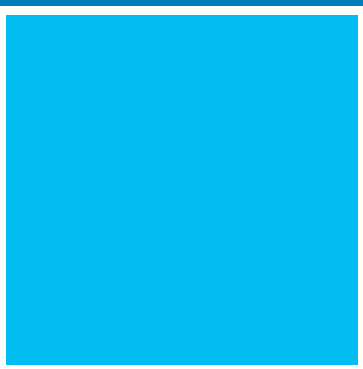
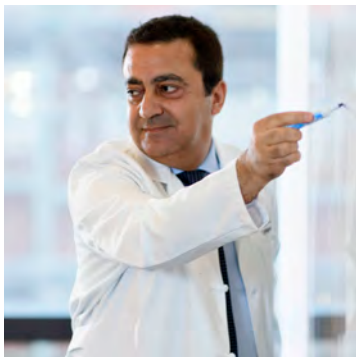
HEMATOLOGIC ONCOLOGY 2015 ANNUAL REPORT



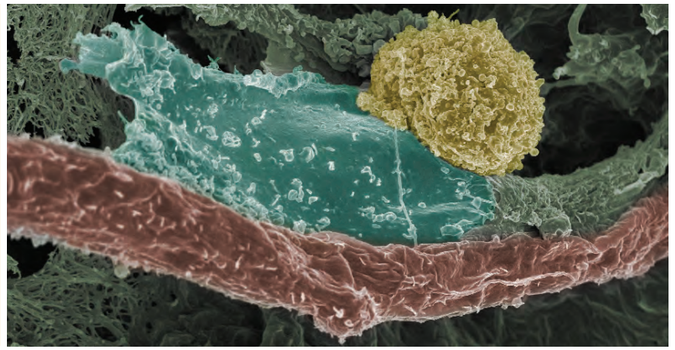



Memorial Sloan Kettering Cancer Center

HEMATOLOGIC ONCOLOGY 2015 ANNUAL REPORT

MEMORIAL SLOAN KETTERING CANCER CENTER

Contents



Scanning electron microscopy image of a bioengineered thymus showing a developing T cell (yellow) on top of a thymic epithelial cell (green) in contact with a fiber (brown) of a three-dimensional polymer scaffold.

CREDIT: ANDREA TUCKETT, PHD, RESEARCH ASSOCIATE, DEPARTMENT OF IMMUNOLOGY

ON THE COVER: TOP: Jodi Mones; RIGHT: Heather Landau; BOTTOM: Jae Park; LEFT: Alexander Lesokhin; CENTER: Anas Younes

Letter from the Division Head

The Division of Hematologic Oncology in the Department of Medicine at Memorial Sloan Kettering Cancer Center is home to 69 faculty members, who belong to one (or more) of 5 services: Adult Bone Marrow Transplantation, Hematology, Leukemia, Lymphoma and Myeloma. Our faculty is devoted to excellence and innovation in a) patient care, b) basic, translational and clinical research and c) education of the next generation of leaders in Hematological Oncology.

The 5th edition of our Annual Report will highlight:

Our outstanding faculty & staff. Personal interviews with a leading nurse practitioner, pharmacist, clinical research nurse coordinator, physician assistant, clinical researcher and two physician scientists.

Comprehensive patient care for cancer patients & survivors. A tour through MSK's Lymphoma Survivorship Clinic and an in-depth look at several of the long-lasting health concerns facing lymphoma patients.

Innovative translational research. Conversations with Dr. Ross Levine about his laboratory's commitment to developing new treatments for myeloproliferative neoplasms (MPNs); Dr. Ola Landgren about a clinical trial for a monoclonal gammopathy of undetermined significance (MGUS); and Dr. Alan Hanash about a novel treatment for graft-versus-host-disease (GVHD) by promoting the regeneration of the lining of the intestines.

Our commitment to improving patient outcomes and access to top-quality cancer care. The Division continued its growth in 2015 by recruiting four new junior faculty members, expanding clinical practice into the MSK Regional Network, and increasing our overall number of patient visits and follow-up appointments.

I hope you will enjoy reading about our accomplishments in 2015.

Regards,

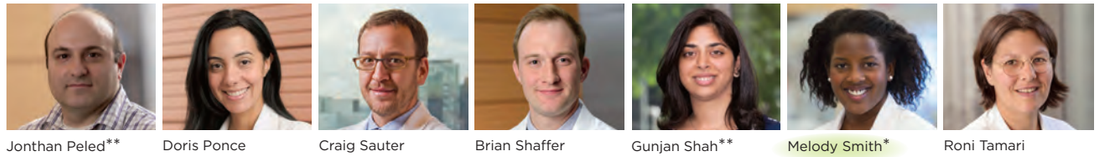
Marcel R.M. van den Brink, MD, PhD
Alan Houghton Chair in Immunology
Head, Division of Hematologic Oncology
Memorial Sloan Kettering Cancer Center

Division of Hematologic Oncology Faculty

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



Jonthan Peled**
Doris Ponce
Craig Sauter
Brian Shaffer
Gunjan Shah**
Melody Smith*
Roni Tamari

HEMATOLOGY

Marcel van den Brink
DIVISION HEAD
James Young
Simon Mantha
Jodi Mones**
Rekha Parameswaran
Lilian Reich
Gerald Soff
CHIEF ATTENDING

LEUKEMIA

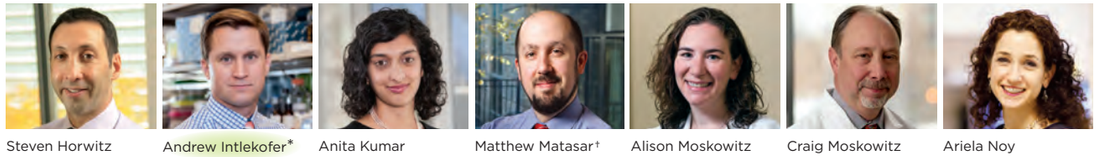
Omar Abdel-Wahab
Ellin Berman
Renier Brentjens
Stephen Chung
Bayard Clarkson
Jacob Glass**
Virginia Klimek

Ross Levine
Peter Maslak
Michael Mauro
Jae Park
Raajit Rampal
David Scheinberg
Alan Shih

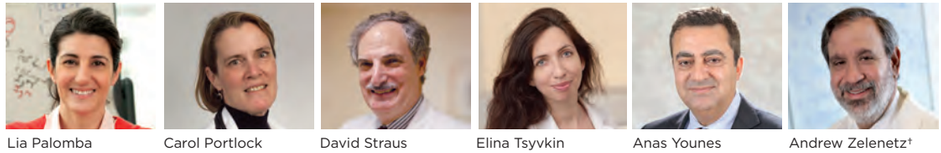
*Joined faculty in 2015 **Joined faculty in 2016 † Physicians who also practice in the Regional Network

LYMPHOMA

Eytan Stein
Martin Tallman
CHIEF ATTENDING
Aaron Viny*
Connie Batlevi**
Helen Chung
John Gerecitano
Paul Hamlin†
CHIEF, BASKING RIDGE MEDICAL ONCOLOGY SERVICE



Steven Horwitz
Andrew Intlekofer*
Anita Kumar
Matthew Matasar†
Alison Moskowitz
Craig Moskowitz
CLINICAL DIRECTOR
Ariela Noy



Lia Palomba
Carol Portlock
David Straus
Elina Tsyvkin
Anas Younes
CHIEF ATTENDING
Andrew Zelenetz†

MYELOMA

Hani Hassoun†
Neha Korde†
Ola Landgren
CHIEF ATTENDING
Nikoletta Lendvai
Alexander Lesokhin
Sham Mailankody*†
Eric Smith**

REGIONAL NETWORK

Philip C. Caron†
Pamela R. Drullinsky†

Audrey M. Hamilton†
Colette Owens**

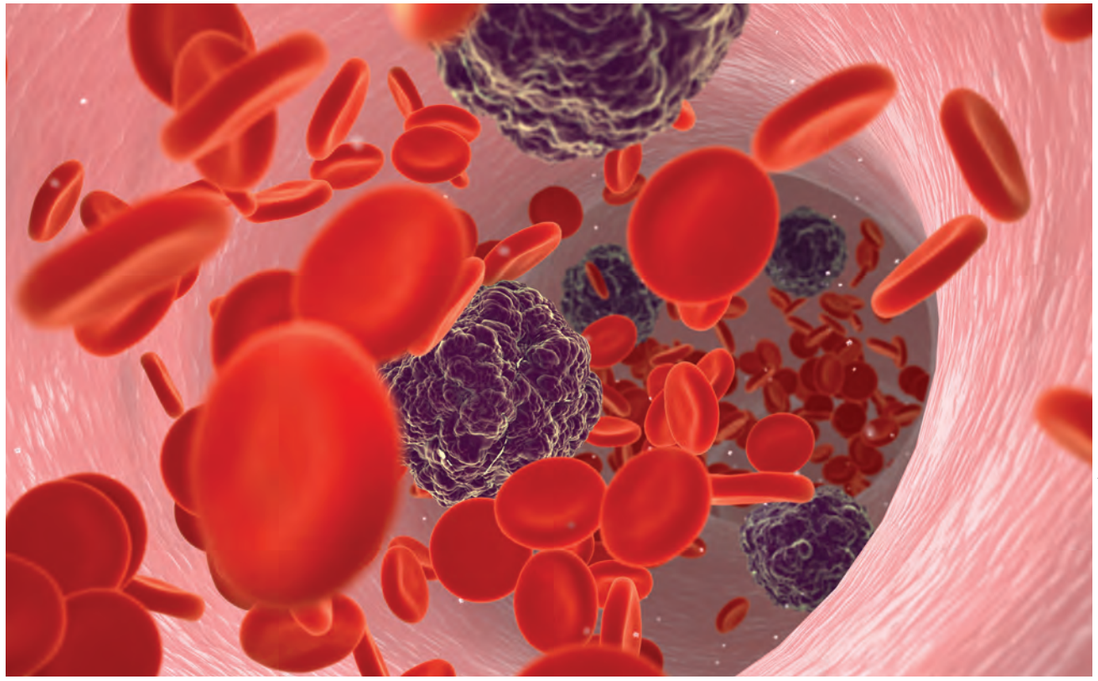
COLLABORATING TEAMS

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 & 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

Discovery Could Boost New Therapies for Myeloproliferative Neoplasms

BY JIM STALLARD



CREDIT: SPRINGER MEDIZIN / SCIENCE SOURCE

Myeloproliferative neoplasms develop when the bone marrow excessively produces several types of blood cells.

Blood cancers called myeloproliferative neoplasms (MPNs) are driven by mutations in a gene called JAK2. Current drugs that inhibit the protein made by mutated JAK2 don't work as well as initially hoped. A new compound that targets this protein when it is in an inactive structural state appears to be more effective and less toxic, raising hopes that this will lead to better drugs for MPNs.

MEMORIAL SLOAN KETTERING researchers are reporting what could be a significant advance in the treatment of blood cancers known as myeloproliferative neoplasms (MPNs). A new compound appears to be effective at blocking a protein, JAK2, that plays a key role in these diseases but has proved stubbornly resistant to current drugs.

The discovery, reported by hematologist/oncologist Ross Levine and colleagues, has energized a therapeutic field that had been foiled by MPN cancer cells' ability to withstand drugs that seemingly hit their target.

"You can feel that the momentum has shifted, and the fact that we have had a major role in changing the momentum is gratifying," said Dr. Levine.

THE TWO FACES OF JAK2

MPNs are diseases in which the bone marrow produces several types of blood cells in excess. Earlier research by Dr. Levine and others found that cancer cells in many people with MPN have a mutation in the JAK2 gene or in other genes that interact with JAK2 as part of the JAK2 pathway, which regulates a number of basic cell functions.

HIGHLIGHTS:

- Myeloproliferative neoplasms (MPNs) are a group of blood cancers.
- MPNs are largely caused by mutations in a gene called JAK2.
- New compounds may work better than current drugs in treating MPNs.
- They target the JAK2 protein in a different structural state.

"You can feel that the momentum has shifted, and the fact that we have had a major role in changing the momentum is gratifying." PHYSICIAN-SCIENTIST ROSS LEVINE

Mutations in the JAK2 pathway can interfere with this process and promote cancer cell growth.

Although the JAK2 protein was a promising target, clinical trials testing drugs that inhibit this protein by binding to it have not led to dramatic clinical responses. The drugs improve disease-related symptoms and reduce spleen size, and one drug — ruxolitinib — was approved by the FDA for MPN patients. But the JAK2 inhibitors failed to bring about the striking molecular responses seen with other targeted therapies — most notably imatinib (Gleevec®), which is very effective against another blood cancer called chronic myelogenous leukemia (CML).

In 2012, Dr. Levine's lab discovered that MPN cancer cells are capable of using an alternate means of maintaining the function of mutated JAK2 even when the cells are exposed to JAK2 inhibitors. This explained why current drugs are relatively ineffective, and it also bolstered the theory that the cancer cells need JAK2 to stay alive.

A NEW APPROACH

Given JAK2's ability to persist in the presence of such inhibitors, Dr. Levine's team considered another line of attack. JAK2 is a type of protein called a kinase, and many kinases actually cycle between an active and an inactive structural state — what biologists call a "conformation." Drugs effective against one conformation might not work in the other.

Conventional JAK2 inhibitors such as ruxolitinib target the kinase in its active conformation. Dr. Levine's lab decided to see whether a drug that binds to JAK2 in the inactive state would work better. This strategy of targeting a different kinase conformation when drugs are ineffective has worked before, he explained.

"[MSK physician-scientist] Charles Sawyers showed that a second-generation drug, dasatinib, worked in CML patients who failed imatinib because dasatinib binds to the target differently," said Dr. Levine. "So there's precedent in leukemias that if you hit the target when it's in a different structural state, you might get better results."

Dr. Levine and his colleagues collaborated with scientists at Novartis to develop a compound called CHZ868, which inhibits JAK2 in the inactive state. When they tested CHZ868 in mouse models of MPN and in patient samples, the drugs proved to be more effective and less toxic than first-generation JAK2 inhibitors. The researchers reported their results in the journal *Cancer Cell*.

RENEWED ENTHUSIASM

"This shows a new path to making JAK2 drugs that will offer better therapeutic options," said Dr. Levine. "I think you're going to see another wave of drug development against JAK2."

Dr. Levine explains that the exact compound used in the experiment may not actually go into patients. Researchers are busy improving upon it, and the final drug will likely be a slightly different compound that will work even better. But the study was essential in proving the effectiveness of targeting JAK2's inactive state — and it underscores once again the importance of keeping the focus on JAK2.

"You're seeing a groundswell, and a renewed enthusiasm among researchers and in industry that this is going to work," said Dr. Levine. "It's been very rewarding to be involved in this field as it's progressed over the past decade — beginning when the role of JAK2 in MPN was first identified, to seeing the first drugs get to our patients, to today when it's looking like we've found a way to something much better." ■

Karen Collum, DNP, RN, OCN

Nurse Leader, Blood and Marrow Transplant Services

FROM THE MOMENT Karen Collum started working with oncology patients during her nursing school internship, she was hooked. In addition to the deep, enduring connections she saw between nurses and patients, Dr. Collum also appreciated that the blood and marrow transplant (BMT) field, in particular, required an extreme attention to detail — one of her strongest traits.

"There was a lot of complexity and nuances to BMT care that I found intriguing," she explains. "I liked being able to help manage these issues. I can handle a lot of things happening at once. Transplant is very rich in the science and evolution of treatments, but it also kept my attention."

Memorial Sloan Kettering is the lucky beneficiary of this quality in Dr. Collum, who joined the staff in 2009 and now helps run the BMT Service as Nurse Leader, Transplant Service within the Department of Nursing Quality. She helped oversee nearly 450 transplants here in 2015, including 40 in pediatric patients.

Much of Dr. Collum's job involves the detail-laden, nuts-and-bolts work of ensuring the Service is compliant with regulatory, institutional and departmental requirements. She also monitors and implements performance improvement projects in her uber-collaborative role and coordinates the BMT Service's quality management initiatives by facilitating regular audits.

"It's really inspiring that everyone here has the opportunity to be heard and involved," she says. "It's very team-oriented, which makes working on different projects just that much more rewarding because it's not usually an uphill battle."

In this interview, Dr. Collum discusses the trajectory of the BMT Service in recent years and how patients continue to stay at the center of all improvement efforts.

How has the BMT program evolved during the course of your tenure here?

So many positive changes have occurred since Dr. Sergio Giralt, Chief of the Adult BMT Service, arrived here six months after me. He restructured the adult program, merging autologous and allogeneic transplants into one true service. The merger gave us a more defined place in the institution. He has taken a huge interest in making sure everyone is at the table — including the nurses, nurse practitioners and physician assistants — throughout the employee continuum and that we're all well-resourced. It's really a team effort, and Dr. Giralt has made lots of strides to let everyone have a voice.

How pivotal is the BMT Service to patients' overall outcomes?

We have a huge focus on all outcomes — patient-centered outcomes as well as statistical outcomes. Statistical outcomes, of course, are extremely important and you need to know institutionally that you're doing a large volume of transplants successfully. It's easy to get bogged down in regulatory requirements, but our program not only meets those, but also takes into account patient-centered outcomes. Survival is something that everyone looks at, but beyond that, what's the quality of that survival? We follow many new studies and protocols to ensure we're not just maintaining that survival, but a standard of survival acceptable to the patient.

How does the BMT Service go the extra mile to improve patient care?

We're always striving to improve care and there are many new initiatives within the institution to achieve that. We've built up our outpatient transplant program so that more patients can spend more time at home instead of the hospital after receiving chemotherapy conditioning or a transplant. This way, patients are in their home, or a homelike environment. This decreases the burden on the patient and builds the quality of that experience, and it's just one of the ways we're focusing on patient-centered outcomes.

How do you choose which performance improvement projects to implement?

Projects come from different avenues. Many stem from conversations during patient reviews or from staff members' comments indicating a particular process was difficult to achieve. I have to decide the objective: Do we need better education? To simplify a process? Review steps so something isn't as difficult next time? If results aren't good on one of our audits, I work with staff to come up with a process to improve them. Staff members suggest ideas and I meet with them to follow up. I look for recurring themes to decide what to improve.

What are your biggest challenges in your role?

Staying current and ensuring that we're able to do what we want for the patients, staff, and program, as well as ensuring there's continuity and quality in what we're doing. It's hard to say that's a challenge; that's the goal. But sometimes making sure everyone is on the same page and has the same vision is challenging. It's something to be mindful of.

What excites you most about your work?

The recognition I feel from the entire Service and the collaboration within different disciplines. Examining quality and regulatory issues isn't by any means underappreciated, but it's not always at the forefront. But we've gotten to a place in our program where these issues are incorporated into a lot of the discussion. It's great to be sought-after when staff members ask me for help or guidance about how we can improve or change something. I don't have to insert myself in the conversation — I'm already recognized and heard. ■

Collaborative Approach Key to Overseeing Adult Pharmacy Services and Pharmacy Residency Program

A TEMPORARY POSITION at Memorial Sloan Kettering led to a calling for Nelly Adel, PharmD.

Arriving here in 2004 for a one-year research project, Dr. Adel quickly decided MSK was the ideal institution to apply her experience in oncology pharmacy gleaned from working at other major centers. A dozen years later, Dr. Adel now helms two MSK pharmacy programs, serving as both manager of Adult Clinical Pharmacy Services and director of the Adult Oncology PGY-2 Residency Program.

"If you love the field of cancer, you're going to work at the best cancer center in the United States, which is Memorial," she says. "If I compare all the hospitals I've worked at to Memorial, the thing that makes us stand out is that our entire team works toward one goal, and that's the patient."

MSK PHARMACISTS INCREASE AS DRUG CHOICES SKYROCKET

A major evolution in oncology treatment over the past decade — with thousands of new medications approved, including targeted drugs and immunotherapy — has called on pharmacists to become more specialized, not just physicians, Dr. Adel says. This progress has also fueled a heavier collaboration between MSK oncologists and pharmacists since she became manager of Adult Clinical Pharmacy Services nine years ago.

Increasing numbers of pharmacists have been hired during her tenure, with the Pharmacy Department now topping 375 employees. About 225 pharmacists serve patients in 25 pharmacy satellites, and the department's annual budget exceeds $500 million.

"In the beginning I was responsible for justifying the value of having clinical pharmacists to every subspecialty team," Dr. Adel says. "Now every team realizes they can't do without the pharmacists. We're fully staffed in the hematological oncology service in both the inpatient and outpatient setting."

"Future goals include expanding further into solid tumor, with about 40 clinical pharmacy specialists currently dedicated to rounding with doctors and helping decide which therapy to give a patient," she adds. "The physicians love and appreciate this interaction."

RESIDENCY PROGRAM FLOURISHES

The Adult Oncology PGY-2 Residency Program has also grown in important ways under Dr. Adel's tutelage. Designed to build on competencies developed during a postgraduate year 1 pharmacy residency, the PGY-2 program now accepts four oncology residents each year, up from two residents when the program began at MSK in July 2007.

Requiring rotations in several disciplines, including leukemia, lymphoma, bone marrow transplant, breast and lung cancers, and gynecological malignancies, among others, the PGY-2 program aims to build the knowledge and clinical skills pharmacists need as independent oncology practitioners.

"In addition to rounding, residents can do research projects they have to present at ASH (American Society of Hematology) or ASCO (American Society of Clinical Oncology) conferences and they have to publish research in manuscript form by the end of the year," Dr. Adel explains, calling the program her "passion."

"Because of this research program, we have built so many good relationships with physicians, so that opens their eyes to seeing how pharmacists are out there doing different things," she adds.

'POSITIVE REINFORCEMENT' PART OF THE CULTURE

Dr. Adel takes pride in the fact that pharmacy residents who complete the PGY-2 program at MSK tell her they've not only learned, but also enjoyed the experience.

"This is what really sets the program apart. Because of my own training, which I considered a little stressful, I learned to identify things that would create a better experience for these residents," she says. "I believe in positive reinforcement and taking things as they are, instead of stressing the residents and pushing them down."

This education and workplace ethos, Dr. Adel believes, is an extension of the overall philosophy at MSK that she holds dear — and what drew her to work here in the first place.

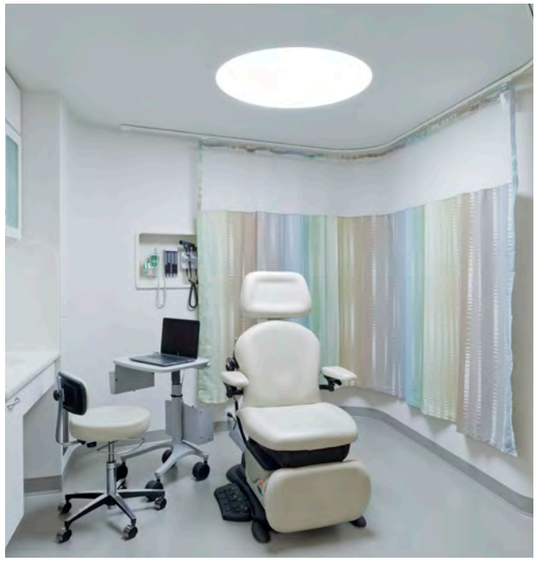
"I want to spend all my life in this field," she says. "I appreciate everyone here who helped pharmacy services survive and be the entity we want to be. I have definitely felt the acceptance of others." ■

> **"The thing that makes us stand out is that our entire team works toward one goal, and that's the patient."** NELLY ADEL

New Clinic Helps Lymphoma Survivors Stay Healthy

BY ANDREA PEIRCE

People are living longer lives after treatment for lymphoma. But the disease can cause lasting health problems — some of which may not show up until many years later. MSK's Lymphoma Survivorship Clinic monitors survivors' health.



THROUGH CAREFUL MONITORING and expert care, MSK's Lymphoma Survivorship Clinic helps people who've survived lymphoma stay healthy by watching for long-term effects of treatment such as heart disease, second cancers, and problems with thinking and memory.

HEMATOLOGIC ONCOLOGIST MATTHEW MATASAR CARES FOR LYMPHOMA SURVIVORS.

Thanks to major advances in the understanding and treatment of lymphoma — one of the nation's most commonly diagnosed cancers — more people than ever are enjoying productive lives for years and even decades after being declared free of the disease. But doctors at Memorial Sloan Kettering and elsewhere have also found that over the course of time, many of these individuals develop complications from the treatment they received.

Even with improvements in approaches to radiation and chemotherapy, people may experience permanent damage that increases the risk for heart disease, skin cancer, lung conditions, and other illnesses.

"Since we know that many of our patients may experience long-term problems, we decided to initiate a program that could help quickly identify and address them," explains hematologic oncologist Matthew Matasar. "And through clinical trials and other research, we're looking for even more ways to keep our survivors healthy."

DEDICATED TO LONG-TERM SURVIVORS

Initiated in 2014 and housed within the Lymphoma Service at MSK's 64th Street Outpatient Center, the Lymphoma Survivorship Clinic welcomes MSK survivors of all ages, as well as people initially treated for the disease at other institutions. Unlike MSK's Adult Long-Term Follow-Up Program (ALTFU) tailored to survivors of a range childhood (and some young adult) cancers, the clinic's sole focus is survivors of lymphoma. The clinic starts caring for people as soon as three years after they end treatment.

> **"We're prepared not only to give people the latest in care, screening, and surveillance, but also to easily send them to our other MSK experts if needed."** MATTHEW MATASAR

HIGHLIGHTS

- More people than ever are living longer after surviving lymphoma.
- Delayed health effects from treatment for the disease are common, however.
- MSK's Lymphoma Survivorship Clinic helps people effectively manage their long-term health.

Depending on such factors as the types of treatments survivors received and their general health when they were diagnosed with lymphoma, Dr. Matasar and two physician assistants in the clinic monitor survivors for:

- Heart disease
- The development of second cancers such as breast, lung, and skin cancer and leukemia
- Thinking and memory problems (commonly known as "chemobrain")
- Lung health
- Bone health
- Stroke
- Problems with teeth and gums
- Reduced thyroid function
- Dry eyes, cataracts, and other eye issues
- Emotional and psychological health

And since the clinic is embedded in a comprehensive cancer center, "we're prepared not only to give people the latest in care, screening, and surveillance, but also to easily send them to our other MSK experts if needed — people at the top of their field in survivorship issues such as heart, lung, and reproductive health," explains Dr. Matasar.

EVIDENCE-BASED EXPERTISE

As part of MSK's larger program in cancer research and survivorship, the clinic is also able to offer access to clinical trials and other research that can help people facing the late effects of lymphoma treatment.

Current investigations are asking such questions as:

- How can doctors anticipate and assist women at risk for long-term sexual and reproductive health issues?
- Which interventions might best help problems with thinking and memory?
- Can cardiac MRI detect early changes in the heart among survivors of Hodgkin lymphoma?

It's high time that lymphoma survivors get a specialized clinic of their own such as this, explains Dr. Matasar. "In part because the clinic is right here, embedded in our Lymphoma Service, we can deliver just the kind of care these patients need." ■

LIVING BEYOND CANCER | SERVICES FOR SURVIVORS

At MSK, we are just as dedicated to helping people live their lives to the fullest as we are to providing our patients as many options as we can to eliminate their disease with as much precision and as little impact as possible on the rest of the body.

Our disease-specific adult survivorship clinics offer comprehensive services to people who have been treated for cancer at MSK. While we anticipate that our patients will lead a healthy, active life, we recognize that they might develop problems as a result of having been treated for cancer. In addition to monitoring for signs of cancer recurrence, we focus on identifying, preventing, and controlling any long-term and late effects associated with treatment to help provide cancer survivors with the best quality of life possible.

To this end, we've built a program for patients and their loved ones that includes counseling and emotional support, resources for life after cancer, rehabilitation and exercise, palliative care and pain management, older patient care, integrative medicine, nutrition, dermatology and skin care, sexual health, fertility, tobacco treatment, genetic testing and counseling and screening services.

OUR DIVISION'S DISEASE-SPECIFIC SURVIVORSHIP CLINICS INCLUDE:

Stem Cell Transplant Survivorship Program
Survivorship follow-up care is provided by a nurse practitioner (NP) who specializes in the care of transplantation survivors. The NP, along with the treatment team, will closely monitor allogeneic transplant patients for signs of graft-versus-host disease (GVHD). Patients who have received either allogeneic or autologous transplants will be monitored for immune system recovery, late complications arising from the high-dose chemotherapy and radiation therapy given prior to transplantation, and any recurrence of cancer.

Allogenic Survivorship Clinic
Provider: Kara Mosesso, NP
Office: 212-639-3225

Autologous Survivorship Clinic
Provider: Sheila Kenny, NP
Office: 212-639-2770

https://www.mskcc.org/cancer-care/treatments/cancer-treatments/blood-stem-cell-transplantation/survivorship

Lymphoma Survivorship Clinic
Physician Assistants (PAs) are medical professionals certified to practice medicine under the supervision of a physician that provide clinical follow-up care for patients in the Lymphoma Survivorship Clinic. Starting three years after completion of therapy for highly curable lymphoma subtypes, the PA monitors patients for cancer recurrence, manages the late effects of treatment, and orders screening tests for secondary cancers.

Lymphoma Survivorship Clinic
Provider: Sharyn Kurtz, PA-C, MPAS, MA
Office: 212-639-5324

https://www.mskcc.org/cancer-care/types/lymphoma/survivorship

Amanda Copeland, RN, MSN, CNS

Acting Director of Clinical Trials Nursing
Clinical Research Nurse Coordinator
Lymphoma Service

ALTHOUGH MOST at Memorial Sloan Kettering understand what clinical trials are, they may be unaware of the pivotal role research nurses play in supporting their implementation. A large part of Amanda Copeland's role at MSK is to act as a proponent and educator of this essential form of research, both for the clinicians and their patients.

Copeland arrived at MSK in 2013 after nine years at MD Anderson Cancer Center. It was during her stint in Houston that Copeland discovered her passion for research. This was during a dynamic period when many innovative lymphoma treatments were emerging. Explaining what research nursing entails and sharing her excitement about the profession is something she looks forward to at every opportunity.

"It's a relatively new branch of nursing," she says. "Patients have been on clinical trials for a long time, but people are just starting to realize this is a specialty type of nursing. We manage patients receiving investigational treatments within the guidance of a research protocol to answer a specific research question." Very exciting for this field of nursing is the American Nurses Association's (ANA) recent recognition of clinical research nursing as a specialty nursing practice.

In this interview, Copeland details the specialized care clinical trial patients receive from research nurses and the challenges she faces in her position.

After you began your career, you realized your true passion was working with novel lymphoma therapies in clinical trials. Explain this evolution in your thinking and practice.

Even though my primary responsibility in my first lymphoma position was managing patients on standard chemotherapy regimens, I frequently interacted with patients on clinical trials. I was intrigued by the process of presenting novel therapies to patients and shared their excitement of trying something new. I knew I wanted to be more a part of that experience. Taking them through that process, especially with so many new and fascinating drugs coming out, was exciting and rewarding.

What are your duties from day to day?

I spend a lot of time educating — not just patients but also staff, sharing with them knowledge about ongoing trials or upcoming trials in the pipeline. Patients considering enrolling in a clinical trial need to learn about its logistics and schedule as well as potential side effects and research nurses play a vital role in this process. Doctors benefit from education provided by a research nurse engaged in the conduct of a particular clinical trial as well. For example, a treating physician may not be seeing all the patients on a particular new drug, but the research nurse most likely is. The nurse is able to share the knowledge of what they've observed with other patients receiving a particular treatment, and what clinical management was used, in addition to what is dictated by the protocol.

Another part of my job is assessing side effects of patients on investigational drugs, because we may need to alter their treatment a bit to maintain the safety of the patient and the integrity of the trial. Trial protocols include very clear guidelines dictating what we can and can't do.

Research nurses play a vital role in the successful implementation of a clinical trial due to their intertwined link between research and clinical care. Their involvement in the entire research process from protocol concept, review and approval, conduction of the trial, including patient care, and reporting of data is essential.

How do your relationships with patients optimize their clinical trial experience?

Patients receive a lot of special attention from a research nurse when they're on a clinical trial. I'm seeing those patients at all their visits; I'm tracking and documenting their experience and condition the whole time. This gives them a sense of security during a time of anxiety when trying a new drug that might not be FDA-approved. They have the reassurance that they're not just going to be put on a new treatment without guidance and close monitoring. I think patients really appreciate that we're bringing them a specialized type of nursing.

What current MSK clinical trials in lymphoma are most compelling?

Therapies that use a patient's own immune system to fight their cancer, such as immunotherapies or bispecific antibodies, are really hot-button drugs right now. Often we combine two types of investigational drugs to see if they work better together than as single agents, which is exciting work. Patients are interested in therapies using their own immune system, because in many cases, they allow patients to go out and live relatively normal lives.

What are the biggest challenges you face in your role?

Many could benefit from education about clinical trials. This includes educating healthcare team members about timing of when to offer a clinical trial to a patient, and educating patients when they are trying to decide whether to enroll on a trial. Efforts need to focus on dispelling a common misunderstanding that a clinical trial is a last-ditch effort. It's actually the opposite. A patient can't enroll on a clinical trial unless they meet specific criteria, which includes in many cases that they're in good overall condition. Clinical trials give patients the opportunity to have access to some amazing, innovative novel drugs they might not otherwise get. Clinical research nurse's involvement in this education to colleagues and patients is invaluable. ■

Advanced Practice Providers Expand Access to Superb Patient Care

A PROJECTED SHORTAGE of oncologists in coming years has shifted attention to the ways advanced practitioners, such as physician assistants and nurse practitioners, can fill the void. Heather Hylton, PA-C, was brought to Memorial Sloan Kettering to help stay ahead of this curve.

Hylton, the Director of PA Services for the Department of Medicine, was recruited in 2012 by Sergio Giralt, MD, Chief of the Adult Bone Marrow Transplant Service, in large part to build and oversee the Department's PA program. It's a role that Hylton — who is both a PA and a classically trained musician — relishes because of the deep collaboration required.

After a six-year stint at Dana-Farber Cancer Institute in Boston, Hylton was only the second PA hired in MSK's Division of Hematologic Oncology, though PAs had been practicing at MSK for several decades. While most of her work responsibilities are administrative in nature, Hylton maintains a clinical practice on the inpatient adult BMT Service.

"Over a short period of time, we have grown to have more than 40 PAs in the Department of Medicine," she explains. "Alongside that, our PA student program has grown significantly as well. We had a few PA students completing clinical rotations in the Department in 2012, but this year have been able to offer more than 30 clinical rotations. We're helping train the future workforce."

> **"Whether NP or PA, it's not the letters after your name, but what you're bringing to the table that matters. That's the model we've taken."**
>
> HEATHER HYLTON

PROCESS STREAMLINED TO FORMALIZE ROLES

When Hylton arrived at MSK four years ago, neither she nor the PA already practicing in BMT could place orders for patients' chemotherapy in the computer system. Investigating further, Hylton found the reason for this is there had been no precedent. The revelation prompted immediate action, resulting in a collaborative effort to establish a basic competency for all advanced practice providers prescribing chemotherapy and biotherapy, thereby streamlining the training and improving quality of care.

"Part of my responsibility is to address clinical practice issues that may arise so we can make operations as streamlined as possible and seamless for our patients," she says. "I work very closely with NP leadership on matters involving advanced practice providers. This collaboration is key: whether NP or PA, it's not the letters after your name, but what you're bringing to the table that matters. That's the model we've taken."

Hylton's efforts to expand MSK's advanced practice workforce has also required close collaboration with Department of Medicine administration; Steven Martin, MD, Vice Chair of Clinical Affairs and Chief Medical Officer for the Department of Medicine; and service chiefs throughout the Department of Medicine, including those from Hematologic Oncology, Survivorship and Supportive Care, General Medicine, Solid Tumor and others. "It's about building teams and expanding access, which is so important," she says.

ADVANCED PRACTITIONERS LEAD KEY INITIATIVES

Hylton can readily point to several key cases demonstrating the role of advanced practitioners in expanding patients' access to optimal care. In the ambulatory Lymphoma practice, for example, two PAs have taken a lead role in the development of a survivorship clinic embedded within the Lymphoma practice. Advanced practice providers also staff a newly developed walk-in clinic at the ambulatory Lymphoma practice to see patients who need to be seen same-day but who do not necessarily need to be seen in an urgent care setting.

As another example, in the inpatient setting, the advanced practice providers on the Leukemia Service have a key role in caring for patients undergoing protocol-based therapy, including CAR T cell treatments. Likewise, the inpatient BMT advanced practice providers have a tremendous role in managing the day-to-day care of patients in one of the best transplant programs in the country.

"We may not necessarily decide what chemotherapy or treatment a patient will receive, but PAs and NPs must be knowledgeable about the different therapies and be proactive about patients' symptoms and how to treat them," she says. "This supportive care is the cornerstone of our clinical practice."

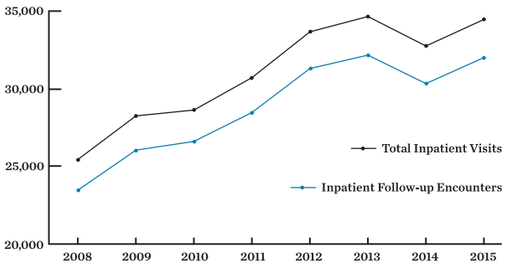
COLLABORATION CRUCIAL TO SUCCESS

Hylton circles back to the collaboration theme when reflecting on how her work and that of her advanced practice colleagues complements the duties of physicians, nurses and other staff members. She's proud of the wealth of advanced practitioners that MSK has very deliberately brought to the team. "I'm very fortunate to work with such fantastic colleagues across MSK," she says.

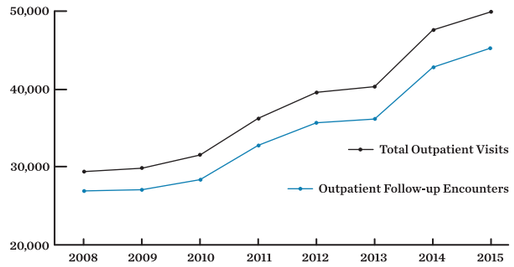
"We're all working toward a common goal, which is to do the most we can for our patients," Hylton says. "We can't achieve that by working in isolation. When we work together, the synergy that results greatly benefits our patients. It's very powerful." ■

Division of Hematologic Oncology Metrics

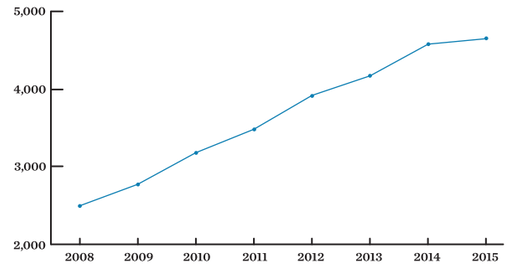
Inpatient | Total Visits



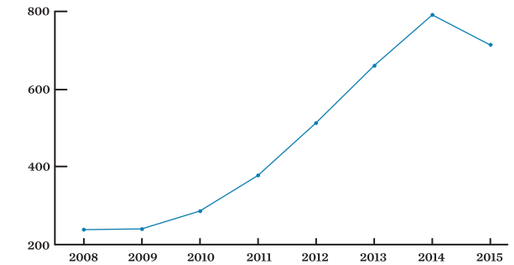
Outpatient | Total Visits



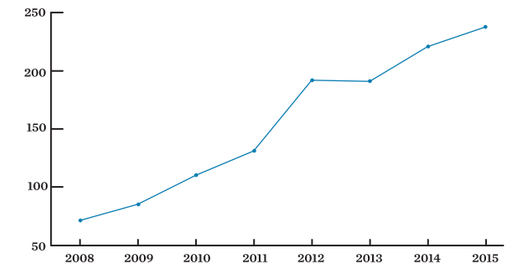
Outpatient | New Visits



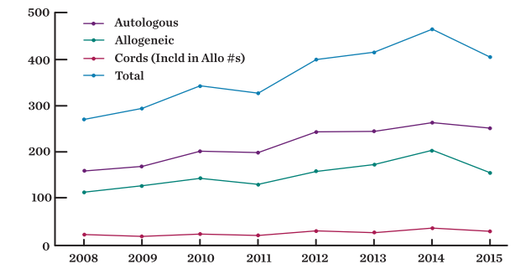
Clinical Trial Accruals



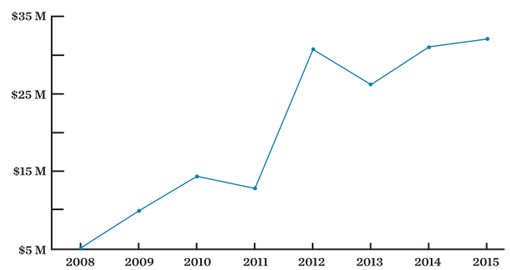
Peer-Reviewed Publications



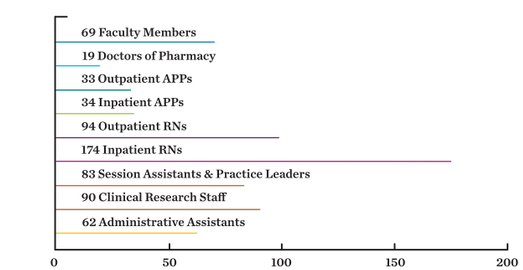
Number of Adult Bone Marrow Transplants



Awarded Grants & Contracts
(in millions)



Staff 2015



Paul Hamlin appointed Chief, Basking Ridge Medical Oncology Service

IN MARCH 2015, Dr. Paul Hamlin, MD, was appointed as Chief of the Basking Ridge Medical Oncology Service, in the Division of Network Medicine Services, Department of Medicine.

Dr. Hamlin is a highly respected clinical trialist and an outstanding clinician on the Lymphoma Service with a strong interest in the care of older patients with lymphoma. He has also demonstrated outstanding administrative skills as the Medical Director in the oversight of the administrative and clinical programs at E. 64th Street, implementing several innovative programs, and establishing close and effective working relationships with nursing and administrative leaders.

With the appointment of Dr. Han Xiao as Head of the Division of Network Medicine Services, a search committee was convened to identify candidates as service chiefs. Dr. Hamlin was recommended by the committee as the lead candidate based upon outstanding clinical skills, strong administrative ability, and excellence as a clinical trialist. His vision statement made clear his commitment to the institutional effort to expand clinical and clinical research opportunities in the network. He intends to maintain his interest in the hematological malignancies and will bring that expertise to Basking Ridge. ■

HEMATOLOGIC ONCOLOGY FACULTY CURRENTLY PRACTICING IN THE REGIONAL NETWORK:

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

* Primary location † Starting 2016

Expert Cancer Care Close to Home

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

MSK Bergen (Spring / Summer 2018)
225 Summit Avenue
Montvale, NJ 07645

MSK Commack
650 Commack Road
Commack, NY 11725

MSK Hauppauge
800 Veterans Memorial Highway
Hauppauge, NY 11788

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

MSK Monmouth (Fall 2016)
480 Red Hill Road
Middletown, NJ 07748

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

MSK Westchester in West Harrison
5000 Westchester Avenue
West Harrison, NY 10604

Agent Orange Linked to Increased Risk of MGUS in Some Vietnam Veterans

BY MIRIAM FALCO

US Air Force veterans who participated in the spraying missions of Agent Orange during the Vietnam War have a more than twofold increased risk of developing a condition called monoclonal gammopathy of undetermined significance, or MGUS, a precursor to multiple myeloma. An association between Agent Orange and multiple myeloma has been suspected based on other studies involving farmers and agriculture workers, but this study provides the first direct evidence linking Vietnam veterans exposed to Agent Orange with MGUS.

Agent Orange was an herbicide spayed during the Vietnam War to strip forests of their protective foliage. New research has linked US Air Force veterans involved in those spraying missions with an increased risk of MGUS.

FIFTY YEARS AFTER the US Air Force began spraying Agent Orange in Vietnam, new research shows that veterans exposed to the herbicide are more than twice as likely to develop monoclonal gammopathy of undetermined significance (MGUS), a precursor to multiple myeloma.

A team of researchers led by Ola Landgren, Chief of Memorial Sloan Kettering's Myeloma Service, analyzed serum samples from 459 US Air Force personnel involved in aerial herbicide spray missions during the Vietnam War, as well as 459 samples from veterans who served there at the same time but were uninvolved in the spraying missions.

All of these veterans served between 1962 and 1971, when the US military dropped more than 19 million gallons of herbicides in Southeast Asia during Operation Ranch Hand.

Researchers tested for the presence of MGUS and also concentrations of TCDD, a contaminant of Agent Orange that's been classified as a human carcinogen since 1997.

They found 7.1 percent of Ranch Hand veterans had MGUS, a precursor of multiple myeloma, compared with only 3.1 percent of the comparison group, says Dr. Landgren — a more than twofold higher risk. The risk of getting MGUS was significantly higher among veterans younger than 70 years of age. The researchers also found that those vets who developed MGUS had higher TCDD levels in their blood samples.

> "This provides the first direct scientific evidence that there is a link between Agent Orange and the development of multiple myeloma." OLA LANDGREN

"This provides the first direct scientific evidence that there is a link between Agent Orange and the development of multiple myeloma [in Ranch Hand participants]," Dr. Landgren explains. The findings were published in JAMA Oncology on September 3, 2015.

WIDE USE AND EXPOSURE

Agent Orange was the most widely used herbicide combination sprayed during the Vietnam War, according to a 2003 Department of Veterans Affairs report. Most adverse events linked to it are blamed on TCDD.

The herbicide was used to protect US troops on the ground by stripping the forests, thereby depriving enemy soldiers of protective foliage. Agent Orange was first used in 1965, according to a 2003 Department of Veterans Affairs report. More than 11 million gallons of the chemical were used as tactical herbicides.

Dr. Landgren advises Vietnam veterans to get a simple blood test to identify MGUS. Research shows that early detection of MGUS results in better outcomes for those who do develop multiple myeloma.

An association doesn't necessarily mean causation. But, as Nikhil Munshi, a multiple myeloma expert at Harvard School of Medicine, explained in an accompanying editorial:

"Although this study associated risk of MGUS with [Agent Orange] exposure, the fact that all [multiple myeloma] cases originate from MGUS provides the first scientific evidence for a direct link between multiple myeloma and Agent Orange exposure."

This new research was made possible by previous work Dr. Landgren led at the National Cancer Institute before coming to MSK. He and his colleagues studied data from more than 77,000 participants in the PLCO (Prostate, Lung, Colorectal, and Ovarian) Cancer Screening Trial, who were cancer-free at the start of the study. Seventy-one participants developed multiple myeloma during the study. Dr. Landgren and his team found that "virtually all multiple myeloma cases were preceded by MGUS."

Previous studies showed an association between pesticide exposure and an increased risk of MGUS and multiple myeloma, but "no studies [had previously] uncovered such an association in Vietnam War veterans," according to the JAMA Oncology study.

There are real clinical implications to be drawn, Dr. Landgren says, and a very specific group of people can and should be screened for MGUS. Even though not everyone with this precursor condition goes on to develop cancer, his work shows that everyone who has multiple myeloma had MGUS first. Prior work by Dr. Landgren and others shows that the risk of transformation from MGUS to multiple myeloma is about 1 percent per year; for example, 30 years of follow-up equals a 30 percent cumulative risk.

Dr. Landgren emphasizes the value of early detection and suggests that Vietnam veterans get a simple blood test to identify MGUS. That's because another recent study by Dr. Landgren and co-workers, also published in JAMA Oncology, shows that patients with MGUS who develop multiple myeloma during clinical monitoring have a 10 to 15 percent better overall survival and experience fewer complications than those with multiple myeloma who never received an MGUS diagnosis. ■

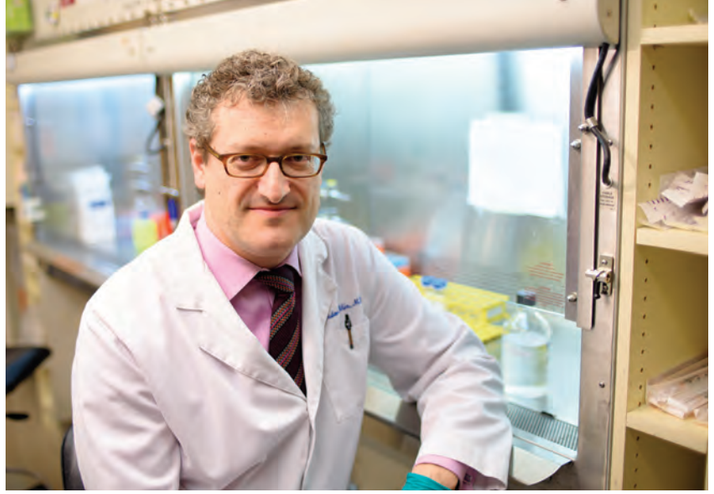
PUBLICATIONS REFERENCED:

1. http://www.ncbi.nlm.nih.gov/pubmed/26181017 Sigurdardottir EE, Turesson I, Lund SH, Lindqvist EK, Mailankody S, Korde N, Björkholm M, Landgren O, Kristinsson SY. The Role of Diagnosis and Clinical Follow-up of Monoclonal Gammopathy of Undetermined Significance on Survival in Multiple Myeloma. JAMA Oncol. 2015. 1(2):168-74. PMID: 26181017

2. http://www.ncbi.nlm.nih.gov/d/?term=Agent+Orange+Exposure+and+Monoclonal+Gammopathy+of+Undetermined+Significance+An+Operation+Ranch+Hand+Veteran+Cohort+Study Landgren O, Shim YK, Michalek J, Costello R, Burton D, Ketchum N, Calvo KR, Caporaso N, Raveche E, Middleton D, Marti G, Vogt RF Jr. Agent Orange Exposure and Monoclonal Gammopathy of Undetermined Significance: An Operation Ranch Hand Veteran Cohort Study. JAMA Oncol. 2015. 1(8):1061-8. PMID: 26335650

Alexander Lesokhin, MD

Assistant Attending, Myeloma Service



ALEXANDER LESOKHIN points to myeloma's "Darwinian" ability to adapt to therapies — eventually diminishing their potency — as one of the biggest obstacles remaining in finding a cure. But Dr. Lesokhin, who came to Memorial Sloan Kettering in 2005 as an oncology fellow and joined the Division of Hematologic Oncology in 2008, has only accelerated his efforts to identify novel treatments in response to myeloma's stealthy ways.

An assistant attending in the Myeloma Service, this physician-scientist develops innovative methods to unleash the power of the immune system to treat cancer by releasing the "brakes" that typically inhibit that response. Much of his lab research has focused on characterizing myeloid-derived suppressor cells (MDSC), a varied group of immune cells originating in bone marrow, and determining how they can help tumors evade the immune response. A relatively new class of drugs that release the brakes on the immune response, called immune checkpoint blockade, have also become a major focus of Dr. Lesokhin's translational research efforts.

The Myeloma Service's consistent growth, including a 35% increase in patient visits in 2015, has heightened the potential impact of his research. Partly as a result of his and colleagues' efforts, the median survival for myeloma patients has been steadily climbing, now extending seven to eight years.

"When I started in the laboratory, immunotherapy was something that had a century-old history, much of it at MSK, and there was a lot of potential on paper but there weren't a lot of successes," he recalls. "And the question I set out asking was, why not?"

Here, Dr. Lesokhin highlights the array of new immunotherapies being tested in myeloma and how his work with patients fuels his research.

How did you zero in on myeloid cells as being potentially pivotal in tumor immunotherapy?

Myeloid cells are important in healing responses, such as wound healing, but they also tamp down T-cell responses. They are an important part of how a tumor such myeloma or other tumor types develop an environment to support their growth and survival. I started looking in preclinical models at what those cells do, and in parallel, the area of regulating T-cell activation through the use of antibodies, or drugs, that release the brakes on T-cell responses — immune checkpoints. Through my work with Dr. Jedd Wolchok, a wonderful mentor, I was able to take this work from lab animals to people. In patients, we looked at how myeloid cells affected response to these drugs, namely ipilimumab, which blocks a T cell-inhibiting protein named CTLA-4. We found a particular group of these myeloid cells were quite important in identifying patients susceptible to this drug, and now we've done a larger analysis essentially showing a prolonged survival time in those with a low quantity of these myeloid cells. This work is ongoing, and additional larger studies will be completed soon.

> **"I think it's up to centers with focused expertise, such as ours, to help guide treatment for patients within the myeloma community."**
>
> PHYSICIAN-SCIENTIST ALEXANDER LESOKHIN

Talk about the most compelling new immunotherapy treatments for myeloma and what they involve:

It's been exciting to see how another immune checkpoint directed therapy, the PD-1 inhibitor nivolumab, has progressed. We studied nivolumab in a signal-seeking basket study — which uses a drug targeting a specific mechanism, not a specific disease — to evaluate the efficacy of nivolumab across a variety of hematologic cancer subtypes. We found really remarkable activity in Hodgkin lymphoma, where there was an 87% response rate in patients who had failed the majority other therapies.

In myeloma, this drug produced interesting responses, and more will come as we continue to study these patients. One thing that's become clear to us and others was that nivolumab seemed to sensitize myeloma patients to traditional myeloma drugs, which has provided rationale for trials studying checkpoint blockade in combination.

What current research efforts do you feel are especially promising?

One trial we'll be starting soon will combine stem cell transplant with immune checkpoint blockade, to modulate how the immune system sees myeloma. It will entail a series of steps, including giving patients immunotherapy drugs, collecting their T-cells before transplant, clearing their body of as much myeloma as possible, and giving their T-cells back to them with additional checkpoint blockade. It's a very exciting study for us because it will evaluate whether we can use this transplant-based therapy in combination with checkpoint blockade as a platform for directed anti-myeloma therapies that enhance T-cell activation and lead to long-term disease control.

Why should myeloma patients seek care at MSK instead of another institution or private practice?

Myeloma has become such a complicated therapeutic space, with five new drugs approved over the last year and new studies and drugs constantly in development. Our treatment paradigms are changing from year to year, so I can imagine that keeping pace with all the latest research developments is really a challenge. I think it's up to centers with focused expertise, such as ours, to help guide treatment for patients within the myeloma community.

At MSK, we have state-of-the-art assays to guide clinical care, such as minimal residual disease (MRD) assessment, with which we can really evaluate whether disease is present at the lowest levels. We know from many studies that individuals who achieve MRD negativity are the ones who do the best, so we can really personalize our treatment approaches and treat patients in adaptive ways using standard of care drugs or our pipeline of clinical trials to see if we can achieve this endpoint for all our patients, and if this will result in long term disease control.

How does your patient care influence your research approach?

I don't think I would know what questions to ask if I weren't seeing patients. The research questions I've asked over the past couple of years have really grown out of clinical observations in the context of a particular treatment. As an example, in one observation we made in the blood of several patients we treated with anti-PD1s, we went to the lab and modeled this observation. Being able to look at this effect in animal models allows us to potentially dissect a variety of mechanistic possibilities and then look back to patients for confirmation. This way we can understand why we're seeing something in the clinic, and perhaps this will help develop new ways to treat patients. How fun is that? It's really cool. ■

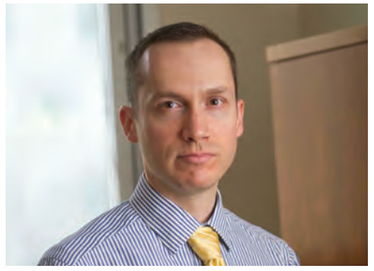
American Society of Hematology (ASH) Meeting 2015, Orlando Florida

THE 57TH ANNUAL MEETING of the American Society of Hematology took place in Orlando, FL in December 2015. Our faculty was well-represented with over 150 abstracts, 54 of which were selected for oral presentation.

The Memorial Hospital Alumni Society hosted their 8th annual ASH reception at the Rosen Centre Hotel in Orlando, FL. The reception was well attended by MSK alumni, current faculty, fellows, and colleagues from other institutions as well as invited guests of the Division of Hematologic Oncology.

Before the ASH Meeting, Dr. Marcel van den Brink and Dr. Edmund Waller of the Winship Cancer Institute of Emory University, co-chaired the 4th Annual BMT Winter Workshop at the University of Central Florida Rosen College. The workshop was attended by 200 physicians and scientists and consisted of short presentations regarding unpublished recent research on Hematopoietic Stem Cell Transplantation. ■

TOP LEFT: Philip Caron, Philip Shulman, Craig Moskowitz, Pamela Drullinsky; TOP RIGHT: Renier Brentjens, David Scheinberg, Kevin Curran, Rubin Benjamin; CENTER LEFT: Valkal Bhatt, Troy Horvat, Aaron Viny; CENTER RIGHT: Neha Mehta-Shah, Mark Geyer, Allison Rosenthal, Jacob Soumerai, Gunjan Shah, Michael Scordo, Justin Taylor; BOTTOM LEFT: Anita Kumar, Parastoo Dahi, Leyla Shune; BOTTOM RIGHT: Alex Lesokhin, Billel Gasmi, David Chung, Eric Smith, Sham Mailankody



Benign Hematology Treatment Crucial to Cancer Outcomes

THE BLEND OF PATIENT CARE and technical expertise inherent in practicing hematology has gelled into the ideal career path at Memorial Sloan Kettering for Simon Mantha, MD, MPH. An associate attending physician in the Hematology Service, Dr. Mantha came to MSK in 2012 from a small Massachusetts hospital, lured by the prospect of doing more and bigger research in a field he finds fascinating.

With a background in vascular medicine and research interests that veer heavily into venous thromboembolism (VTE) — a clotting condition comprised of deep vein thrombosis and its byproduct, pulmonary embolism — Dr. Mantha feels MSK is the ultimate environment to delve into benign hematologic disorders that can prove just as dangerous to patients as cancer itself.

"Hematology is both personal and technical, things I really like a lot," he says. "It's very important because it's part of supportive care in cancer — it helps prevent complications, and that really helps improve outcomes."

PROMISING RESEARCH ON NEWER ANTICOAGULANT

Dr. Mantha's practice encompasses the full spectrum of blood-related issues — topped by blood clots, low blood counts, hemorrhage, and anemia — cancer patients may experience either because of their malignancy or its treatment. Cancer is a major risk factor for VTE, accounting for up to one-fifth of cases, and approximately 80% of Dr. Mantha's consults in the Hematology Service pertain to the use of anticoagulants in patient care.

"Thrombosis, or clotting, is by far the most common problem," he says. "Bleeding is much less of a problem overall, and anemia is very common too, but typically not lethal."

Because of the prevalence of abnormal clotting among cancer patients — as well as Dr. Mantha's interest in it — he has plunged into research investigating the use of new anticoagulants. One important effort centers on a Quality Assurance Initiative to use the oral anticoagulant rivaroxaban, known by the brand name Xarelto, to treat cancer-associated thrombosis.

The U.S. Food and Drug Administration approved rivaroxaban in 2012 for the treatment of pulmonary embolism and deep vein thrombosis, but a knowledge gap remained regarding its use in cancer patients. Many with cancer-related clotting problems had previously been prescribed low molecular weight heparin, an injectable anticoagulant that was painful, expensive and inconvenient to receive.

An abstract presented by Dr. Mantha and a bevy of MSK colleagues in December 2015 at the American Society of Hematology annual meeting indicated rivaroxaban was just as safe and effective as low molecular weight heparin among the first 200 patients entered into the Quality Assurance Initiative, and patient burden was lower.

"Obviously it's much more convenient to take a pill once a morning than take injections twice a day," he says. "We have found that rivaroxaban is likely as safe and effective, but we haven't proven it 100% and need to follow up in more patients."

> **"If the work I produce ends up changing the standard of care for venous thromboembolism (VTE), it can impact thousands of patients ..."** SIMON MANTHA

PROGRESS IN TREATING ARRAY OF CANCER-ASSOCIATED BLOOD DISORDERS

Dr. Mantha is also part of pioneering efforts at MSK to tackle low platelet counts associated with chemotherapy, or thrombocytopenia, which can lead to abnormal bleeding and prevent patients from staying on their intended chemotherapy dose and schedule.

Launched by Hematology Service Chief Gerald Soff, MD, a rigorous clinical study examining the use of the platelet-boosting drug romiplostim — known commercially as Nplate — has been undertaken at MSK. Dr. Soff initially published more preliminary data showing that all 20 patients treated with Nplate for thrombocytopenia experienced a benefit and were able to resume full-dose chemotherapy.

"We've seen our experience with Nplate really grow and we're very comfortable using it now," Dr. Mantha says. "That's an advance."

Some aspects of benign hematology still need more of a research emphasis, Dr. Mantha says. This list includes an uncommon disease known as atypical hemolytic-uremic syndrome, which causes abnormal blood clots to form in the small vessels of the kidneys, potentially triggering kidney failure. MSK's renown equates to more cases of this vexing condition landing on its doorstep.

While all his benign hematology work proves fulfilling to Dr. Mantha, he hopes in particular that his efforts to more effectively treat VTE will have widespread, lasting impact.

"If the work I produce ends up changing the standard of care for VTE, it can impact thousands of patients all over the world because of the frequency of the problem," he says. "If I help the field, I help many individuals." ■

The Mortimer J. Lacher Lecture & Fellows Conference

TOP ROW LEFT TO RIGHT: Aaron Viny, Melody Smith, Colette Owens, Eric Smith, Marcel van den Brink; FRONT ROW LEFT TO RIGHT: Neha Mehta-Shah, Charles Sawyers, Mortimer Lacher, Connie Batlevi

ON MAY 15, 2015, the Division held its annual Mortimer J. Lacher Lecture and Fellows Conference. 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 and currently serves as a Consultant in MSK's Department of Medicine. Every year, The Lymphoma Foundation provides funding for Medical Oncology/Hematology fellows at MSK and specific projects in the laboratories of MSK physician scientists.

The Sixth Annual Mortimer J. Lacher Lecture, "Reflections on Precision Medicine," was delivered by Charles L. Sawyers, MD, Investigator at Howard Hughes Medical Institute, and Chairman of the Human Oncology & Pathogenesis Program at Memorial Sloan Kettering Cancer Center. ■

THE 2015 LACHER FELLOWS ARE LISTED BELOW ALONG WITH THEIR ABSTRACT TITLES:

- **Neha Mehta-Shah, MD**
  Mentor: Steven Horwitz, MD
  Assessing the Importance of Epigenetic Modification in T-cell lymphomas: A Phase Ib/IIa Trial of Romidepsin and Lenalidomide in Patients with Relapsed/Refractory Lymphoma and a Phase Ib/IIa Study of Romidepsin, Lenalidomide and Carfilzomib in Relapsed Refractory Lymphoma
- **Melody Smith, MD**
  Mentor: Marcel van den Brink, MD, PhD
  CD19-CAR Donor T cells Exert Potent Graft-versus-Lymphoma Activity without Graft-versus-Host-Disease
- **Eric Smith, MD, PhD**
  Mentor: Renier Brentjens, MD, PhD
  CAR T-cells for Plasma Cell Dyscrasias
- **Aaron Viny, MD, MS**
  Mentor: Ross Levine, MD
  The Role of the Cohesin Complex in Oncogenic Transformation of AML
- **Colette Owens, MD**
  Mentor: Paul Hamlin, MD
  Prednisone and Rituximab Prephase May Decrease Early Toxicity in Older DLBCL Patients (pts) Receiving RCHOP within an NHL Specific Comprehensive Geriatric Assessment (CGA) Trial
- **Connie Batlevi, MD, PhD**
  Mentor: Anas Younes, MD
  Functional Genomics in Lymphoma Management
- **John Cuaron, MD**
  Mentor: Joachim Yahalom, MD, FACR
  Identification of Gene Expression Signatures to Predict the Response of Low-grade Lymphomas to Very Low Dose Radiation Therapy

TOP LEFT: John Cuaron; TOP RIGHT: Charles Sawyers; BOTTOM LEFT: Connie Batlevi; BOTTOM RIGHT: Colette Owens

Highlights | Nurses and Physician Assistants

HIGHLIGHTS

- **Teresa Scardino, PA-C, MPAS, Michelle Wisniewski, MS, PA-C, Sharyn Kurtz, PA-C, MA, MPAS, Jason Carter, MSHS, MPH, PA-C,** and **Nadia Kralovic, MS, PA-C** have been an integral part of the Lymphoma Walk In Clinic that launched in January 2015 to reduce UCC admissions. Their efforts were recognized at the 2015 Quality and Performance Improvement Fair with the Judges' Honor Award.
- **Teresa Scardino, PA-C, MPAS, Michelle Wisniewski, MS, PA-C, Sharyn Kurtz, PA-C, MA, MPAS, Jason Carter, MSHS, MPH, PA-C,** and **Nadia Kralovic, MS, PA-C** were featured in a MSKLife Article in 2015 titled: "Physician Assistants on MSK's Lymphoma Service: Changing How Care is Delivered": https://one.mskcc.org/sites/pub/MSKLife/Pages/PAs_Lymphoma.aspx.
- **Heather Hylton, MS, PA-C** was elected as a Director at Large for the Association of Physician Assistants in Oncology for 2015-2016. She also led a Capitol Hill Day initiative in September 2015 for the Association of Physician Assistants in Oncology where nearly 40 PAs from 14 states advocated on Capitol Hill for robust funding support for the National Institutes of Health/National Cancer Institute and for federal oral parity legislation.
- **Apryl Sarabia, MS, PA-C, Carolyn Canonica, MMSc, PA-C, Elaina Preston, MPH, MSHS, PA-C, Whitney Quitta, MS, PA-C, Catherine Bender, MPAC, PA-C, Abigail Staible, MMS, PA-C, Teresa Scardino, PA-C, MPAS, Sharyn Kurtz, PA-C, MA, MPAS, Natalie Concannon, MMSc, PA-C**, and **Heather Hylton, MS, PA-C** served as primary preceptors for 11 PA students who rotated in Adult BMT and Medical Oncology during calendar year 2015.
- In February 2015, the outpatient BMT and Leukemia APPs successfully implemented an independently operated bone marrow clinic on main campus serving the BMT, Hematology, and Leukemia Services. Approximately 200 bone marrows are performed monthly.

ALL NAMES ARE LISTED LEFT TO RIGHT. TOP LEFT: Sheila Kenny, Meighan Palazzo, Kara Mosesso; TOP RIGHT: Joanne Taylor, Barbara Morcerf, Jessie Dechene, Jason Chan; BOTTOM LEFT: Ginevra Castagna, Hannah Rigney, Jennifer McLoughlin, Megan Rambone, Kim Ford; BOTTOM RIGHT: UPPER ROW: Teresa Scardino, Susan McCall, Jason Carter, Emily Panzner; LOWER ROW: Sharyn Kurtz, Jillian Solomon, Nadia Kralovic, Peggy Lynch

- **Karen Collum, DNP, RN, OCN** presented on "Transplant Continuing Education Activities — Who Does This Affect & Examples on How to Comply" at the ASBMT Tandem Meeting in February 2015. In May of 2015, Karen Collum also completed her degree for her Doctorate of Nursing Practice in Executive Leadership.
- The Outpatient Chemotherapy nurses and Leukemia Office Practice Nurses/NPs successfully transitioned care for patients receiving HiDac for consolidation to the outpatient setting. Patients receive both doses of chemotherapy via a CADD pump at home. Also, in July of 2015, they opened 2 new infusion suites, Suites 5 and 6 in the Haupt Building on the 4th floor. One is for Chemo 1275 and one is supporting the Red Team.
- The M8, M9 and M14 Nursing Teams were all awarded with the Spirit of Transplant Award in June of 2015.
- The Outpatient Chemotherapy nurses and Leukemia Office Practice Nurses/NPs are in the midst of their first home care visit with a patient on the Pilot Trial for Homebound Transplant and everything is running smoothly so far.

PUBLICATIONS

- **Ranaghan CP**, Boyle K, Fraser P, Meehan M, Moustapha S, Concert C. *JBI Database System Rev Implement Rep.* 2015 Sep 16;13(8):54-69. doi: 10.11124/jbisrir-2015-2323. The effectiveness of a patient navigator on patient satisfaction in adult patients in ambulatory care settings: a systematic review protocol.
- Yuan A, **Kurtz SL**, Barysauskas C, Pilotte AP, Wagner AJ, Treister NS. *Oral Oncology.* 2015. 51 (11): 1026-33. Oral Adverse
Events in Cancer Patients Treated with VEGEF- Directed Multi-targeted Tyrosine Kinase Inhibitors.
- **Hylton H, Featherstone C, and Sauter C.** *Biology of Blood Marrow Transplant.* 2015. 21(2):5355-56. Management of cytokine release syndrome in patients undergoing chimeric antigen receptor modified T cell therapy following autologous stem cell transplant.
- **Heather Hylton, MS, PA-C**. *ASCO Daily News.* 2015 June 1. Professional Burnout and the Oncology Workforce: A Perspective on Physician Assistants and Nurse Practitioners.
- **Kara Mosesso, MSN, RN, ANP-BC, AOCNP.** *American Journal of Nursing.* 2015 Nov. Adverse Late and Long-Term Treatment Effects in Adult Allogeneic Hematopoietic Stem Cell Transplant Survivors.

PRESENTATIONS

- **Sharyn Kurtz, PA-C, MA, MPAS** presented "A Matter of Life and Death: Physician Assistant Attitudes on Physician Assisted Dying" at the MSK Ethics Committee in November 2015.
- **Sharyn Kurtz, PA-C, MA, MPAS** presented "Bioethics: A brief history, review, and case presentation for PAs" at Memorial Sloan Kettering Physician Assistant Grand Rounds in January 2015 and at the New York State Society of Physician Assistants Annual Conference in October 2015.
- **Sharyn Kurtz, PA-C, MA, MPAS** presented a poster "A Matter of Life and Death: Physician Assistant Attitudes on Physician Assisted Dying" at the 17th Annual American Society for Bioethics and Humanities Annual Meeting in October 2015.
- **Heather Hylton, MS, PA-C, Catherine Featherstone, FNP, BC,** and **Craig Sauter, MD** presented a poster "Management of cytokine release syndrome in patients undergoing chimeric antigen receptor modified T cell therapy following autologous stem cell transplant" at the BMT Tandem Meetings in 2015.
- **Bernadette Cuello, Cornelia Melendez, Christopher Brooks, Margaret Brennan,** and **Elizabeth Rodriguez** presented "Transitioning high dose chemotherapy for acute myeloid leukemia to the outpatient setting improves patient experience" at the Oncology Nursing Society National Congress in May 2015. ■

Highlights | Department of Pharmacy

PUBLICATIONS IN 2015

- **Afifi S,** Michael A, Azimi M, **Rodriguez M,** Lendvai N, Landgren O. Role of Histone Deacetylase Inhibitors in Relapsed Refractory Multiple Myeloma: A Focus on Vorinostat and Panobinostat. *Pharmacotherapy.* 2015 Dec;35(12): 1173-88.
- **Buie LW, Pecoraro JJ, Horvat TZ,** and **Daley RJ.** Blinatumomab: A First-in-Class Bispecific T-cell Engager for Precursor B-cell Acute Lymphoblastic Leukemia. *Ann Pharmacotherapy.* 2015;49:1057-67.
- **Dang TO,** Ogunniyi A, Barbee MS, Drilon A. Pembrolizumab for the treatment of PD-L1 positive advanced or metastatic non-small cell lung cancer. *Expert Rev Anticancer Ther.* 2015 Dec 10:1-8.
- **Horvat TZ, Adel NG, Dang TO,** et al. Immune-related adverse events, need for systemic immunosuppression, and effects on survival and time-to-treatment failure in melanoma patients treated with ipilimumab at Memorial Sloan Kettering Cancer Center. *J Clin Oncol.* 2015 Oct 1;33(28):3193-8.
- **Horvat TZ, Pecoraro JJ, Daley RJ, Buie LW,** et al. Erwinia Asparaginase Safety and Feasibility during Therapy for Acute Lymphoblastic Leukemia in Adult Patients with Pegaspargase Hypersensitivity or Severe Toxicity. *Blood* 2015 Dec 10;126(23):4915.
- Shoushtari AN, Postow MA, **Horvat TZ,** et al. Safety of pembrolizumab (pem) in patients (pts) who stopped ipilimumab (ipi) due to immune-related adverse events. *J Clin Oncol.* 33, 2015 (suppl; abstr e20023).
- Barbee M, Ogunniyi A, **Horvat TZ, Dang TO** et al. Current Status and Future Directions of the Immune Checkpoint Inhibitors Ipilimumab, Pembrolizumab, and Nivolumab in Oncology. *Ann Pharmacotherapy.* 2015 Aug;49(8):907-37.

POSTER PRESENTATIONS IN 2015

- **King Amber,** Barbee Meagan, **Adel N.** et al. "Efficacy of Discontinuation or Omission of Vincristine in the Rituximab, Methotrexate, Vincristine, and Procarbazine (R-MVP) Regimen for First Line Treatment of Primary CNS Lymphoma (PCNSL)." Hematology/Oncology Pharmacy Association 11th Annual Conference. Austin, TX. March 2015.
- **Bhatt Valkal,** Leyla Shune, Emily Lauer, Marissa Lubin, Sean Devlin, Andromachi Scaradavou, Nancy A. Kernan, Sergio Giralt, Rekha Parameswaran, Miguel-Angel Perales, Doris M. Ponce, Gerald A. Soff, Juliet Barker. "Autoimmune Hemolysis (AH) & Immune Thrombocytopenic Purpura (ITP) after Cord Blood Transplantation (CBT) May be Life-Threatening & Warrant Early Therapy with Rituximab." American Society for Blood and Marrow Transplantation Tandem Meeting, San Diego, CA, March 2015.
- **Bhatt Valkal,** Michael Scordo, Meier Hsu, Antonio M. Omuro, Lisa DeAngelis, **Andrew Lin,** Matthew J. Matasar, Parastoo B. Dahi, Craig H. Moskowitz, Sergio A. Giralt and Craig S. Sauter. "Outcomes of pharmacokinetically (PK) directed busulfan in combination with thiotepa and cyclophosphamide (TBC) conditioning with HDT-ASCT in patients with primary and secondary CNS Lymphoma." American Society of Hematology 57th Annual Meeting. Orlando, FL. December 2015.
- **Bhatt Valkal,** Meighan Palazzo, Kathleen Kilroy, Patrick Hilden, Molly Maloy, Juliet N. Barker, Hugo R. Castro-Malaspina, David J. Chung, Parastoo B. Dahi, Katharine C. Hsu, Alan M. Hanash, Ann A. Jakubowski, MD, Robert R. Jenq, Guenther Koehne, Heather Landau, Esperanza B. Papadopoulos, Miguel-Angel Perales, Craig S. Sauter, Roni Tamari, Marcel van den Brink, James W. Young, Sergio A. Giralt and Doris M. Ponce. "Low dose unfractionated heparin is a safe strategy for prevention of hepatic SOS in adult allogenic stem cell recipients."

BMT CLINICAL PHARMACY SPECIALISTS
LEFT TO RIGHT: Tony Proli II, Andrew Lin, Valkal Bhatt, Kristen Beyer
NOT PICTURED: Carmen Lau, Meagan Griffin

LEUKEMIA CLINICAL PHARMACY SPECIALISTS
LEFT TO RIGHT: Troy Horvat, Larry Buie, Amber King, Josh Pecoraro, Ryan Daley

LYMPHOMA & MULTIPLE MYELOMA CLINICAL PHARMACY SPECIALISTS
LEFT TO RIGHT: Thu Dang, Salma Afifi, Tim Peterson, Mabel Rodriguez, Laura Tang
NOT PICTURED: Kristen Poppiti

American Society of Hematology 57th Annual Meeting. Orlando, FL. December 2015.

- **Peterson Tim, Andrew Lin,** Patrick Hilden, Sean Devlin, **Nelly G Adel,** and Jae H Park. "Effects of Obesity on the Efficacy and Toxicity of Induction Chemotherapy in Adult Acute Lymphoblastic Leukemia (ALL)." American Society of Hematology 57th Annual Meeting. Orlando, FL. December 2015.
- Reiss SN, **Buie LW, Adel NG,** and Douer D. "Effect of serum albumin levels on methotrexate (MTX) clearance and toxicity." Hematology/Oncology Pharmacy Association 11th Annual Conference. Austin, TX. March 2015.
- Reiss SN, **Buie LW, Adel NG,** et al. "Hypoalbuminemia is significantly associated with increased clearance time of high doses of methotrexate." American Society of Hematology 57th Annual Meeting. Orlando, FL. December 2015.

NATIONAL PRESENTATIONS IN 2015

Salma Afifi:
- Invited Speaker for Debates in Hematology Transplant versus no Transplant for Multiple Myeloma Patients at the Hematology/Oncology Pharmacy Association (HOPA) 11th Annual Meeting in Austin, TX.

Larry Buie:
- Invited speaker for the Chronic Lymphocytic Leukemia Review at the Hematology/Oncology Pharmacy Association (HOPA) 11th Annual Meeting in Austin, TX.
- Invited speaker at University of Illinois at Chicago College of Pharmacy, "Immunologic Therapies for Hematologic Malignancies Targeting Cancer: Annual Update in Oncology Pharmacy."
- Invited speaker for the Barbara M. DiLascia Oncology Lecture Series at Albany college of Pharmacy and Health Sciences, "Epigenetic Modification and Peripheral T-Cell Lymphomagenesis: Understanding the Role of Histone Deacetylase Inhibitors (HDACIs)".

NATIONAL COMMITTEE REPRESENTATION

Valkal Bhatt:
- Served as a member of the Educational Committee for the American Society for Blood and Marrow Transplantation (ASBMT).

Larry Buie:
- Served as a member of the Council of Continuing Education for the Hematology/Oncology Pharmacy Association (HOPA).
- Served as the Hematology Oncology Secretary/Treasurer for American College of Clinical Pharmacy (ACCP) Practice and Research Network.
- Served as Network Facilitator for Oncology with the American Society of Health-Systems Pharmacists (ASHP).

Mabel Rodriguez:
- Served as a member of the Session Proposal Review Work Group for the Hematology/Oncology Pharmacy Association (HOPA).

SPECIAL AWARDS

Valkal Bhatt:
- Valkal was granted the "Spirit of Transplant" Award 2015. It was granted for the first time to a Clinical Pharmacy Specialist by the Department of Medicine, Hematology Division, at MSK in New York.

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

- **Tony Proli II, Andrew Lin, Valkal Bhatt, Kristen Beyer, Larry Buie, Josh Pecoraro, Ryan Daley, Thu Dang, Salma Afifi,** and **Mabel Rodriguez** successfully continued their board certification in oncology pharmacy (BCOP).
- **Valkal Bhatt** successfully continued his board certification in pharmacotherapy (BCPS).
- New BCOP certifications for 2015 included **Troy Horvat**. ■

Transplant Survivors Celebrate Life

THE 20TH ANNUAL Blood and Marrow (BMT) Survivors Celebration on October 21, 2015 brought together 325 recipients of blood and marrow transplants and their donors, family members and friends, doctors, nurses, and other MSK staff. The event, intended to honor the courage and continued success of survivors, included a short speaking program, live jazz music, food, and drinks. The joyous atmosphere keeps participants coming back year after year to see fellow survivors and members of their care team who supported them through their transplant process. ■

TOP: Dr. Sergio Giralt; BOTTOM LEFT: Dr. Juliet Barker; BOTTOM RIGHT: Dr. Richard O'Reilly

Dr. Marcel van den Brink, Dr. Sergio Giralt

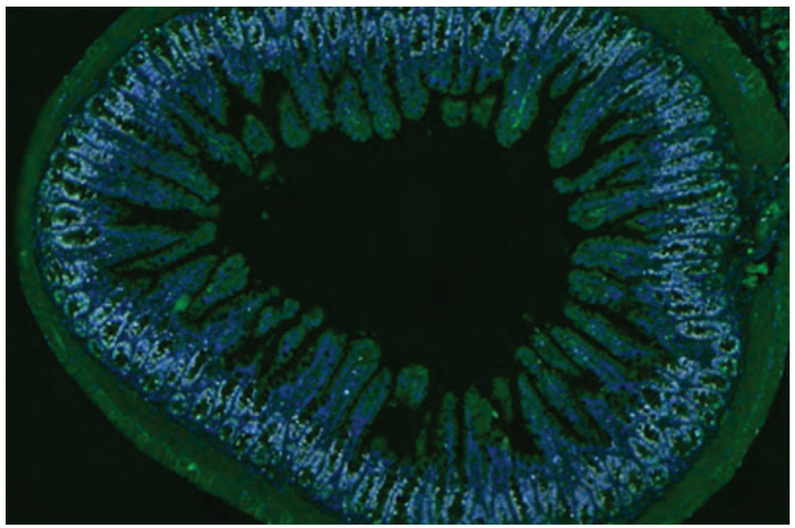
2015 Richard O'Reilly Stem Cell Transplant Lectureship

ON JUNE 24, 2015, the annual Richard O'Reilly Stem Cell Transplant Lecture was delivered by Dr. Marcel van den Brink. This lectureship pays tribute to one of the most distinguished physicians within the field of bone marrow transplantation, Dr. Richard J. O'Reilly, Chair of the Department of Pediatrics, Chief of the Pediatric Bone Marrow Transplant Service and Claire L. Tow Chair in Pediatric Oncology Research at MSK.

In his talk, Dr. van den Brink discussed the emerging role of the composition of the intestinal flora on critical outcomes in patients in allogenic bone marrow transplant patients, such as graft-versus-host disease, infections and malignant relapse. ■

Immune System Molecule Could Become New Treatment for Graft-Versus-Host Disease

BY JIM STALLARD



This cross section of a mouse intestine shows dividing cells (stained white) in the epithelial layer of the intestine, which lines the organ. These proliferating cells help restore intestinal tissue after damage from graft-versus-host disease (GVHD).

Graft-versus-host disease (GVHD) is a complication of blood and marrow stem cell transplantation. A new study reveals how the patient's immune system restores the intestinal lining following damage from GVHD and points to a strategy for a potential therapy to alleviate the effects.

GRAFT-VERSUS-HOST DISEASE (GVHD) is a major complication of bone marrow and blood stem cell transplantation. Although these transplants can cure patients with leukemia, lymphoma, or other blood disorders by replacing diseased blood-forming cells with healthy ones, GVHD can seriously impair recovery and even cause death.

Memorial Sloan Kettering researchers are studying how the intestinal tract heals from GVHD in hopes of developing new treatments for this serious condition. In a study published recently in Nature, an MSK team reports a discovery on how the patient's immune system helps repair intestinal damage caused by GVHD. The findings also suggest that drugs based on a molecule from the immune system could be used as an effective GVHD treatment.

DONATED TISSUE ATTACKS

GVHD occurs after a transplant when donor immune cells called T cells recognize the recipient's tissue as foreign and attack it. This complication can damage the liver, skin, digestive tract, or other organs. One of the most common sites of injury in GVHD is a section of the intestine called the epithelial layer, which lines the organ.

MSK physicians have pioneered a groundbreaking procedure for reducing GVHD risk by removing T cells from the group of donor cells prior to the transplant. However, not every patient can receive this type of transplant, and it has risks of its own.

Memorial Sloan Kettering physician-scientist Alan Hanash, who treats blood stem cell transplant patients, suggests the search for new therapies may benefit by expanding focus beyond the donor T cells to find ways to boost tissue repair after damage occurs.

"Much of the work in our field has centered on suppressing T cells without a lot of understanding of what's actually happening in the tissues," he says. "Our research group has begun concentrating on how the tissues are being damaged and, more importantly, how they recover from that damage."

AN UNEXPECTED IMMUNE SYSTEM ROLE

In 2012, Dr. Hanash and Marcel van den Brink, Head of the Division of Hematologic Oncology, discovered that an immune signaling molecule called interleukin-22 (IL-22) helps the intestines recover from GVHD damage.

"It's a very exciting development, because we have a way to treat GVHD using a completely different approach than any that has been tried." ALAN HANASH

Immune cells that can produce IL-22 reside within the intestines, ready to respond when needed after infections or tissue damage. These cells help protect the body against infections and maintain the barrier between intestinal tissue and bacteria.

In the 2012 study, the MSK team discovered that these immune cells have another function: after the intestinal epithelial cells are damaged — as in GVHD — IL-22 also somehow protects the intestinal stem cells necessary for maintaining the epithelial layer. However, how this happens was unclear.

"There are multiple epithelial cell types in the intestinal tract," Dr. Hanash says. "There are the mature intestinal epithelial cells, which are maintained by the stem cells, and there are niche cells that help to nurture and support the stem cells. We didn't know whether IL-22 was acting only on mature cells, directly targeting the stem cells, indirectly helping the stem cells by promoting the function of the supportive niche cells — or perhaps all of these things."

DIRECT STIMULATION OF STEM CELLS

Fast-forward to now: In the new study, Dr. Hanash's team found that IL-22 acts directly upon the intestinal stem cells to stimulate creation of new intestinal cells.

"Normally, the stem cells are able to maintain and replenish the tissue sufficiently," Dr. Hanash says. "We now believe that when the intestinal epithelial tissue is damaged, IL-22 gets turned on and directly signals the stem cells to go into overdrive to promote recovery of the tissue, indicating that we're no longer in maintenance mode — we're now in recovery mode."

The researchers used both mouse models and human tissue to study epithelial regeneration. This approach allowed them to tease apart the various biological signals and to show that IL-22 acts directly on the stem cells.

In one experiment, the scientists created three-dimensional "mini-guts" grown from intestinal stem cells that resemble the main features of the normal epithelium in the human gut. When they exposed these mini-guts to IL-22, the stem cells proliferated and dramatically increased the growth of the mini-guts.

In another experiment, mice that received bone marrow transplants and began to develop GVHD had reduced intestinal damage and a much better chance of surviving if they were treated with IL-22.

"This suggests that treatment with IL-22 can have real therapeutic effects," Dr. Hanash says.

NEW HOPE FOR TRANSPLANT PATIENTS

To speed this treatment to patients, the MSK researchers have partnered with a pharmaceutical company that has developed a modified, potentially more potent form of IL-22. They plan to launch a phase II clinical trial at MSK in early 2016 to treat transplant patients experiencing GVHD of the intestinal tract. The drug will be given promptly when the complication emerges to head off serious damage, which is more difficult to treat.

"It's a very exciting development, because we have a way to treat GVHD using a completely different approach from any that's been tried so far," Dr. Hanash says.

Sergio Giralt, Chief of MSK's Adult Bone Marrow Transplantation Service, says the findings hold great promise for transplant patients, as well as for other patients suffering intestinal damage.

"Dr. Hanash's work now allows us to explore a strategy that can enhance healing of the gastrointestinal tract from the damages of graft-versus-host disease," he says. "If successful, IL-22 could also be used for other causes of severe gastrointestinal damage that require tissue regeneration."

Dr. Hanash emphasized the cross-disciplinary nature of this research, which involved immunologists and stem cell biologists. He says the interplay between specialties is increasingly important as evidence accumulates that the role of the immune system is broader than generally thought.

"It's not a case of your intestines, your heart, or your liver all functioning independently — that's not the way our bodies work," he says. "Things are very interconnected. And one of those connections seems to be the immune system. It's not just fighting off foreign invaders — it's also deeply involved in tissue maintenance and repair." ■

PAPER REFERENCED IN ARTICLE:

http://www.ncbi.nlm.nih.gov/pubmed/?term=Interleukin-22+promotes+intestinal-stem-cell-mediated+epithelial+regeneration

Lindemans CA, Calafiore M, Mertelsmann AM, O'Connor MH, Dudakov JA, Jenq RR, Velardi E, Young LF, Smith OM, Lawrence G, Ivanov JA, Fu YY, Takashima S, Hua G, Martin ML, O'Rourke KP, Lo YH, Mokry M, Romera-Hernandez M, Cupedo T, Dow L, Nieuwenhuis EE, Shroyer NF, Liu C, Kolesnick R, van den Brink MRM*, Hanash AM*.

*shared last authorship

Interleukin-22 Promotes Intestinal Stem Cell-Mediated Epithelial Regeneration.

Nature. 2015; 528(7583):560-4. PMID: 26649819; PMC4720437

The Susan and Peter Solomon Divisional Genomics Program

Susan and Peter Solomon

THE SUSAN AND PETER SOLOMON Divisional Geonomics Program is a collaborative, multidisciplinary program comprised of clinical and research experts led by Marcel van den Brink, Ross Levine and Elli Papaemmanuil. Scientific meetings are held regularly to review research progress, discuss novel technologies and analysis approaches, and to conceive of new collaborative research opportunities.

Initiated in 2010, the Solomon Divisional Genomics Program has pioneered efforts to develop genomics platforms to look for genetic mutations in the tumor samples of patients with different blood cancers. The program has also invested in new and innovative technologies that have contributed to discovery and translational research in hematologic malignancies, including DNA/RNA sequencing and proteomic approaches, which allows MSK to invest in our clinical and laboratory investigators and to recruit additional world leaders in blood cancer research.

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

Hematologic Oncology Tissue Bank

BACK ROW FROM LEFT: Jim Young, Emily Leede, Sean Quach, Haivy Luu, Juliann Orfini, Keimya Sadeghi; FRONT ROW FROM LEFT: Christie Mallek, Jessica Schulman, Amber Turner

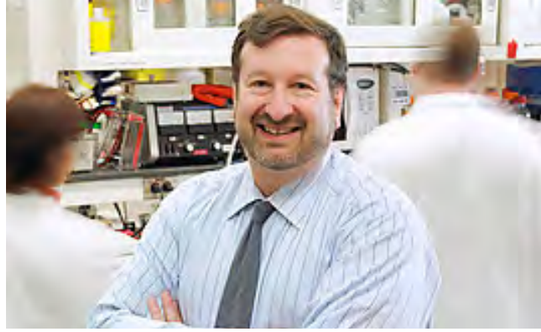
THE DIVISION OF HEMATOLOGIC ONCOLOGY established the Hematologic Oncology Tissue Bank (HOTB) in 2010 to support the many different research projects of Memorial Hospital and Sloan Kettering Institute investigators.

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

When the bank was first established, about 150 samples were processed each month. Sample processing has since increased to more than 2400 per month. The HOTB currently has an inventory of more than 133,000 including peripheral blood components (plasma, serum, granulocyte pellets and mononuclear cells), buccal swabs for DNA, bone marrow mononuclear cells, skin, and lymphoid tissue.

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. ■

Translational Research



Physician-Scientist David Scheinberg Pioneers Targeted Immunotherapies, Helping MSK Lead Field

BY HIS OWN ADMISSION, David A. Scheinberg, MD, PhD, has long had a "singular focus" on translating laboratory discoveries into therapeutic advances in cancer. But over the 30-plus years of his career — all spent at Memorial Sloan Kettering — this physician-scientist's single-mindedness has fueled a team approach in creating novel agents making headway against a variety of malignancies.

Internationally recognized in the development of targeted immunotherapies, Dr. Scheinberg wears many hats at MSK: He is the Vincent Astor Chair and Chairman of the Molecular Pharmacology Program in the Sloan Kettering Institute; he also founded and chairs the Center for Experimental Therapeutics and formerly, the Nanotechnology Center. He also founded and is a Director of the Tri-Institutional Therapeutics Discovery Institute of Cornell, Rockefeller, and MSK, which develops drugs for the community.

"I think I was able to work beyond my initial expectations because of the resources and support of the institution," he says. "Not only have I been able to translate lab discoveries into therapeutic advances for my own research, our programs have been able to help dozens of faculty members at MSK do the same."

DISCOVERIES IN HEMATOLOGIC CANCERS FUEL OTHERS

As Leukemia Chief for more than a decade, Dr. Scheinberg initially focused on developing new drugs for acute and chronic leukemias. Among the eight therapeutic agents Dr. Scheinberg has helped create that have reached human clinical trials are the first humanized antibodies to treat acute leukemia and the first cancer vaccines for acute and chronic myeloid leukemia (CML). But the scope of his bench-to-bedside work in the clinic and lab expanded as years passed to include a variety of other cancer types, including lymphomas, myeloma, and solid tumors.

Dr. Scheinberg has discovered and developed many immunotherapeutic agents, including monoclonal antibodies that target the cell surface of cancers; targeted radiopharmaceuticals that deliver radioactive particles via nanodevices that selectively kill cancer cells; and therapeutic vaccines that target the oncogene products causing cancers.

"I've always believed that the hematologic malignancies served as the stalking horse for discoveries that are then applied to solid tumors," he says. "We know more about the causes of hematologic cancer and the proteins on the cell surface, and have more tools and therapeutic opportunities in hematologic cancers. Using them, we can make more rapid advances that then become applicable to a variety of other cancers using the same approaches."

MULTIDISCIPLINARY TEAM SPEEDS TRANSLATION OF BASIC SCIENCE

Dr. Scheinberg's launch in 2002 of the Center for Experimental Therapeutics — designed to test novel ideas pharmaceutical companies are unlikely to tackle — has succeeded on all levels. The center includes physicians and scientists from nearly every MSK department and program, both on the basic science side and the hospital, who meet weekly to discuss new therapeutic science and unite in their goal of understanding how to make drugs work better.

"We support large teams of physicians and scientists working together to develop new drugs," says Dr. Scheinberg, the published author of more than 250 papers, chapters and books on his research. "It's a highly integrated, multidisciplinary operation, which can efficiently translate ideas in both directions."

"One of the advantages we have in being a lab and a clinical investigation unit here is we can immediately translate our ideas into the hospital, learning how drugs work. Then we bring them back into the lab and make them better," he adds. "That process is highly efficient at a place like MSK."

MSK DEFINED BY LONG TRADITION OF IMMUNOTHERAPY

Despite his intense focus on translational research, Dr. Scheinberg greatly values his work with patients and feels his novel drug discoveries wouldn't be possible without his clinical activity.

"I've always felt that treating patients has allowed me to understand what the most pressing problems and needs are for patients, and what are realistic and practical solutions for them," says the frequent honoree, who has received the Doris Duke Distinguished Clinical Science Professorship and is elected into the American Society of Clinical Investigation, the American Association of Physicians, and the Interurban Club. "Neither of those essential pieces of information are readily available unless you're actually treating patients."

Dr. Scheinberg would like to see many of the new, currently experimental immunotherapies advance to U.S. Food and Drug Administration approval so they can be used to help patients around the world "live longer and better lives."

"There are dozens of new immunotherapies in the pipeline, not just from MSK, but also from around the world," he says. "It's a huge field that is expanding, and at MSK we are among the leading proponents. MSK has been a leader in immunotherapies for cancer since the early 20th century, so we have a long tradition and culture of trying to use the immune system to selectively kill cancer cells." ■

"We can immediately translate our ideas into the hospital, learning how drugs work. Then we bring them back into the lab and make them beter." DAVID SCHEINBERG

Appointments 2015

ANDREW INTLEKOFER, MD, PHD JOINED LYMPHOMA SERVICE

Andrew Intlekofer, MD, PhD joined the Lymphoma Service as an Assistant Attending Level I Physician. After receiving his MD and PhD from the University of Pennsylvania, Dr. Intlekofer completed residency training in Internal Medicine at the New York-Presbyterian Hospital/Weill Cornell Medical Center, and did his fellowship in Medical Oncology at MSK. Dr. Intlekofer will care for patients on the Lymphoma Service and conduct basic and translational research in the laboratory of Dr. Craig Thompson.

SHAM MAILANKODY, MBBS JOINED MYELOMA SERVICE

Sham Mailankody, MBBS, joined the Myeloma Service as an Assistant Attending Level 1 Physician. Dr. Mailankody received his MBBS from the K S Hegde Medical Academy in India, completed a residency in Internal Medicine at Georgetown University/Washington Hospital Center, and did a clinical fellowship at the National Cancer Institute, NIH. He will work in the Myeloma Service and provide consultation in multiple myeloma, both at MSK's Main Campus and at MSK's Commack location.

Promotions 2015

JULIET BARKER PROMOTED TO MEMBER

Juliet Barker, MBBS, FRACP was promoted to Attending Physician on the Adult Bone Marrow Transplant Service, Member at MSK, and Professor of Medicine at the Weill Cornell Medical College. Dr. Barker originally received her MBBS from Adelaide University in Australia and joined MSK in 2005. Her clinical expertise includes bone marrow transplantation with a focus on allogeneic transplantation, and specifically the use of cord blood derived hematopoietic (blood-forming) stem cells to treat diseases of the blood and bone marrow. Dr Barker is Director of the Cord Blood Transplantation Program at MSKCC.

PAUL HAMLIN, MD PROMOTED TO CHIEF, BASKING RIDGE MEDICAL ONCOLOGY SERVICE

Paul Hamlin, MD, was promoted to Chief of the Basking Ridge Medical Oncology Service in the Division of Network Medicine Services. Dr. Hamlin is a highly respected clinical trialist and an outstanding clinician on the Lymphoma Service with a strong interest in the care of older patients with lymphoma. He has also demonstrated outstanding administrative skills as the Medical Director in the oversight of the administrative and clinical programs at E 64th Street, implementing several innovative programs, and establishing close and effective working relationships with nursing and administrative leaders. Dr. Hamlin intends to maintain his interest in the hematological malignancies and will bring that expertise to Basking Ridge.

VIRGINIA KLIMEK PROMOTED TO ASSOCIATE MEMBER

Virginia Klimek, MD was promoted Associate Member at MSK, Associate Attending Physician on the Leukemia Service, and Associate Professor of Clinical Medicine at Weill Cornell Medical College. Dr. Klimek received her medical degree from the University of Medicine and Dentistry of New Jersey Robert Wood Johnson Medical School. She then completed a residency in Internal Medicine at North Shore University Hospital. She joined MSK in 1996 as Assistant Chief Medical Resident. She also completed her Hematology/Oncology fellowship training at MSK. Dr. Klimek's clinical expertise focuses on bone marrow failure syndromes, including myelodysplastic syndromes (MDS) and aplastic anemia. Her clinical research interests also include the study of "therapy-related" MDS and leukemia, which can develop after treatment with radiation or chemotherapy for another cancer.

MELODY SMITH, MD JOINED ADULT BONE MARROW TRANSPLANT SERVICE

Melody Smith, MD joined the Adult Bone Marrow Transplant Service as an Instructor-level physician. Dr. Smith received her MD with Distinction in Research from the University of Texas Southwestern Medical School and completed a residency in Internal Medicine at the University of Texas Southwestern Medical Center in Dallas, Texas. She then completed a fellowship in Hematology and Oncology at MSK. Dr. Smith researches the use of donor-derived CD19 CAR T cells in the post transplant setting, and provides consultation in immunotherapy and bone marrow transplant.

ALEXANDER LESOKHIN PROMOTED TO ASSISTANT MEMBER

Alex Lesokhin, MD was promoted to Assistant Attending Physician on the Myeloma Service, Assistant Member at MSK, and Assistant Professor of Medicine at Weill Cornell Medical College. Dr. Lesokhin received his MD from the Albert Einstein College of Medicine. He then completed his residency training at Columbia University and his hematologic oncology fellowship training at MSK. Dr. Lesokhin's research focuses on tumor immunology, specifically on ways to modulate the immune response toward eliminating cancer. He has also established a focus in immunotherapy clinical trials and in the care of patients with multiple myeloma.

MATTHEW MATASAR PROMOTED TO ASSISTANT MEMBER

Matthew Matasar, MD, MS was promoted to Assistant Attending Physician in the Lymphoma Service, Assistant Member at MSK and Assistant Profession of Medicine at Weill Cornell Medical College. Dr. Matasar received his medical degree from Harvard Medical School and subsequently graduated with a Masters of Science from Mailman School of Public Health at Columbia University. He then completed his internship and residency in Internal Medicine at Columbia Presbyterian, where he was appointed Chief Resident from 2003-2004. He first joined MSK as a Fellow in Hematology and Medical Oncology in 2005. Dr. Matasar has clinical expertise in Hodgkin and non-Hodgkin lymphoma as well as in autologous stem cell transplant. He has a grant-supported research program in cancer survivorship investigating late effects of lymphoma therapy. He is also exploring new treatments in the management of relapsed non-Hodgkin lymphoma.

AARON VINY, MD, MS JOINED LEUKEMIA SERVICE

Aaron Viny, MD, MS joined the Leukemia Service in the Department of Medicine as an Instructor-level physician. Dr. Viny received his MD/MS Master's in Biomedical Investigation from the Cleveland Clinic Lerner College of Medicine. He then completed residency training at the New York-Presbyterian Hospital/Weill Cornell Medical Center and fellowship in Hematology and Oncology at MSK. Dr. Viny served as Hematology Chief Fellow from 2014-2015. Dr. Viny's research in the Levine lab focuses on cohesin mutations in myeloid neoplasms, characterizing their clinical importance as well as studying mouse models to delineate cohesin's function in normal and malignant hematopoiesis. His special interests in bone marrow failure and myeloid neoplasms aim to translate novel epigenetic insights into clinical care.

LIA PALOMBA PROMOTED TO ASSOCIATE CLINICAL MEMBER

Lia Palomba, MD was promoted to Associate Clinical Member at MSK, Associate Attending Physician on the Lymphoma Service and Associate Professor of Clinical Medicine at the Weill Cornell Medical College. Dr. Palomba received her medical degree from University of Pavia in Italy. She then completed a fellowship in Hematology at the University Hospital of Pavia and an internship and residency in Internal Medicine at the Harvard Medical School-affiliated Mt. Auburn Hospital in Cambridge, MA. She joined MSK in 1999 as a Hematology/Medical Oncology fellow. Her clinical expertise is in the study and treatment of lymphoma, with a focus on the development of novel therapies for patients with B cell lymphoma, particularly the indolent lymphomas, Waldenstrom macroglobulinemia and chronic lymphocytic leukemia. She was part of the team that conducted a pivotal clinical trial of ibrutinib for patients with Waldenstrom Macroglobulinemia, which resulted in the first ever drug approval by the FDA for this disease. She is a member of the Cellular Therapy Center, focusing on CAR T-cell therapy for patients with lymphoma. Dr. Palomba's laboratory interest is in understanding the signaling mechanisms underlying lymphoma growth and proliferation.

Awards & Recognition 2015

The following faculty members received Steven Greenberg Lymphoma Research Awards in 2015: **Omar Abdel-Wahab** 1, **Andrew Intlekofer** 2, **Lia Palomba** 3, **and Hans-Guido Wendel** 4.

Omar Abdel-Wahab 1 also received the 2015 Joanne Levy Memorial Award for Outstanding Achievement, which is awarded to an ASH Scholar with the highest-scoring abstract for the ASH annual meeting. He also received the Leukemia & Lymphoma Society Clinical Scholar Award in 2015.

Andrew Intlekofer 2 also won a Special Fellow Career Development Award from the Leukemia & Lymphoma Society.

Stephen Chung 5 received the inaugural Jake Wetchler Foundation ASH Scholar Award for Pediatric Innovation for his research on the mechanisms of bone marrow failure syndromes.

Steven Horwitz 6 received a Leukemia & Lymphoma Society Specialized Center of Research (SCOR) grant for his project, "Translational discoveries in T-cell lymphoma."

Malin Hultcrantz 7, an Advanced Oncology Fellow at MSK, received the 2015 Research Fellow Award from the Multiple Myeloma Research Foundation.

The M8, M9 and M14 Nursing Teams 8 were all awarded with the Spirit of Transplant Award in June of 2015.

Memorial Sloan Kettering 9 received a 2015 "Top 25 Environmental Excellence Award" from Practice Greenhealth, an organization that promotes environmental stewardship and sustainability excellence in healthcare institutions.

Ariela Noy 10 received the first of five years of a UM1 award from the National Cancer Institute for the AIDS Malignancy Consortium as the MSK site Principal Investigator and additional funding for her role as Lymphoma Working Group Chair.

Rekha Parameswaran 11 won the Hematology Teaching Attending of the Year in 2015.

Jonathan Peled 12 received an SITC-Merck Cancer Immunotherapy Clinical Fellowship Award, an ASCO Young Investigator Award, and the MSK Clinical Scholars Biomedical Research Training Program Award through the Charles A. Dana Foundation.

Miguel Perales 13 was appointed as a Member of the Board of Directors for Be The Match/National Marrow Donor Program. He also received the Purple Heart Award for Exemplary Service from the Blood and Marrow Transplantation Clinical Trials Network.

Doris Ponce 14 received an MSK Society Research Grant in 2015.

Raajit Rampal 15 received the 2015 Gilead Sciences Research Scholars Program Award in Hematology/Oncology.

Eric Smith 16 **and Renier Brentjens** 17 received a 2015 MSKCC Technology Development Fund Award for their work on novel CAR T-cell therapy for the treatment of multiple myeloma.

Eric Smith 16 also received an ASCO Young Investigator Award and recognition as an ISCT-ASBMT Cell Therapy Training Course Scholar.

Gerald Soff 18 won the 2015 Willet F. Whitmore Award for Clinical Excellence.

Marcel van den Brink 19 received the Delete Blood Cancer Award at the ninth annual Delete Blood Cancer Gala in 2015 and the Immunology Letters Lecture Award from the European Federation of Immunological Societies. He also presented the 2015 Memorial Lecture for the annual City of Hope Celebration of Life Hematopoietic Cell Transplantation Reunion.

Aaron Viny 20 received a Damon Runyon Cancer Research Foundation Postdoctoral Fellow Award and an ASCO Young Investigator Award.

Olga Guryanova (Senior Research Scientist), Ross Levine, Adriana Rodriguez Gonzalez (medical student)

Clinical Training and Education

Programs Train the Leaders of the Future

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

MEDICAL ONCOLOGY/HEMATOLOGY FELLOWSHIP

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

The three-year program is the largest of its kind in the country, attracting more than 450 applicants each year for just 15 coveted spots. In addition to being outstanding physicians, fellows must have a specific interest in clinical research or laboratory investigation and demonstrate scientific curiosity and motivation.

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

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

BONE MARROW TRANSPLANTATION FELLOWSHIP

The Adult Hematopoietic Stem Cell Transplantation Fellowship Program at Memorial Sloan Kettering was launched in 2007 as an independent, one-year program designed to prepare physicians for academic careers in stem cell transplantation, including experience with clinical research. The fellowship provides training in inpatient and outpatient settings, with a specific focus on the different subspecialties within hematopoietic stem cell transplantation, as well as exposure to the different disciplines that relate to this field. These include radiation oncology and clinical laboratory rotations.

Fellows have opportunities to participate in ongoing research projects or to initiate an independent project. This process is helped by the assigning of a mentor throughout the fellowship, who ensures that the objectives of the fellow are met for the training year.

The program also includes a wide variety of conferences which complement the clinical aspects. These are based on a disease management concept and group physicians from different specialties who treat the disease in question. In addition to these patient-based conferences, a weekly research meeting is held.

Since 2007, the Program has trained 14 fellows. Thirteen of the 14 graduates are now full time faculty on BMT services in academic centers in the U.S. and abroad. The 14th graduate is working in industry as medical director for a CAR-T program.

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

Swim Across America

SINCE ITS ESTABLISHMENT IN 1987 as a small grassroots effort in Nantucket, Massachusetts, Swim Across America (SAA) has grown to include events at aquatic venues across the nation. Today, over 5000 recreational swimmers, masters swimmers, and even kayakers and boaters participate in swimming-related events in communities from coast to coast.

The SAA community has raised over $60 million for cancer research, prevention and treatment, since 1993. One of its major research beneficiaries is MSK, which has received $7 million in support of research that has led to historic breakthroughs in the burgeoning field of immunotherapy and cancer.

Dr. James Young, an Attending Physician on the Adult BMT Service and avid distance swimmer, began swimming the Long Island Sound Open Water event in 2006. In 2009, a patient and fellow distance swimmer 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 MSKCC.

Since 2009, Team Transplant has raised nearly $200,000 for much needed support of the research efforts that ensure the successful use of transplantation to cure patients with leukemia, lymphoma, multiple myeloma, and other cancers of the blood and bone marrow. In 2015, "Team Transplant" raised nearly $35,000 in funds that went directly to MSKCC's bone marrow and stem cell transplantation program.

Team Transplant MSKCC, SWIM ACROSS AMERICA Long Island Sound Open Water Swim, July 2015

Team Transplant swam for its seventh consecutive year on July 25th, 2015 in the Long Island Sound Open Water Swim event. Three former patients (4,10, and 20 yrs out from their transplants) and MSKCC nurse practitioners, Emily Panzner and Kara Mosesso, swam the course along with other members of Team Transplant. Most of the team swam the 2K course, but one of the previously transplanted patients swam the 5K course. Team Transplant will be swimming for its eighth consecutive year on July 30th, 2016. ■

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

Team Transplant's webpage:
http://www.swimacrossamerica.org/site/TR/OpenWater/LongIslandSound?team_id=18303&pg=team&fr_id=3941

Fred's Team 2015

FRED'S TEAM IS MEMORIAL SLOAN KETTERING'S athletic fundraising program dedicated to bringing us closer to a world without cancer. The program 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 2015, members raised more than $5.3 million.

On November 1, 2015, 939 Fred's Team members — including 60 Memorial Sloan Kettering staff members — ran the 26.2 mile 2015 TCS New York City Marathon, taking them through all five NYC boroughs to raise funds for the institution's lifesaving mission.

Named after running legend Fred Lebow, the program has raised over $65 million since 1995. In 2015, the Division of Hematologic Oncology received nearly $347,393.99 from Fred's Team participants.

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

PARTICIPANTS FROM THE DIVISION INCLUDED:

Jessica Ardizzone
Valkal Bhatt
Nadia Kralovic
Christine Liebertz
Michael Mauro
Roni Tamari
Marcel van den Brink

Dr. Roni Tamari

Cycle for Survival 2015

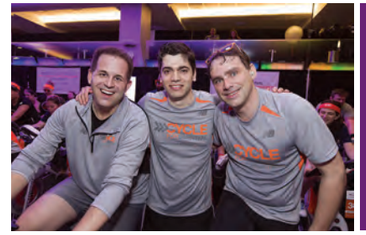
MEMORIAL SLOAN KETTERING'S CYCLE FOR SURVIVAL is the movement to beat rare cancers. Cycle for Survival's high-energy indoor team cycling events provide a tangible way for participants to fight back against cancer. One hundred percent of all money raised goes directly to lifesaving research. Within six months of the annual events, all donations are allocated to pioneering studies and clinical trials led by MSK. With support from founding partner Equinox, Cycle for Survival has raised over $105 million for rare cancer research, which has led to new and better treatments for patients worldwide.

In 2015, Cycle for Survival kicked off the year in a big way with the second annual Times Square Takeover, featuring powerful speeches, performances from Broadway stars, and an appearance on *Good Morning America*. Also in 2015, Cycle for Survival introduced #ThisIsMyBattleCry and encouraged riders and supporters to use the hashtag on social media to share who or what inspires them to fund rare cancer research. Over 21,000 people participated in 2015 to raise a record-breaking $25 million at events across the country led by Equinox instructors in 13 cities: New York City; Chicago; Roslyn, Long Island; Washington, DC; Boston; Greenwich, CT; Miami; Summit, NJ; Dallas; Los Angeles; Palo Alto; San Francisco and Seattle.

For more information, please visit: www.cycleforsurvival.org. ■

TOP, LEFT TO RIGHT:
Craig Thompson, Seth Meyers, Jose Baselga

BOTTOM, LEFT TO RIGHT:
Ross Levine, David Hyman, David Solit



PARTICIPANTS FROM THE DIVISION INCLUDED:

The Mighty M&Ms
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Tiana Barnwell
Mathieu Boulad
Nailah Cummings
Sarah Kerr
Ola Landgren
James Nguyen
Ashley Poliak
Stephanie Primiani
Allison Sams
Rachel Simms
Kayla Smith
Amanda Stellman
Ioanna Tsakos (captain)
Heather Wendel
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MSKCC Fellows
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Sheng Cai
Lara Dunn (captain)
Anya Litvak
Neha Mehta-Shah
Jarushka Naidoo
Nitya Raj
Prithvi Raj
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Aaron Viny

MSKCC Leukemia Research Team
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Christina Bravo
Morgan Coleman
Chris Famulare
Talal Khawaja
Virginia Klimek
Kristina Knapp
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Kelsey Malone (captain)
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Minal Patel
Raajit Rampal
Diane Stopka
Nour Elise Tabbara
Yasaman Zarbafian
Guadalupe Zúñíga-Estrada

Scrubbed Crusaders
Famatta Fallah
Mary Griffin
Katie Hambright
Andrea Karikas
Morgan Kurpiel
Sharon Lynch
Sue Posthumus
Tessa Rabinowitz
Biana Ryzhik
Jenna Sell
Aizza Zuno

T-cell Racers
Kurt Bantilan
Heather Coggins (captain)
Donald Etheridge
Stephanie Fox
Rebecca Green
Steven Horwitz
Gabriella John
Soyeon Lee
Shoshana Miller
Sumi Nair
Mark Scheuerman
Tamir Sholklapper
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Amanda Bernard
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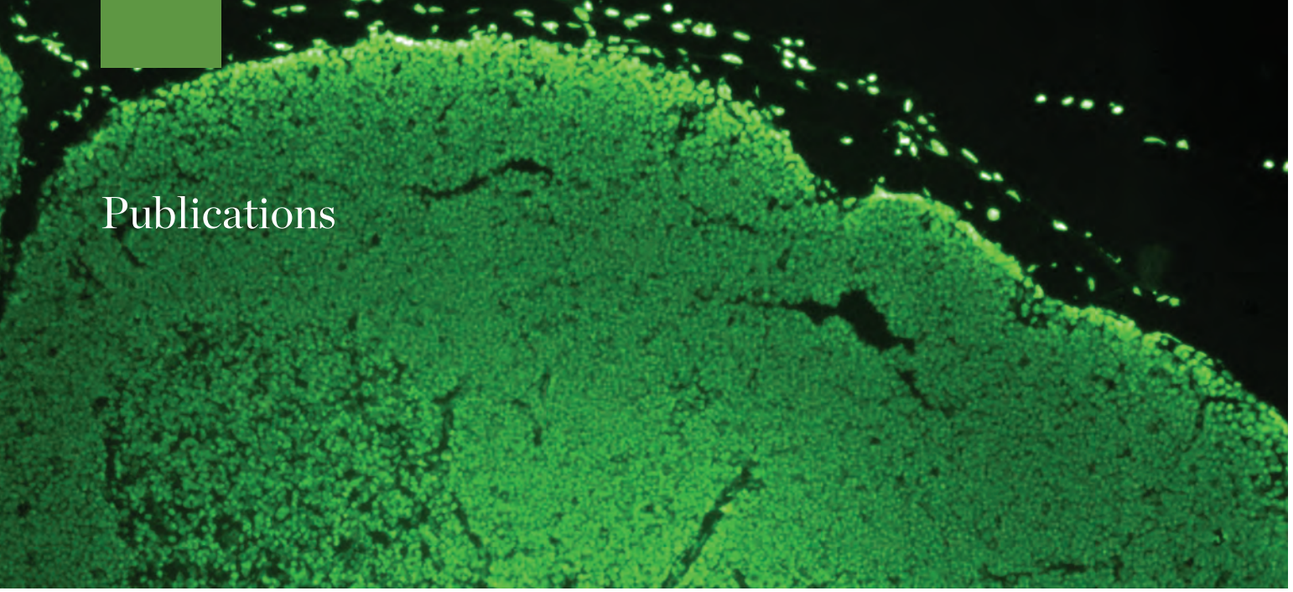
Katie Drinkwater
Arnab Ghosh
Laura Hirschfield
Yvette Murillo
Miguel Perales (captain)
Karina Ramirez
Matias Sanchez
Apryl Sarabia
Craig Sauter
Allison Slater
Jenna Strauss
Whitney Quitta
Joanna Zizzo

Team HOPP – NYC
Omar Abdel-Wahab
Manuel Arguelles
Natalie Barragan and Mitchell Clark
Baselga Family
Michael Berger and Anna Varghese
Nyree Cabrera-Lugo
cBioPortal MSKCC
Magali Cavatore
Debyani Chakravarty
Sarat Chandarlapaty
Nidia Claros
Caitlin Gallagher
Meighan Gallagher and Ralph Alfano
Emma Hatton
Kety Huberman
Jason Huse
David Hyman
Richard Koche
Lee and Laura Krug
Kelly Lafaro
Nathalie Lailler
Steven Leach
Christophe Lemetre
Ross and Erica Levine
Juan Li
Paul Miranda
David, Amy and Brooke Nagler
Lisa Newman
Moriah Nissan
Ederlinda Paraiso
Christie Park
Christopher Park
Anna Patruno and Richie Bolognese
Abby Poteshman
Jen & Zach Resnick
Ajay Riddhika
Julia Rudolph
Leonard Saltz
Charles and Susan Sawyers
Dan Scacalossi
Howard and Deborah Scher
Barry Taylor and Rachel Schwartz
Garner Smythe
David and Barbara Solit (captain)
Rebecca Solit
Sabrena Thomas
Craig Thompson and Tullia Lindsten
Kajsa Thompson
Michael Trapani
Daria Valerio
Teresa Valderrama
Agnes Viale
Gael Westby
Daoqi You
Ahmet Zehir
Jeffrey Zhao

Team HOPP – Long Island
Jennifer Ben-Levi
Lisa Freifeld
Lara Gatz
Nicole Hirschfield
Douglas Jaffe
Marisa Jaffe
Elisa and Craig Kandel
Corey Kandel
Marcy Kandel
Ross and Erica Levine (captain)
Sima Lis



Publications

Thymus low: Very simplistic cellularity of a rescued thymus. CREDIT: SUSAN PROCKOP

These are a few articles out of the 237 total articles published by the Division of Hematologic Oncology faculty in 2015.

ADULT BONE MARROW TRANSPLANT

Prognostic Importance of Pretransplant Functional Capacity after Allogeneic Hematopoietic Cell Transplantation.

Jones LW, Devlin SM, Maloy MA, Wood WA, Tuohy S, Espiritu N, Aquino J, Kendig T, Michalski MG, Gyurkocza B, Schaffer WL, Ali B, Giralt S, Jakubowski AA.
Oncologist. 2015; 20(11):1290-7. PMID: 26446235 PMCID: PMC4718429
http://www.ncbi.nlm.nih.gov/pubmed/26446235

- Normal processes of aging can be "accelerated" by allogeneic hematopoietic cell transplantation (HCT) therapy-related direct toxicity to the cardiovascular-musculoskeletal system and indirect physiological consequences secondary to therapy such as exercise intolerance and loss of muscle mass. The purpose of this study was to investigate the prognostic importance of functional capacity (using the 6 minute walk distance test [6MWD]) pretransplant and changes in the same test over the course of the transplant. Our data showed that the pretransplant 6MWD was a significant univariate predictor of clinical outcomes that provided incremental prognostic information beyond chronological age. Although that relationship became nonsignificant after adjustment for performance status (PS), a 6MWD of ≥400 m was associated with a 31% and 27% reduction in NRM and OS (after controlling for PS) suggesting that this test might provide distinct, complementary information.

High Disease-Free Survival with Enhanced Protection against Relapse after Double-Unit Cord Blood Transplantation When Compared with T Cell-Depleted Unrelated Donor Transplantation in Patients with Acute Leukemia and Chronic Myelogenous Leukemia.

Ponce DM, Hilden P, Devlin SM, Maloy M, Lubin M, Castro-Malaspina H, Dahi P, Hsu K, Jakubowski AA, Kernan NA, Koehne G, O'Reilly RJ, Papadopoulos EB, Perales MA, Sauter C, Scaradavou A, Tamari R, van den Brink MR, Young JW, Giralt S, Barker JN.
Biol Blood Marrow Transplant. 2015; 21(11):1985-93. PMID: 26238810 PMCID: PMC4768474
http://www.ncbi.nlm.nih.gov/pubmed/26238810

- Neonatal publically banked cord blood units are a rapidly available stem cell source for adults with high-risk hematologic malignancies requiring transplantation but without other stem cell sources. We analyzed 166 patients who underwent allogeneic stem cell transplantation (111 unrelated donor and 55 cord blood) for the treatment of acute leukemias and chronic myeloid leukemia. We found that the 3-year disease-free survival in cord blood transplantation was similar to the standard of matched unrelated donor transplants and higher than mismatched unrelated donor transplants. Our findings support performing cord blood transplants in adults in preference to mismatched unrelated donor and suggest cord blood transplantation is a readily available alternative to matched unrelated donor in patients requiring an urgent transplant.

CD34-Selected Hematopoietic Stem Cell Transplants Conditioned with Myeloablative Regimens and Antithymocyte Globulin for Advanced Myelodysplastic Syndrome: Limited Graft-versus-Host Disease without Increased Relapse.

Tamari R, Chung SS, Papadopoulos EB, Jakubowski AA, Hilden P, Devlin SM, Goldberg JD, Perales MA, Ponce DM, Sauter CS, Maloy MA, Herman DY, Klimek V, Young JW, O'Reilly RJ, Giralt SA, Castro-Malaspina H.
Biol Blood Marrow Transplant. 2015; 21(12):2106-14. PMID: 26187863 PMCID: PMC4764129
http://www.ncbi.nlm.nih.gov/pubmed/26187863

- This paper summarizes the experience of patients with myelodysplastic syndrome who underwent T-cell depleted allogeneic stem cell transplant at Memorial Sloan Kettering, and highlights the long term survival with very low risk of acute and chronic graft versus host disease.

Intestinal Blautia Is Associated with Reduced Death from Graft-versus-Host Disease.

Jenq RR, Taur Y, Devlin SM, Ponce DM, Goldberg JD, Ahr KF, Littmann ER, Ling L, Gobourne AC, Miller LC, Docampo MD, Peled JU, Arpaia N, Cross JR, Peets TK, Lumish MA, Shono Y, Dudakov JA, Poeck H, Hanash AM, Barker JN, Perales MA, Giralt SA, Pamer EG, van den Brink MR.
Biol Blood Marrow Transplant. 2015; 21(8):1373-83. PMID: 25977230 PMCID: PMC4516127
http://www.ncbi.nlm.nih.gov/pubmed/25977230

- In this study of 115 allogeneic BMT patients at MSKCC, we found that a group of bacteria called "Blautia" was more common in patients that were protected from lethal graft-versus-host disease.

LEUKEMIA

Targeting Mutant BRAF in Relapsed or Refractory Hairy-Cell Leukemia.

Tiacci E, Park JH, De Carolis L, Chung SS, Broccoli A, Scott S, Zaja F, Devlin S, Pulsoni A, Chung YR, Cimminiello M, Kim E, Rossi D, Stone RM, Motta G, Saven A, Varettoni M, Altman JK, Anastasia A, Grever MR, Ambrosetti A, Rai KR, Fraticelli V, Lacouture ME, Carella AM, Levine RL, Leoni P, Rambaldi A, Falzetti F, Ascani S, Capponi M, Martelli MP, Park CY, Pileri SA, Rosen N, Foà R, Berger MF, Zinzani PL, Abdel-Wahab O, Falini B, Tallman MS.
N Engl J Med. 2015; 373(18):1733-47. PMID: 26352686 PMCID: PMC4811324
http://www.ncbi.nlm.nih.gov/pubmed/26352686

- This paper reports clinical trial results using the BRAF inhibitor drug vemurafenib in patients with hairy cell leukemia, a form of leukemia where all patients contain an activating mutation in the oncogene BRAF. This paper also describes the first case of BRAF inhibitor resistance in this disease.

Dose-dependent role of the cohesion complex in normal and malignant hematopoiesis.

Viny AD, Ott CJ, Spitzer B, Rivas M, Meydan C, Papalexi E, Yelin D, Shank K, Reyes J, Chiu A, Romin Y, Boyko V, Thota S, Maciejewski JP, Melnick A, Bradner JE, Levine RL.
J Exp Med. 2015; 212(11):1819-32. PMID: 26438361 PMCID: PMC4612085
http://www.ncbi.nlm.nih.gov/pubmed/26438361

- We delineated for the first time the role of cohesin complex mutations in acute myeloid leukemia and rpvided novel insight into the role of the cohesin complex in normal and malignant hematopoiesis, and developed the first mouse model of cohesin mutant AML.

Diverse and Targetable Kinase Alterations Drive Histiocytic Neoplasms.

Diamond EL, Durham BH, Haroche J, Yao Z, Ma J, Parikh SA, Wang Z, Choi J, Kim E, Cohen-Aubart F, Lee SC, Gao Y, Micol JB, Campbell P, Walsh MP, Sylvester B, Dolgalev I, Aminova O, Heguy A, Zappile P, Nakitandwe J, Ganzel C, Dalton JD, Ellison DW, Estrada-Veras J, Lacouture M, Gahl WA, Stephens PJ, Miller VA, Ross JS, Ali SM, Briggs SR, Fasan O, Block J, Héritier S, Donadieu J, Solit DB, Hyman DM, Baselga J, Janku F, Taylor BS, Park CY, Amoura Z, Dogan A, Emile JF, Rosen N, Gruber TA, Abdel-Wahab O.
Cancer Discov. 2016; 6(2):154-65. PMID: 26566875 PMCID: PMC4744547
http://www.ncbi.nlm.nih.gov/pubmed/26566875

- This paper describes a series of mutations driving a group disorders, termed histiocytic neoplasms. These are cancers formed from blood cells which are normally called monocytes and macrophages and they are treated very effectively with drugs targeting specific mutations found in these patients.

JAK-STAT pathway activation in malignant and nonmalignant cells contributes to MPN pathogenesis and therapeutic response.

Kleppe M, Kwak M, Koppikar P, Riester M, Keller M, Bastian L, Hricik T, Bhagwat N, McKenney AS, Papalexi E, Abdel-Wahab O, Rampal R, Marubayashi S, Chen JJ, Romanet V, Fridman JS, Bromberg J, Teruya-Feldstein J, Murakami M, Radimerski T, Michor F, Fan R, Levine RL.
Cancer Discov. 2015; 5(3):316-31. PMID: 25572172 PMCID: PMC4355105
http://www.ncbi.nlm.nih.gov/pubmed/25572172

- We showed how production of cytokines (inflammatory mediators), from both tumor cells and normal, non-cancerous cells, contribute to the pathogenesis of myeloid leukemias.

SRSF2 Mutations Contribute to Myelodysplasia by Mutant-Specific Effects on Exon Recognition.

Kim E, Ilagan JO, Liang Y, Daubner GM, Lee SC1, Ramakrishnan A, Li Y, Chung YR, Micol JB, Murphy ME, Cho H, Kim MK, Zebari AS, Aumann S, Park CY, Buonamici S, Smith PG, Deeg HJ, Lobry C, Aifantis I, Modis Y, Allain FH, Halene S, Bradley RK, Abdel-Wahab O.
Cancer Cell. 2015; 11;27(5):617-30. PMID: 25965569 PMCID: PMC4429920
http://www.ncbi.nlm.nih.gov/pubmed/25965569

- Most patients with blood cancers known as myelodysplastic syndromes (MDS) have mutations in RNA splicing factors, the proteins that control how DNA is coverted to RNA. In this paper we identified how mutations in the RNA splicing factor called SRSF2 actually cause MDS and provided the first mouse model of MDS driven by a splicing factor mutation.

LYMPHOMA

Brentuximab vedotin as consolidation therapy after autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): a randomised, double-blind, placebo-controlled, phase 3 trial.

Moskowitz CH, Nademanee A, Masszi T, Agura E, Holowiecki J, Abidi MH, Chen AI, Stiff P, Gianni AM, Carella A, Osmanov D, Bachanova V, Sweetenham J, Sureda A, Huebner D, Sievers EL, Chi A, Larsen EK, Hunder NN, Walewski J; AETHERA Study Group.
Lancet. 2015; 385(9980):1853-62. PMID: 25796459
http://www.ncbi.nlm.nih.gov/pubmed/25796459

- The AETHERA study was the largest study done in relapsed or refractory Hodgkin lymphoma. At 3 and a half years of follow-up, 61% of the patients who received brentuximab vedotin maintenance or consolidation were progression-free, vs 44% of the patients who received placebo. This treatment is now standard of care worldwide.

PET-adapted sequential salvage therapy with brentuximab vedotin followed by augmented ifosamide, carboplatin, and etoposide for patients with relapsed and refractory Hodgkin's lymphoma: a non-randomised, open-label, single-centre, phase 2 study.

Moskowitz AJ, Schöder H, Yahalom J, McCall SJ, Fox SY, Gerecitano J, Grewal R, Hamlin PA, Horwitz S, Kobos R, Kumar A, Matasar M, Noy A, Palomba ML, Perales MA, Portlock CS, Sauter C, Shukla N, Steinherz P, Straus D, Trippett T, Younes A, Zelenetz A, Moskowitz CH.
Lancet Oncol. 2015; 16(3):284-92. PMID: 25683846
https://www.ncbi.nlm.nih.gov/pubmed/25683846

- This was the first study evaluating single-agent brentuximab vedotin in the pre-transplant setting for relapsed and refractory Hodgkin lymphoma. In this study, patients with relapsed or refractory disease after only one line of therapy were treated with brentuximab vedotin. Those achieving complete response on PET proceeded directly to transplant while those with persistent abnormalities on PET received additional chemotherapy with ICE before proceeding to transplant. This study confirmed the feasibility of PET adapted treatment in relapsed and refractory Hodgkin lymphoma and demonstrated high efficacy of sequential therapy with brentuximab vedotin and ICE in the pre-transplant setting.

Ibrutinib in previously treated Waldenström's macroglobulinemia.

Treon SP, Tripsas CK, Meid K, Warren D, Varma G, Green R, Argyropoulos KV, Yang G, Cao Y, Xu L, Patterson CJ, Rodig S, Zehnder JL, Aster JC, Harris NL, Kanan S, Ghobrial I, Castillo JJ, Laubach JP, Hunter ZR, Salman Z, Li J, Cheng M, Clow F, Graef T, Palomba ML, Advani RH.
N Engl J Med. 2015; 372(15):1430-40. PMID: 25853747
http://www.ncbi.nlm.nih.gov/pubmed/25853747

- This is a pivotal clinical trial of ibrutinib for patients with Waldenstrom Macroglobulinemia, which resulted in the first ever drug approval by the FDA for this disease

Targeting BCL2 with Venetoclax in Relapsed Chronic Lymphocytic Leukemia.

Roberts AW, Davids MS, Pagel JM, Kahl BS, Puvvada SD, Gerecitano JF, Kipps TJ, Anderson MA, Brown JR, Gressick L, Wong S, Dunbar M, Zhu M, Desai MB, Cerri E, Heitner Enschede S, Humerickhouse RA, Wierda WG, Seymour JF.
N Engl J Med. 2016; 28;374(4):311-22. PMID: 26639348
http://www.ncbi.nlm.nih.gov/pubmed/?term=26639348

- Venetoclax is the first approved drug to target the BCL-2 protein, which is overexpressed in CLL and many lymphomas and helps keep tumor cells alive. This article reports the results of the first arm of a study showing that venetoclax given alone yields high response rates that are deep and long-lasting in patients with Chronic Leukocytic Leukemia (CLL). Results from the second arm, in which venetoclax was studied in patients with non-Hodgkin Lymphoma, have been submitted for publication.

Hypoxia Induces Production of L-2-Hydroxyglutarate.

Intlekofer AM, Dematteo RG, Venneti S, Finley LW, Lu C, Judkins AR, Rustenburg AS, Grinaway PB, Chodera JD, Cross JR, Thompson CB.
Cell Metab. 2015; 22(2):304-11. PMID: 26212717 PMCID: PMC4527873
http://www.ncbi.nlm.nih.gov/pubmed/26212717

- Normal stem cells and cancer stem cells prefer to reside in low oxygen niches within the body, but the reasons for this preference remain poorly understood. The paper by Drs. Intlekofer and Thompson demonstrates that oxygen limitation triggers cellular production of a metabolite that promotes stem-like features.

PD-1 blockade with nivolumab in relapsed or refractory Hodgkin's lymphoma.

Ansell SM1, Lesokhin AM, Borrello I, Halwani A, Scott EC, Gutierrez M, Schuster SJ, Millenson MM, Cattry D, Freeman GJ, Rodig SJ, Chapuy B, Ligon AH, Zhu L, Grosso JF, Kim SY, Timmerman JM, Shipp MA, Armand P.
N Engl J Med. 2015 Jan 22;372(4):311-9. doi: 10.1056/NEJMoa1411087. Epub 2014 Dec 6.
http://www.ncbi.nlm.nih.gov/pubmed/25482239

- This article was the 1st experience with anti-PD1 in Hodgkin lymphoma and revealed a remarkable degree of clinical activity (87% response rate).

HEMATOLOGY

Cancer-Associated Venous Thromboembolic Disease, Version 1.2015.

Streiff MB, Holmstrom B, Ashrani A, Bockenstedt PL, Chesney C, Eby C, Fanikos J, Fenninger RB, Fogerty AE, Gao S, Goldhaber SZ, Hendrie P, Kuderer N, Lee A, Lee JT, Lovrincevic M, Millenson MM, Neff AT, Ortel TL, Paschal R, Shattil S, Siddiqi T, Smock KJ, Soff G, Wang TF, Yee GC, Zakarija A, McMillian N, Engh AM.
J Natl Compr Canc Netw. 2015; 13(9):1079-95. PMID: 26358792
http://www.ncbi.nlm.nih.gov/pubmed/26358792

- This paper summarizes the NCCN guidelines for management of thrombosis in cancer patients.

Ovarian vein thrombosis after debulking surgery for ovarian cancer: epidemiology and clinical significance.

Mantha S, Sarasohn D, Ma W, Devlin SM, Chi DS, Roche KL, Suidan RS, Woo K, and Soff GA.
Am J Obstet Gynecol. 2015; 213(2):208.e1-4. PMID: 25743130 PMCID: PMC4863445
http://www.ncbi.nlm.nih.gov/pubmed/25743130

- We showed that ovarian vein thrombosis is common after surgery for ovarian cancer and can usually be followed expectantly without treatment with anticoagulants.

Indirect comparison of dabigatran, rivaroxaban, apixaban and edoxaban for the treatment of acute venous thromboembolism.

Mantha S, Ansell J.
J Thromb Thrombolysis. 2015; 39(2):155-65. PMID: 24989022
http://www.ncbi.nlm.nih.gov/pubmed/24989022

- We compared the results of previously published studies on the treatment of venous thromboembolic disease with new anticoagulants. Our results suggest that apixaban might be associated with a lower risk of bleeding compared with the other drugs.

MYELOMA

Treatment with Carfilzomib-Lenalidomide-Dexamethasone with Lenalidomide Extension in Patients With Smoldering or Newly Diagnosed Multiple Myeloma.

Korde N, Roschewski M, Zingone A, Kwok M, Manasanch EE, Bhutani M, Tageja N, Kazandjian D, Mailankody S, Wu P, Morrison C, Costello R, Zhang Y, Burton D, Mulquin M, Zuchlinski D, Lamping L, Carpenter A, Wall Y, Carter G, Cunningham SC, Gounden V, Sissung TM, Peer C, Maric I, Calvo KR, Braylan R, Yuan C, Stetler-Stevenson M, Arthur DC, Kong KA, Weng L, Faham M, Lindenberg L, Kurdziel K, Choyke P, Steinberg SM, Figg W, Landgren O.
JAMA Oncol. 2015; 1(6):746-54. PMID: 26181891
http://www.ncbi.nlm.nih.gov/pubmed/26181891

- Carfilzomib-lenalidomide-dexamethasone therapy is a tolerable regimen for Newly Diagnosed Multiple Myeloma patients and High-risk Smoldering Myeloma patients that yields high rates of MRD negativity.

Minimal residual disease in multiple myeloma: bringing the bench to the bedside.

Mailankody S, Korde N, Lesokhin AM, Lendvai N, Hassoun H, Stetler-Stevenson M, Landgren O.
Nat Rev Clin Oncol. 2015; 12(5):286-95. PMID: 25622976
http://www.ncbi.nlm.nih.gov/pubmed/25622976

- Minimal residual disease (MRD) testing is increasingly used in the management of patients with hematologic malignancies. This comprehensive review outlines the technologies used and prognostic implications of MRD testing in multiple myeloma.

Agent Orange Exposure and Monoclonal Gammopathy of Undetermined Significance: An Operation Ranch Hand Veteran Cohort Study.

Landgren O, Shim YK, Michalek J, Costello R, Burton D, Ketchum N, Calvo KR, Caporaso N, Raveche E, Middleton D, Marti G, Vogt RF Jr.
JAMA Oncol. 2015; 1(8):1061-8. PMID: 26335650
http://www.ncbi.nlm.nih.gov/pubmed/26335650

- Prior occupational studies have shown that pesticides (ie, insecticides, herbicides, fungicides) are associated with excess risk of multiple myeloma and its precursor state, monoclonal gammopathy of undetermined significance (MGUS). This study including 479 US Air Force personnel who participated in Operation Ranch Hand (Ranch Hand veterans) and 479 other US Air Force personnel who had similar duties in Southeast Asia during the same time period but were not involved in herbicide spray missions (comparison veterans) was designed to examine the relationship between MGUS and exposure to Agent Orange, including its contaminant 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Operation Ranch Hand veterans have a significantly increased risk of MGUS, supporting an association between Agent Orange exposure and multiple myeloma.

On being less tolerant: enhanced cancer immunosurveillance enabled by targeting checkpoints and agonists of T cell activation.

Lesokhin AM, Callahan MK, Postow MA, Wolchok JD.
Sci Transl Med. 2015; 7(280):280sr1. PMID: 25810313
http://www.ncbi.nlm.nih.gov/pubmed/25810313

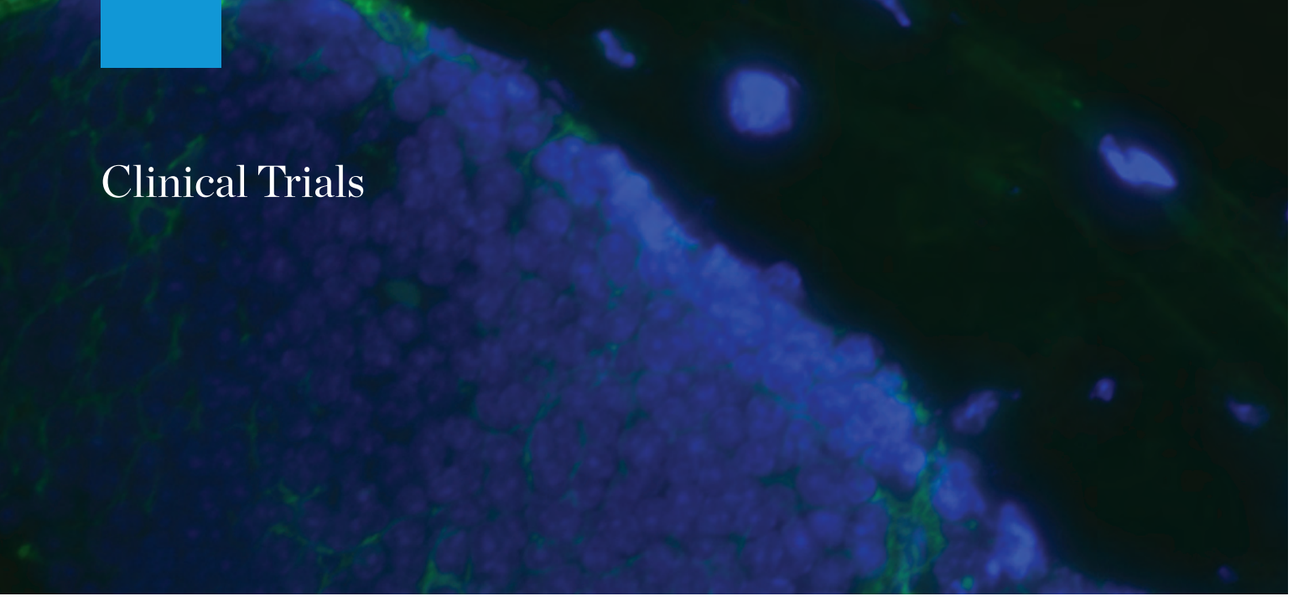
- This paper is a review of the state of the art in immunotherapy focused on drugs that modify the way patient's own T cells stay activated against cancer cells. The paper reviewed advances in our clinical knowledge of responders to therapies that block T cells from turning off, the side effects of these therapies, and possible predictors of susceptibility to treatment. Also reviewed were drugs that further enhance T cell activation. Finally, available data describing combinations therapies that use drugs that inhibit T cell off switches or enhance T cell on switches together with radiation or other standard cancer treatments.

The Role of Diagnosis and Clinical Follow-up of Monoclonal Gammopathy of Undetermined Significance on Survival in Multiple Myeloma.

Sigurdardottir EE, Turesson I, Lund SH, Lindqvist EK, Mailankody S, Korde N, Björkholm M, Landgren O, Kristinsson SY.
JAMA Oncol. 2015; 1(2):168-74. PMID: 26181017
http://www.ncbi.nlm.nih.gov/pubmed/26181017

- Multiple myeloma is consistently preceded by the precursor state, monoclonal gammopathy of undetermined significance (MGUS). This population-based study included all patients with multiple myeloma diagnosed in Sweden (n = 14,798) from 1976 to 2005 (with follow-up until 2007); 394 (2.7%) had previously been diagnosed as having MGUS. Patients with multiple myeloma with prior knowledge of MGUS had better multiple myeloma survival, suggesting that earlier treatment of multiple myeloma leads to better survival. Among MM patients with prior knowledge of MGUS, low M-protein concentration (<0.5 g/dL) at MGUS diagnosis was associated with poorer multiple myeloma survival, reflective of less frequent clinical follow-up. These observations stress the importance of clinical follow-up in patients with MGUS, regardless of risk stratification. ■

Clinical Trials



Thymus cellularity rescued after stem cell transplant demonstrating normalization of architecture by cytokeratin and lymphoid cellularity by Dapi.
CREDIT: SUSAN PROCKOP

These are a few highlighted therapeutic clinical trials in the Division of Hematologic Oncology. For more information, please visit: https://www.mskcc.org/cancer-care/clinical-trials

ADULT BONE MARROW TRANSPLANT

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

IRB #: 14-263; PI: Miguel-Angel Perales

- Dr. Perales is the national co-Chair of this randomized phase 3 study that will seek to prove that CD34 selection of the stem cell graft (T-cell depletion) improves outcomes in patients undergoing stem cell transplant for acute leukemia or MDS by reducing the risk of chronic graft-versus-host disease (GVHD). This approach was pioneered at MSK over two decades ago and this study may change the current standard of care in the most common indications for transplant.

Phase II Study of Palifermin with Leuprolide Acetate for the Promotion of Immune Recovery Following Total Body Irradiation Based T-Cell Depleted Allogeneic Hematopoietic Stem Cell Transplantation

IRB #: 12-077; PI: Miguel-Angel Perales

- T-cell depletion of the stem cell graft reduces the risk of graft-versus-host disease (GVHD), one of the main complications of a stem cell transplant without increasing the risk of relapse in patients with acute leukemia and MDS. One limitation, however, is a delay in recovery of the immune system and an increased risk of infections. Based on work in Dr. van den Brink's lab, this study seeks to improve immune recovery by protecting the thymus using palifermin and leuprolide.

Analysis of the Effects of Treatment with Low Dose 5′-Azacitidine After Allogeneic T-cell Depleted Transplant on BM and Peripheral Blood Samples

IRB: 14-060; PI: Roni Tamari

- After analyzing the outcomes of patients with myelodysplastic syndrome who underwent T cell depleted transplant (the paper above), we learned that high risk cytogenetic abnormalities are associated with higher risk for post-transplant relapse. In collaboration with Dr. Stephen Chung, from the Leukemia Service, we study how a maintenance treatment with low doze Azacitidine in patients with high risk cytogenetic abnormalities can reduce the relapse risk post transplant.

A Multi-center Randomized Phase II Study of the Impact of CD34+ Cell Dose on Progression-free Survival Following High-dose Therapy and Autologous Stem Cell Transplantation for Relapsed and Refractory Diffuse Large B-cell Lymphoma (DLBCL)

IRB #: 15-193; PI: Craig Sauter

- In retrospective studies, the amount of blood stem cells received at the time of autologous transplantation has suggested improved survival of patients with relapsed or primary refractory diffuse large B cell lymphoma. We are leading a nine institution multicenter study to prospectively investigate the prognostic impact of blood stem cell dose at the time of autologous transplantation in these patients.

A Randomized Phase III Trial Comparing Conventional-Dose Chemotherapy Using Paclitaxel, Ifosfamide, and Cisplatin (TIP) with High-Dose Chemotherapy Using Mobilizing Paclitaxel Plus Ifosfamide Followed by High-Dose Carboplatin and Etoposide (TI-CE) as First Salvage Treatment in Relapsed or Refractory Germ Cell Tumors (Alliance A031102) (CIRB)

IRB #: 15-154, PI: Darren Feldman

- IRB #15-154, also known as the "TIGER trial" is an international phase 3 cooperative group clinical trial that seeks to determine the optimal second-line chemotherapy treatment for patients with advanced germ cell tumors. The study is comparing a conventional-dose chemotherapy regimen developed at MSKCC known as TIP with a high-dose chemotherapy and autologous stem cell transplant program also developed at MSKCC, known as TI-CE. The primary endpoint of the trial is overall survival, meaning the study seeks to identify which treatment results in more patients being alive. It will enroll 420 patients (210 to each arm) in more than 7 countries across 3 continents over a 5 year period.

LEUKEMIA

A Phase 1, Multicenter, Open-Label, Dose-Escalation and Expansion, 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

- AG-221 is a small molecule inhibitor that blocks the action of mutated IDH-2, an abnormality found in about 15% of patients with acute myeloid leukemia (AML). To date, the results of this phase 1, dose escalation and dose expansion trial have been remarkable. The overall response rate of this very poor risk patient population is 40%, with many patients achieving a complete remission. The study is ongoing and entering a second dose expansion phase to look more closely at the efficacy of AG-221 in a patients with relapsed and refractory AML.

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

IRB #: 12-200; PI: Jae Park

- HCL is characterized by nearly 100% frequency of the BRAFV600E mutation that is the key driver in HCL development. We investigated the efficacy of the BRAF inhibitor, Vemurafenib, in relapsed HCL by conducting the first U.S. multicenter, investigator-initiated, phase II clinical trial. We have enrolled 26 patients with relapsed HCL, and observed 100% overall response rates (CR+PR) in this refractory patient population. While longer follow up is needed to confirm the durability of response, this trial provides a proof-of-concept and validates mutant BRAF as a rational therapeutic target in HCL.

The ROCKET Study: A Phase 2, Single-arm, Multicenter Trial to Determine the Efficacy and Safety of JCAR015 in Adult Subjects with Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia

IRB #: 15-099; PI: Jae Park

- We have previously shown that we can take patients' own immune cells called T cells and re-engineer them to express an artificial T cell receptor called chimeric antigen receptor (CAR) that is designed to recognize and selectively kill cancer cells expressing CD19 antigen. Using these CD19-targeted CAR modified T cells, we then demonstrated 80% complete response rates in adult patients with relapsed B-cell acute lymphoblastic leukemia (B-ALL) in our phase I clinical trial (IRB#09-114). Based on these encouraging results, a multi center phase II trial, the ROCKET study (IRB#15-099), has opened at MSKCC to determine the efficacy of CD19-targeted CAR T cells in a larger cohort of adult patients with relapsed B-ALL.

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

IRB #: 14-168; Michael Mauro

- ABL001 represents a significant breakthrough in the evolution of oral small molecule inhibitors for patients with Philadelphia-chromosome positive leukemias. By blocking the Bcr-Abl kinase central in these cancers in a new and distinct way, phase I trial results have shown excellent safety and clear activity in cases where all five previously developed medicines have failed. The phase I trial continues globally in a greatly expanded format and we are delighted to be a significant contributor at MSKCC.

A Phase I Trial of SGN-CD33A in Patients with CD33-positive Acute Myeloid Leukemia

IRB #: 13-137; Eytan Stein

- SGN-CD33A is an antibody against CD33 which is found on the malignant cells of most patients with acute myeloid leukemia. This antibody is linked to a potent chemotherapeutic agent and allows direct delivery of the chemotherapy to the leukemic cell and avoids some of the toxicity associated with systemic chemotherapy that is given intravenously. When given in combination with a class of drugs called hypomethylating agents, SGN-CD33A appears quite effective, with a complete remission rate of over 70%.

LYMPHOMA

A Phase Ib/II Study Evaluating the Safety and Efficacy of MPDL3280A in Combination with Either Obinutuzumab plus Bendamustine or Obinutuzumab Plus CHOP In Patients With Follicular Lymphoma Or Diffuse Large B-cell Lymphoma

IRB #: 16-006; PI: Younes, Anas, MD

- This study will evaluate the safety, efficacy, and pharmacokinetics of induction treatment consisting of atezolizumab in combination with either obinutuzumab plus bendamustine (MPDL-G-benda) in participants with follicular lymphoma (FL) or obinutuzumab plus cyclophosphamide/doxorubicin/vincristine/prednisone (CHOP) (MPDL-G-CHOP) in participants with FL or diffuse large B-cell lymphoma (DLBCL), followed by post-induction treatment consisting of either atezolizumab plus obinutuzumab (MPDL-G) in participants with FL who achieve a complete response (CR) or partial response (PR) at end of induction (EOI) or atezolizumab alone in participants with DLBCL who achieve a CR at EOI.

A Phase 1, First-in-Human, Open-Label, Dose Escalation Study of JNJ-64052781, a Humanized CD19 x CD3 Dual-Affinity Re-Targeting (DART®) Protein in Subjects with Relapsed or Refractory B-cell Malignancies

IRB #: 15-125; PI: Younes, Anas, MD

- The purpose of this study is to evaluate the safety, tolerability, dose-limiting toxicities (any harmful effect of a drug) (DLT), maximum tolerated dose (MTD), recommended Phase 2 dose (RP2D) and preliminary clinical activity of JNJ-64052781 when administered intravenously to participants with relapsed or refractory B-cell malignancies [diffuse-large B cell lymphoma (DLBCL), follicular lymphoma (FL), mantle-cell lymphoma (MCL), chronic lymphocytic leukemia (CLL), and acute lymphoblastic leukemia (ALL)].

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

IRB #: 14-130 ; PI: Zelenetz, Andrew, MD, PhD

- Chemoimmunotherapy with rituximab with cyclophosphamide/doxorubicin/vincristine/prednisone (R-CHOP) is the standard of care for patient with untreated DLBCL; however, only approximately 60% of patients are cured. Venetoclax is a drug that promotes death of tumor cells by inhibition of BCL2. The study evaluates the combination of R-CHOP with venetoclax to determine the safety and efficacy of the combination, response duration, progression free survival and overall survival.

Sequential Chemotherapy and Lenalidomide Followed by Rituximab and Lenalidomide Maintenance for Untreated Mantle Cell Lymphoma: A Phase II Study

IRB #: 15-196 ; PI: Kumar, Anita, MD

- To improve outcomes for untreated mantle cell lymphoma patients, we are testing a new treatment approach in a phase II study that incorporates the highly active, immune modulatory drug lenalidomide with a standard induction chemotherapy backbone including RCHOP and high-dose cytarabine. Given emerging data that maintenance therapy is highly effective in mantle cell lymphoma and may have equivalent benefit when compared to high dose therapy and autologous stem cell transplant, in this study induction chemotherapy is followed by rituximab and lenalidomide maintenance for six months. In this study, we will also be evaluating the prognostic value of interim PET scans and minimal residual disease testing using a deep-sequencing based platform. These radiographic and molecular biomarkers of response may be predictive of outcomes in MCL and help establish a basis for future risk-adapted therapies in MCL.

A Phase II Clinical Trial of MK-3475 (Pembrolizumab) in Subjects with Relapsed or Refractory (R/R) Classical Hodgkin Lymphoma (cHL)

IRB #: 15-166 ; PI: Moskowitz, Craig, MD

- This is a Pembrolizumab trial for patients with relapsed or refractory classical Hodgkin lymphoma. This is a Memorial led study.

HEMATOLOGY

A Open Label Phase II Study for Chemotherapy Induced Thrombocytopenia

IRB: 13-132; PI: Gerald Soff

- This is an ongoing clinical trial of romiplostim for treatment of chemotherapy-induced thrombocytopenia.

MYELOMA

Lenalidomide Maintenance in Plasma Cell Myeloma

IRB #: 15-129; PI: Ola Landgren

- This study is designed to focus on longitudinal monitoring in parallel with lenalidomide maintenance therapy in patients with multiple myeloma. Main focus is to study long-term minimal residual disease (MRD) negative disease states with regard to the bone marrow microenvironment and to circulating immune cells in the peripheral blood. For patients who are MRD positive, the study is investigating the role of the bone marrow microenvironment and to circulating immune cells in the peripheral blood in relation to host-immune control of low level residual disease.

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

IRB #: 15-310; PI: Nikoletta Lendvai

- This is a single institution study of a fully oral regimen for relapsed myeloma. We are evaluating the safety and efficacy of combining the first recently FDA approved oral proteasome inhibitor, ixazomib with selinexor and dexamethasone. Selinexor (KPT-330) is a very exciting, first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound that has been shown to have single agent activity against myeloma. Selinexor functions by inhibiting the nuclear export protein XPO1, leading to the accumulation of tumor suppressor proteins in the cell nucleus, which results in increasing their tumor suppressor function that may in turn lead to apoptosis (programmed cell death) of myeloma cells.

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

IRB #: 15-294; PI: Sham Mailankody

- Smoldering multiple myeloma is a precursor disease that is currently managed with watchful monitoring. The advent of effective and safe treatment options has prompted clinical trials focusing on early treatment initiation in smoldering myeloma. This pilot clinical trial is evaluating treatment with ixazomib, an oral proteasome inhibitor and dexamethasone in patients with high risk smoldering multiple myeloma.

A Randomized Phase 2 Trial to Evaluate Three Daratumumab Dose Schedules in Smoldering Multiple Myeloma

IRB #: 15-168; PI: Ola Landgren

- This study is designed to investigate 3 different dosing schedules of single drug daratumumab (anti-CD38) monoclonal antibody targeting patients with highrisk smoldering myeloma. The goal of the study is to delay and/or prevent development of multiple myeloma by early intervention.

VLX1570 and Low-Dose Dexamethasone in Relapsed or Relapsed and Refractory Multiple Myeloma: A Clinical and Correlative Phase 1/2 Study

IRB #: 14-274; PI: Ola Landgren

- Proteasome inhibition is one of the most effective targets for the treatment of multiple myeloma. This first-time-in-man phase 1/2 clinical trial with Dr. Landgren as the lead-PI uses a novel approach to inhibit the 19S proteasome upstream of current 20S proteasome inhibitors (e.g., velcade, carfilzomib). Preclinical data show strong effect in velcade resistant myeloma cell lines. ■

SPECIAL THANKS TO SUSAN PROCKOP, MD, FOR HER CONTRIBUTION OF THE SCIENTIFIC IMAGES USED IN THE DIVISION OF HEMATOLOGIC ONCOLOGY'S 2015 ANNUAL REPORT.

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

Below is a list of patrons who donated $50,000 or more in 2014.

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Vital Projects Fund, Inc.
John and Barbara Vogelstein Foundation
Estate of Kathryn D. Wriston

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 866-815-9501.

DONATING BLOOD

Blood donations can be designed for a particular patient or for our general blood inventory. For more information or an appointment, call 212-639-8177 or 212-639-7648.

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.

The 3D Genome

Nucleolar staining of bone marrow stem and progenitor cells from mice with haploinsufficiency of Smc3 reveal supernumerary and fragmented nucleoli similar to patients with Roberts Syndrome, where Smc3 is functionally impaired.

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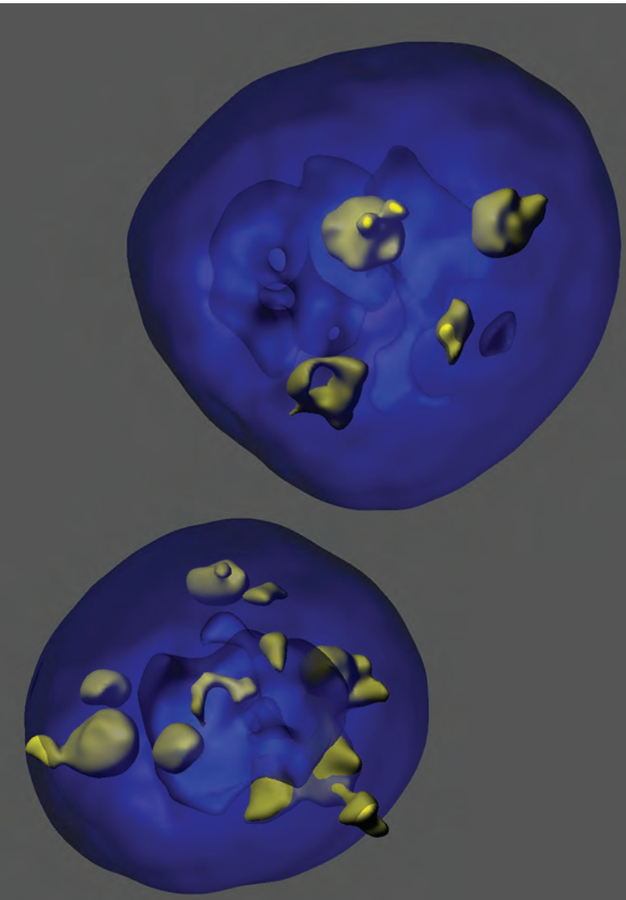

Architectural rendering of MSK's 74th Street building, the future home of our Division.

Memorial Sloan Kettering Cancer Center

GENERAL INFORMATION
212-639-2000

PHYSICIAN REFERRAL SERVICE
800-525-2225

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