning Labs at an Acute Care Oncology Setting” — Megan Leary, RN, BSN; Linda Ouyang RN, BSN; Jacqueline Patterson RN, BSN

2012 ASBMT conference

(poster presentations from M8 staff)

- “Expanding Beyond Our Borders : Creation of an Overflow Unit”
- “Collaborating with our Colleagues to Enhance Patient Care: A Multidisciplinary Workflow for Busulfan PK Serum Levels”
- “Just-In-Time Training for Travel Nurses: Unit-Specific Competency for Adult Inpatient Bone Marrow Transplant”

M8 staff members continue to share their nursing knowledge of the transplant process by mentoring staff from NewYork-Presbyterian Hospital. They continue to develop the staff’s knowledge of transplant nursing by presenting a two-day seminar called “Overview of Hematological Malignancies and Nursing Considerations,” a one-day seminar called “Bone Marrow

Transplant Specialty Day,” and a one-day seminar called “Hematopoietic Stem Cell Transplant for the Advanced Learner.”

ASBMT 2013 Tandem Meetings (poster presentations)

- “Implementation of FACT Guidelines Improves Donor Screening” — Bernadette Cuello, NP
- “Experience of Establishing a Post-Hematopoietic Stem Cell Transplant Immunization Clinic” — Jill Vanak, NP, and Melanie Bushnell, NP

Oncology Nursing Society 2

013 Annual Congress

- “Gene-Modified T-Cell Infusions for Chronic Lymphocytic Leukemia: Innovations in Outpatient Nursing Care Delivery” — Cheryl Caravano, RN (podium presentation)

Stem Cell Transplant Survivors Gather to Celebrate

More than 200 people who were treated for cancer or blood disorders with hematopoietic stem cell transplantation gathered in October 2012 with family, friends, and Memorial Sloan Kettering staff for MSK’s 17th annual Stem Cell Transplant Survivors Celebration.

The event drew a total of more than 600 guests and allowed Memorial Sloan Kettering stem cell transplant patients to meet one another and reunite with the doctors, nurses, and other staff who cared for them.

Sergio Giralt, Chief of the Adult Bone Marrow Transplant Service, extolled the gravity of celebrating lives saved with



DR. MIGUEL PERALES, DR. SERGIO GIRALT, DR. RICHARD O'REILLY

stem cell transplantation at Memorial Sloan Kettering. “Of all the things we do, this is one of the most beautiful events we have,” he said. “Every year, we get together to celebrate you fighting the battle and hopefully winning the war.” Two

patients and a caregiver also made brief remarks, praising the care they received at Memorial Sloan Kettering during treatment and recovery, and reflecting on how the experience had transformed their lives.

Appointments and Promotions



Scott Armstrong, MD, PhD
Department of Pediatrics and Human
Oncology and Pathogenesis Program
Grayer Family Chair

Scott Armstrong joined MSK in June 2012. He specializes in treating children and young adults with leukemia, and has a particular interest in developing new therapies that are less toxic and more effective.

A pediatric oncologist, Dr. Armstrong uses technologies to characterize the molecular pathways responsible for leukemia development, with a focus on the relationship between normal and leukemic stem cells. In particular, he has made major contributions to the understanding of the pathogenesis of a high-risk form of acute leukemia associated with a distinctive rearrangement of chromosomes that occurs in both children and adults. He has made major contributions to our understanding of how leukemia develops, and his landmark research findings have pointed to potential new leukemia therapies.

Dr. Armstrong earned his MD and PhD degrees from the University of Texas Southwestern Medical School. He completed an internship and residency at Boston Children's Hospital and a clinical fellowship at Dana-Farber Cancer Institute.



Stephen Chung, MD
Department of Medicine

Stephen Chung is a medical oncologist on the Leukemia Service who specializes in the care of patients with leukemia and bone marrow failure syndromes, including acute myeloid leukemia and myelodysplastic syndromes. In the laboratory, he studies molecular alterations in the hematopoietic (blood-forming) stem and progenitor cells that underlie the development of acute myeloid leukemia and myelodysplastic syndromes.

Dr. Chung received his MD degree from Washington School of Medicine in St. Louis. He completed his residency at Massachusetts General Hospital and a fellowship at MSK.



Alan Hanash, MD, PhD
Department of Medicine

Alan Hanash is a physician-scientist who joined the Bone Marrow Transplant Service and is an authority on allogeneic bone marrow transplantation, hematologic malignancies, and graft-versus-host disease (GVHD, a potential complication of transplantation in which cells from the donor attack tissues of the recipient). In his research, he is seeking to cure more cancer and prevent disease relapse by improving transplantation through the use of experimental models.

Dr. Hanash received his MD and PhD degrees from the University of Miami Medical School. He completed his residency training at the University of Chicago Medical Center and a fellowship at MSK.



Simon Mantha, MD
Department of Medicine

Simon Mantha is a hematologist with expertise in vascular medicine whose clinical practice encompasses the whole spectrum of benign blood conditions, including bleeding disorders and anemias. His research interests include venous thromboembolic disease and new anticoagulants, with a focus on the study of cancer-associated thrombosis.

Dr. Mantha received his MD degree from the Faculté de Médecine de l'Université Laval, in Quebec City, and an MPH degree from Harvard School of Public Health. He did his fellowship training at the Université Laval Hospital Network and then completed fellowships at NewYork-Presbyterian/Columbia University Medical Center and Yale-New Haven Hospital.



Raajit Rampal, MD, PhD
Department of Medicine

Raajit Rampal is a hematology-oncology physician who specializes in the treatment of leukemia and myeloproliferative diseases (MPDs). He is also an active researcher seeking to develop innovative approaches to treating MPDs and leukemia. He is working to understand the genetic events that contribute to the development and progression of leukemia and MPDs, with the hope of designing new targeted therapies for patients with these diseases.

Dr. Rampal earned his MD degree and a PhD in Molecular and Cellular Biology from Stony Brook University. He completed his residency training at University of Chicago Hospitals and a fellowship at MSK.

PROMOTIONS



Omar Abdel-Wahab, MD
Appointed Assistant Attending
in 2012



Robert Jenq, MD
Appointed Assistant Attending
in 2012

Programs Train the Leaders of the Future

Memorial Sloan Kettering attracts applicants from all over the world for two distinguished fellowship programs 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 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 ONCOLOGIST DEAN BAJORIN CONSULTS WITH MEDICAL ONCOLOGY/HEMATOLOGY FELLOW JEAN LEE.

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>.

Fundraising

The Division of Hematologic Oncology is grateful to the many supporters of our efforts. Our own staff members have also stepped up on multiple occasions to swim, cycle, and run to raise vital funds for our research and patient care programs. Here is a sample of those initiatives.

ADULT BONE MARROW TRANSPLANTATION PROGRAM BENEFITS FROM SWIMMERS' EFFORTS

A team of swimmers including James Young, Associate Chair of the Department of Medicine and a physician on the Bone Marrow Transplant Service, three bone marrow transplant survivors, and two of their spouses, have participated regularly in Swim Across America to support MSK's Adult Bone Marrow Transplantation Program. Team Transplant raised \$35,000 in 2012 and over \$27,000 more in 2013, braving the waters of Long Island Sound to complete a 1.25-mile swim.

Dr. Young, an avid distance swimmer, has been participating in the event since 2006. Another distance swimmer, who had recovered from an allogeneic transplant for acute leukemia, proposed starting a Swim Across America team in 2009. The team has since raised more than \$100,000 to support research efforts at MSK that ensure the successful use of transplantation to cure patients with leukemia, lymphoma, multiple myeloma, and other

cancers of the blood and bone marrow.

Swim Across America is dedicated to raising money and awareness for cancer research, prevention, and treatment through swimming. Memorial Sloan Kettering has been one of its major beneficiaries.

MEMORIAL SLOAN KETTERING RESEARCHERS APPOINTED TO STAND UP TO CANCER IMMUNOLOGY "DREAM TEAM"

Michel Sadelain, Director of the Center for Cell Engineering, and Jedd Wolchok, Director of Immunotherapy Trial Development and Monitoring for Memorial Sloan Kettering's Ludwig Center for Cancer Immunotherapy, were appointed to a new Stand Up To Cancer (SU2C) "Dream Team" dedicated to immunotherapy research. Immunotherapy treatments harness the body's own immune system to attack cancer.

The new Dream Team is being funded jointly by SU2C, a nonprofit program that raises funds to accelerate the pace of translational research, and the Cancer Research Institute (CRI), a nonprofit that provides funding for cancer immunology research at every stage of discovery. The joint project, known as "Immunologic Checkpoint Blockade and Adoptive Cell Transfer in Cancer Therapy," provides up to \$10 million during a three-year period.

The Immunology Dream Team will pursue the study of two research techniques.

- The first, being led by Dr. Wolchok, involves exploring how a type of white blood cell called a T lymphocyte (T cell) can kill cancer cells.
- The second, directed by Dr. Sadelain, focuses on adoptive cell transfer (ACT). (See page 4 for more information.) This part of the Dream Team's research will investigate several ways to use ACT as a cancer therapy.



Fundraising

FRED'S TEAM MEMBERS KEEP RUNNING FOR MSK

Fred's Team enables athletes of all abilities to raise funds directly for Memorial Sloan Kettering by competing in marathons, half-marathons, triathlons, cycling races, and other endurance events worldwide. Whether running the New York City Marathon, the 155-mile Sahara Race, or climbing Mt. Kilimanjaro, thousands of athletes have competed for Fred's Team in various events. Every dollar raised goes directly to MSK, and in 2012 the Division of Hematologic Oncology received nearly \$337,000 from Fred's Team participants.

"To me, being a member of Fred's Team means raising funds for pioneering research done by the physicians I work with every day at MSK, and contributing in



another way to the shared goal of making a difference in the lives of those affected by cancer," says Brynna Lipson, a clinical

research coordinator and Fred's Team runner.

DIVISION MEMBERS SADDLE UP FOR CYCLE FOR SURVIVAL

Cycle for Survival is an indoor team cycling event that raises funds directly for Memorial Sloan Kettering. It was founded in 2007 by the late Jennifer Goodman Linn and her husband, Dave Linn, to benefit research on rare cancers conducted at MSK. In 2012, over 7,000 indoor cyclists participated to raise \$8.3 million at events in Los Angeles, San Francisco, Long Island, Chicago, New York, and Washington, DC.



NADINE MANOSALVA, SHANNON DURAND, EMILY LAUER, ASHLEY HELMES

The Division of Hematologic Oncology received funds through Cycle for Survival donations to support multiple clinical trials.

To date, Cycle for Survival has raised \$31 million, with participation nearly doubling every year.

In 2012, participants from the Hematologic Oncology Division included:

Team BMT

1. Ayaz Alam
2. Amanda Bernard
3. Chelsea Chin
4. Shannon Durand
5. Eric Fama
6. Mary Griffin
7. Kathleen Hammond
8. Ashley Helmes
9. Greg Ivancich
10. Emily Lauer
11. Jessica Magnoli
12. Nadine Manosalva
13. Alana Mihovics
14. Naomi Paul
15. Miguel Perales (captain)
16. Martin Toulouse
17. Allison Tucker
18. Carly Turro
19. Nicole Ventura

Team ABMT

1. Christina Bello
2. Cristi Ciolino (captain)
3. Djamalia Dierov
4. Katie Evans
5. Allison Feldman
6. Anne Marie Gonzales
7. Maria Gonzalez
8. Elizabeth Hoover
9. Lauren Lechner
10. Rachel Lehrman
11. Marissa Lubin
12. Molly Maloy
13. Sarah Rivas
14. Kevin Robinson
15. Sarah Alandra Weaver
16. Yeon Yoo

Team T-Cell Racers

1. Regina Byrne
2. Steve Horwitz
3. Nisha Lund
4. Matthew Lunning
5. Peggy Lynch
6. Shani Miller (captain)
7. Patty Mysliwiec
8. Erika Pamer
9. Stephen Randolph
10. Daniel Toscano
11. Janelle Walkley

Publications

In 2012, our faculty published 191 articles in peer-reviewed journals online or in print. In this section, we highlight some of those publications. A complete list can be found online at libguides.MSK.org/hem-onc.

BONE MARROW TRANSPLANT

Perales MA et al. Recombinant human interleukin-7 (CYT107) promotes T cell recovery following allogeneic stem cell transplantation. Blood. 2012;120:4882-91.

This study reported how cytokines could be used to promote the recovery of T cells. The investigators performed a phase 1 clinical trial of r-hIL-7 (CYT107) in recipients of T cell-depleted allogeneic hematopoietic stem cell transplants (allo-HSCTs). The results showed that r-hIL-7 can enhance immune recovery after a T cell-depleted allo-HSCT without causing significant graft-versus-host disease or other serious toxicity

Dobrovina E et al. Adoptive immunotherapy with unselected or EBV-specific T cells for biopsy-proven EBV+ lymphomas after allogeneic hematopoietic cell transplantation. Blood. 2012; 119: 2644-2656.

This study reported on the MSK experience using adoptive cell therapy after transplantation for potentially lethal Epstein-Barr virus-associated lymphomas. Investigators evaluated HLA-compatible donor leukocyte infusions (DLIs) and HLA-compatible or HLA-disparate EBV-specific T cells (EBV-CTLs) in 49 hematopoietic cell transplantation recipients with biopsy-proven EBV-lymphoproliferative disease (EBV-LPD). They concluded that either unselected DLIs or EBV-specific CTLs can

eradicate both untreated and rituximab-resistant lymphomatous EBV-LPD, with failures ascribable to impaired T-cell recognition of tumor-associated viral antigens or their presenting HLA alleles.

Hanash AM et al. Interleukin-22 protects intestinal stem cells from immune-mediated tissue damage and regulates sensitivity to graft versus host disease. Immunity. 2012;37(2):339-50.

Early laboratory evidence suggests that the cytokine IL-22 protects the intestine in GvHD. In this study, the investigators demonstrated that deficiency of recipient-derived IL-22 increased acute graft-versus-host disease (GVHD) tissue damage and mortality, that intestinal stem cells (ISCs) were eliminated during GVHD, and that ISCs as well as their downstream progenitors expressed the IL-22 receptor. The findings reveal IL-22 as a critical regulator of tissue sensitivity to GVHD and a protective factor for ISCs during inflammatory intestinal damage.

Jenq RR et al. Regulation of intestinal inflammation by microbiota following allogeneic bone marrow transplantation. J Exp Med. 2012;209(5):903-11.

Researchers are increasingly gaining a better understanding of the intestinal microbiota — the collective bacteria that inhabit the intestinal tract. MSK researchers found that while bone marrow transplantation (BMT) has only a minimal impact on the microbiota, graft-versus-host disease (GVHD) has a profound impact, causing a dramatic loss of diversity and leading to an overgrowth of a group of bacteria known as Lactobacillales. Furthermore, eliminating Lactobacillales from the flora of mice before BMT aggravated GVHD, whereas reintroducing Lactobacillales produced protection against GVHD. The results show

that the intestinal microbiota can impact on the severity of intestinal inflammation and suggest that flora manipulation may improve outcomes for allogeneic BMT recipients.

LEUKEMIA

Patel JP et al. Prognostic relevance of integrated genetic profiling in acute myeloid leukemia. N Engl J Med. 2012;366(12):1079-89.

This paper from the laboratory of Ross Levine (collaborating investigators include Omar Abdel-Wahab and Martin S. Tallman) represents a truly landmark study in integrating molecular genomic profiling into clinical practice in acute myeloid leukemia (AML). By analyzing 398 patients with AML for the presence of 18 genes known to be recurrently mutated in this disease and correlating these mutations with clinical outcome, investigators identified key genetic predictors of prognosis and response to therapy. These findings have already begun to refine our ability to use mutational profiling to inform prognostic and therapeutic decision-making in AML patients.

Abdel-Wahab O et al. ASXL1 mutations promote myeloid transformation through loss of PRC2-mediated gene repression. Cancer Cell. 2012;22(2):180-93.

Recently, a series of new somatic genetic alterations have been found in patients with myeloid malignancies in genes whose known or assumed function involves the epigenetic regulation of gene transcription. In this paper, researchers in the laboratory of Ross Levine (with studies spearheaded by Omar Abdel-Wahab) characterized the function of mutations in the gene Addition of Sex Combs Like 1 (ASXL1), which is among the most common genetic

alterations in patients with myelodysplastic syndromes, chronic myelomonocytic leukemia, and elderly patients with AML. They found that mutations in ASXL1 are loss of function mutations which affect the ability of the Polycomb Repressive Complex 2 to methylate histone residues on histone H3 lysine 27. This results in disordered gene regulation and promotes the aggressiveness of myeloid malignancies induced by co-occurring genetic alterations such as oncogenic mutations in NRAS.

Callahan MK et al. Progression of RAS-mutant leukemia during RAF inhibitor treatment. N Engl J Med. 2012;367(24):2316-21.

In this case report, Raajit Rampal, Omar Abdel-Wahab, Virginia Klimek, and Ross Levine collaborated with investigators from the Melanoma Service to describe an unexpected side effect of a selective RAF inhibitor (vemurafenib) used to treat metastatic melanoma. While vemurafenib inhibits ERK signaling in BRAF V600E-mutant cells, it has been described to paradoxically activate ERK signaling in BRAF-wild type cells, leading to the development of RAS mutant squamous cell skin cancers in patients treated with RAF inhibitors. In this paper, investigators demonstrate that this phenomenon can also drive the progression of RAS-mutant leukemias, with reversal of this effect upon drug withdrawal. This finding has important implications for the monitoring of patients and proposed use of RAF inhibitors in clinical trials.

LYMPHOMA

Hartridge-Lambert SK et al. ABVD alone and a PET scan complete remission negates the need for radiologic surveillance in early-stage, nonbulky Hodgkin lymphoma. Cancer. 2013;119(6):1203-9. [Epub 2012 Nov 6]

This retrospective study examined the value of post-treatment imaging following a PET-negative response to ABVD in early-stage Hodgkin lymphoma and suggested that routine follow-up imaging can be omitted in these patients.

Moskowitz AJ et al. Phase II study of bendamustine in relapsed and refractory Hodgkin lymphoma. J Clin Oncol. 2013;31(4):456-60. [Epub 2012 Dec 17]

This study confirmed the efficacy of bendamustine in heavily pretreated patients with Hodgkin lymphoma (HL). These results support current and future studies evaluating bendamustine combinations in relapsed and refractory HL, including an ongoing MSK phase I trial of bendamustine in conjunction with a poly ADP ribose polymerase (PARP) inhibitor.

Leonard JP et al. Selective CDK4/6 inhibition with tumor responses by PD0332991 in patients with mantle cell lymphoma. Blood. 2012;119(20):4597-607.

MSK researchers participated in this consortium pilot study demonstrating that CDK4/6 inhibition using targeted therapy could result in radiographic and clinical benefit in patients with mantle cell lymphoma.

MYELOMA

McCarthy PL et al. Lenalidomide after stem-cell transplantation for multiple myeloma. N Engl J Med. 2012;366(19):1770-81.

This paper described the results of a CALGB-sponsored randomized phase III study of lenalidomide maintenance after autologous stem cell transplant for patients with multiple myeloma. Lenalidomide treatment resulted in significantly prolonged disease-free and overall survival after autologous stem transplantation. MSK researchers featured prominently in this multi-institutional trial that established lenalidomide maintenance as a new standard of care after autologous stem cell transplantation for multiple myeloma.

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;27:823-828. [Epub 2012 Sep 27]

This paper described the results of a phase II study using a treatment approach that included up-front risk-adapted melphalan and stem cell transplant (SCT) followed by consolidation with bortezomib and dexamethasone (BD) for amyloidosis (AL) patients with less than a complete response. In newly diagnosed AL, BD following SCT rapidly and effectively improved responses (ORR increased from 45 percent at 3 months to 79 percent at 12 months post SCT), resulting in high CR rates (58 percent) and maintained organ improvement.

Landau H et al. Bortezomib, liposomal doxorubicin and dexamethasone followed by thalidomide and dexamethasone is an effective treatment for patients with newly diagnosed multiple myeloma with International Staging System stage II or III, or extramedullary disease. Leuk Lymphoma. 2012;53(2):275-81.

This study evaluated sequential bortezomib, liposomal doxorubicin, and dexamethasone (BDD) followed by thalidomide and dexamethasone (TD) in patients achieving at least a partial response (PR), and bortezomib and TD (BTD) in patients who failed to achieve a PR in clinically high-risk untreated patients with multiple myeloma. After BDD, the overall response rate (ORR) was 81 percent, with 40 percent achieving at least a very good partial response (VGPR), and 26 percent achieving near complete and complete responses (nCR/CR). After TD or BTD, the ORR was 83 percent, with 60 percent achieving at least a VGPR, including 43 percent nCR/CR, indicating deeper responses following sequential therapy. *Zamarin D et al. Patterns of relapse and progression in multiple myeloma patients after auto-SCT: implications for patients' monitoring after transplantation. Bone Marrow Transplant. 2013;48(3):419-24. [Epub 2012 Aug 13]*

This retrospective study examined the patterns of relapse after first-line transplant in 273 patients, using established criteria. Investigators showed that at the time of relapse, only 2 percent of patients had

no associated serological evidence of relapse, and 85 percent had asymptomatic relapse first detected by serological testing without organ damage. Fifteen percent had symptomatic relapse with aggressive disease, early relapse, and short survival, with poor cytogenetics and younger age identified as risk factors. Researchers also found that yearly skeletal surveys and urine testing were poor at heralding relapse. They found a consistent association between paraprotein types at diagnosis and at relapse. The findings provide important evidence-based recommendations that strengthen current monitoring guidelines after first-line ASCT in multiple myeloma.

Tyler EM et al. WT1-specific T-cell responses in high-risk multiple myeloma patients undergoing allogeneic T cell-depleted hematopoietic stem cell transplantation and donor lymphocyte infusions. Blood. 2013;121(2):308-17. [Epub 2012 Nov 16]

This work suggested an association between the emergence of WT1-CTL and graft-versus-myeloma effect in patients treated for relapsed multiple myeloma after allogeneic T cell-depleted hematopoietic stem cell transplantation and donor lymphocyte infusions, supporting the development of adoptive immunotherapeutic approaches using WT1-CTL in the treatment of multiple myeloma.

Philanthropic Donors over \$50,000

Alex's Lemonade Stand Foundation
Anonymous (5)
Bergstein Family Foundation
Mr. and Mrs. Norman Brownstein
CLL Global Research Foundation
Connecticut Sports Foundation, Inc.
Gabrielle's Angel Foundation for Cancer Research
Mr. and Mrs. Robert S. Goldberg
Grand Street Fund of Fidelity Charitable Fund
The Grinberg Family Foundation
The Grodetsky Family Foundation
Mr. and Mrs. Thomas C. Israel
J. C. Kellogg Foundation
William Lawrence & Blanche Hughes Foundation
Fran and Ralph Levine
The Lymphoma Foundation
Nonna's Garden Foundation
Trust of Nina Nordlicht
Perry Capital LLC
Mr. and Mrs. Jack Rudin
May and Samuel Rudin Family Foundation
Mr. and Mrs. Stephen Scherr
Mr. and Mrs. Robert H. Silver
Trust of Leonard & Ruth Silverman
Peter J. Solomon Family Foundation
St. Baldrick's Foundation
Vital Projects Fund, Inc.
The Washington Post Company

You Can Help

PHILANTHROPY

The Campaign for Memorial Sloan-Kettering is an ambitious fundraising initiative designed to support every area of the Center's mission. Contributions to the Campaign can take a variety of forms including gifts of cash paid outright in a single installment or as a pledge to be fulfilled over a period of several years.

Other ways of giving include:

- Gifts of securities
- Planned gifts (life income plans or a bequest)
- Gifts of real estate and personal property
- Gifts from qualified plans such as a 401 (k) or 503 (b)

For additional information or to make a gift, please call 646-227-3529.

DONATING BLOOD

Blood donations can be designated for a particular patient or for our general blood inventory. For more information or an appointment, call 212-639-8177.

DONATING TO FRED'S TEAM

For information on donating, visit Fred's Team at: www.fredsteam.org.

DONATING TO CYCLE FOR SURVIVAL

For information on donating, visit Cycle for Survival at: www.cycleforsurvival.org.



Memorial Sloan-Kettering Cancer Center

Division Head of Hematologic Oncology
646-888-2304

1275 York Avenue
New York, NY 10065

General Information
212-639-2000

Physician Referral Service
800-525-2225

On the Internet
www.mskcc.org

Follow us
www.facebook.com/sloankettering
www.twitter.com/sloan_kettering
www.youtube.com/mskcc