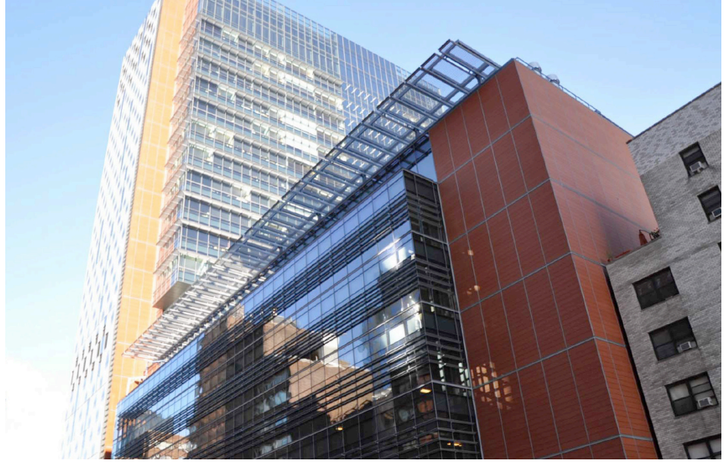
DIVISION OF SUBSPECIALTY MEDICINE

2018 REPORT

Memorial Sloan Kettering Cancer Center

Contents

On the cover: Clockwise from top center: Mini Kamboj, R. Michael Tuttle, Jennifer Liu, Catherine Bautista, Ilya Glezerman, and left to right, Emmy Ludwig, Hans Gerdes, and Robin Mendelsohn.



A Note from the Division Head

You may not be a NASCAR fan, but you have likely seen the amazingly efficient and coordinated midrace servicing and fueling of race cars by dedicated pit crews as they push their car and driver toward the checkered flag. Getting to the winner's podium requires teamwork and a dedicated, masterful pit crew.

OK, comparing cancer treatment to a car race vastly oversimplifies what we do at MSK, but we all agree that optimal patient care depends on teamwork, with multiple pit crews supporting patients as they make their way through the twists and turns of cancer care. While cancer treatments are becoming more effective and increasingly curative, toxicities involving the heart, kidneys, liver, and immune system frequently accompany this success and require specialized care.

The six services of MSK's Division of Subspecialty Medicine (the Cardiology; Endocrine; Gastroenterology, Hepatology, and Nutrition Services; Infectious Diseases; Pulmonary, and Renal Services) provide unique clinical expertise that is essential for optimal responses to cancer treatment. Approaches to cure previously untreatable cancers include the following:

- replacing a patient's immune system by stem cell transplantation
- administering antibodies that bind to and kill cancer cells
- boosting immune effector mechanisms by blocking inhibitory receptors
- infusing lymphocytes that are genetically engineered to kill cancer cells

These rapidly evolving treatments, however, are also associated with infectious or inflammatory complications that require super-specialized expertise.

Our medical subspecialists, nurses, physician assistants, and administrative staff team up with our oncologists and surgeons to optimize responses to cancer therapy by discovering, treating, and preventing complications, such as infections of the immunocompromised host; inflammation resulting from immune activation; and heart, liver, intestinal, kidney, lung, and endocrine toxicities associated with cancer treatment.

Through our fellowship programs, we are also training the next generation of medical subspecialists and providing them with expertise in the treatment and prevention of the complications associated with cancer treatment. The following pages outline some of the exciting, ongoing work within our Subspecialty Medicine Division.

ERIC G. PAMER, MD
HEAD, DIVISION OF SUBSPECIALTY MEDICINE

Division of Subspecialty Medicine Faculty

ATTENDINGS

CARDIOLOGY SERVICE

Richard Steingart
Chief, Cardiology Service

Michael Baum
Attending

Angel Chan
Instructor

Carol Chen
Associate Attending

Paul Cohen
Assistant Attending

Dipti Gupta
Assistant Attending

Michelle Johnson
Clinical Director
Attending

Jennifer Liu
Attending

Eileen McAleer
Assistant Attending

Nancy Rolstacher
Attending

Wendy Schaffer
Associate Attending

Jonathan Weinsaft
Associate Attending

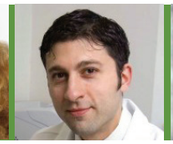
Howard Weinstein
Associate Attending

Anthony Yu
Assistant Attending

ENDOCRINOLOGY SERVICE

James Fagin
Chief, Endocrinology Service

Laura Boucai
Associate Attending

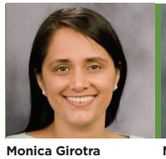


Azeez Farooki
Associate Attending

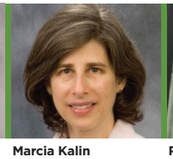
Stephanie Fish
Associate Attending

James Fiory
Assistant Attending

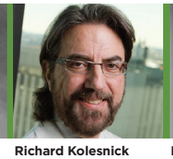
Eliza Geer
Associate Attending



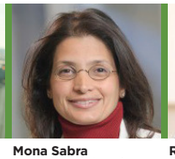
Monica Girotra
Associate Attending



Marcia Kalin
Associate Attending



Richard Kolesnick
Attending



Mona Sabra
Associate Attending

R. Michael Tuttle
Clinical Director
Attending

GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION SERVICE

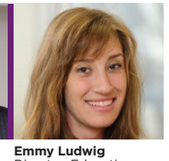
Mark Schattner
Chief, Gastroenterology, Hepatology, and Nutrition Service

Delia Calo
Assistant Attending

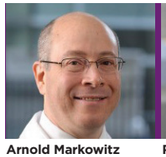
Maya Gambarin-Gelwan
Director, Hepatology
Associate Attending

Hans Gerdes
Director, Endoscopy Unit
Attending

Robert Kurtz
Attending

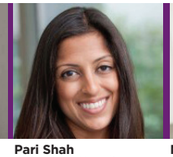


Emmy Ludwig
Director, Education
Associate Attending

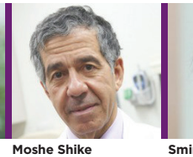


Arnold Markowitz
Director, Gastroenterology Fellowship Program
Attending

Robin Mendelsohn
Clinical Director
Assistant Attending



Pari Shah
Asistant Attending



Moshe Shike
Director, Clinical Nutrition
Attending

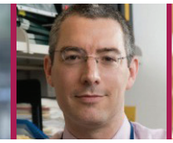
Smirta Sinha
Instructor

INFECTIOUS DISEASES SERVICE

Tobias Hohl
Chief, Infectious Diseases Service

Arthur Brown
Chief and Medical Director, EHWS
Attending

Cesar Figueroa Ortiz
Clinical Director
Assistant Attending



Michael Glickman
Attending

Lena Heung
Assistant Attending

Anna Kaltsas
Director, Infectious Diseases Fellowship Training Program
Assistant Attending

Mini Kamboj
Director, Infection Control
Assistant Attending

Yeon Joo Lee
Assistant Attending

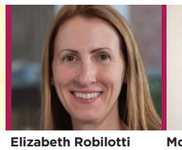
Peter Mead
Assistant Attending

Sejal Morjaria
Instructor

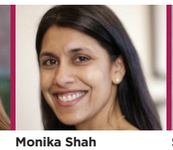
Eric Pamer
Head, Division of Subspecialty Medicine
Attending

Genovefa Papanicolau
Director, of Clinical Trials
Attending

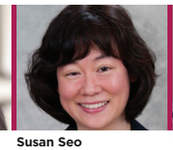
Gil Redelman-Sidi
Assistant Attending



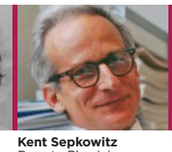
Elizabeth Robilotti
Assistant Attending



Monika Shah
Vice Chair, Education, Department of Medicine
Chair, CME Committee
Associate Attending



Susan Seo
Director, Antibiotic Management Program
Associate Attending



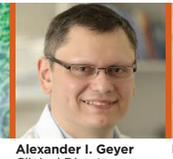
Kent Sepkowitz
Deputy Physician-in-Chief for Quality and Safety

Ying Taur
Assistant Attending

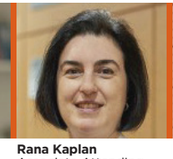
PULMONARY SERVICE

Mohit Chawla
Chief, Pulmonary Service
Director, Section of Interventional Pulmonology

Marc Feinstein
Associate Attending



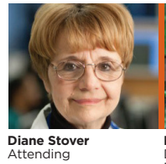
Alexander I. Geyer
Clinical Director
Co-Supervising Physician, Pulmonary Advanced Practice Provider Program



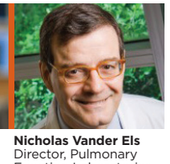
Rana Kaplan
Associate Attending

Robert P. Lee
Director, Pleural Diseases
Assistant Director, Section of Interventional Pulmonology
Co-Supervising Physician, Pulmonary Advanced Practice Provider Program

Jean Santamauro
Director, Pulmonary Medicine Fellowship Program



Diane Stover
Attending

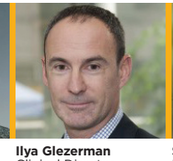


Nicholas Vander Els
Director, Pulmonary Function Laboratories
Attending

RENAL SERVICE

Edgar A. Jaimes
Chief, Renal Service

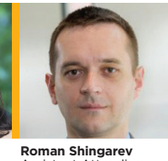
Carlos Flombaum
Attending



Ilya Glezerman
Clinical Director
Associate Attending

Sheron Latcha
Program Director, Nephrology Fellowship
Associate Attending

Insara Jaffer Sathick
Assistant Attending



Roman Shingarev
Assistant Attending

ADVANCED PRACTICE PROVIDERS

CARDIOLOGY SERVICE

Neisha DeJesus
Physician Assistant

Ashlee Jones
Physician Assistant

Natalie Mercier-Munoz
Physician Assistant

Anna Plundo
Physician Assistant

Dylana Possiel
Physician Assistant

Sofia Romero
Physician Assistant

Lina Saab
Nurse Practitioner

Victoria Vallejo
Physician Assistant

Eileen Vella
Physician Assistant

Alison Wiesenmaier
Nurse Practitioner

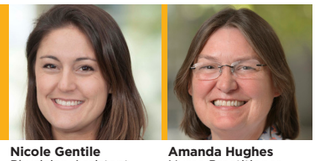
INFECTIOUS DISEASES SERVICE

Melissa Bacchus
Physician Assistant

Alexa Joanow
Physician Assistant

Elizabeth Schmidt
Physician Assistant

RENAL SERVICE



Nicole Gentile
Physician Assistant
(Inpatient)

Amanda Hughes
Nurse Practitioner
(Inpatient)

"Working on the Renal Service has been a great learning experience for me as it has allowed me to see patients with many different types of cancers and related kidney injuries. In addition, I find it enjoyable to work on a collaborative team with the other services."

— NICOLE GENTILE
PHYSICIAN ASSISTANT
RENAL SERVICE

PULMONARY SERVICE

Ngoke Aun (Kelly) Chu
Physician Assistant

Kathy La
Physician Assistant

Sally Sa
Physician Assistant

ENDOCRINOLOGY SERVICE

Ritka Chitkara
Nurse Practitioner

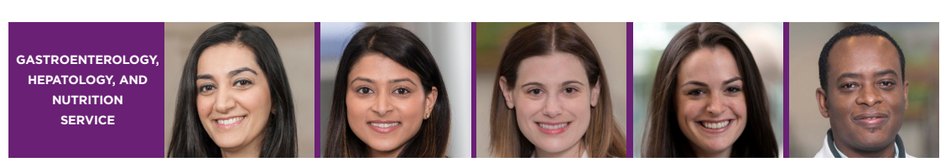
Janet McKiernan
Nurse Practitioner

Rebecca Zueren
Nurse Practitioner

"I will be the recipient of the 2018 Excellence in Cancer Prevention & Early Detection Award and will be recognized as the recipient of this award during the Oncology Nursing Society 43rd annual congress."

— JANET MCKIERNAN
NURSE PRACTITIONER
ENDOCRINOLOGY SERVICE

GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION SERVICE



Shaifa Farooqui
Physician Assistant
(Inpatient)

Jeana Joseph
Nurse Practitioner
(Nutrition)

Alexis Kaiman
Nurse Practitioner
(Nutrition)

Jaclyn Newfield
Nurse Practitioner
(Hepatology)

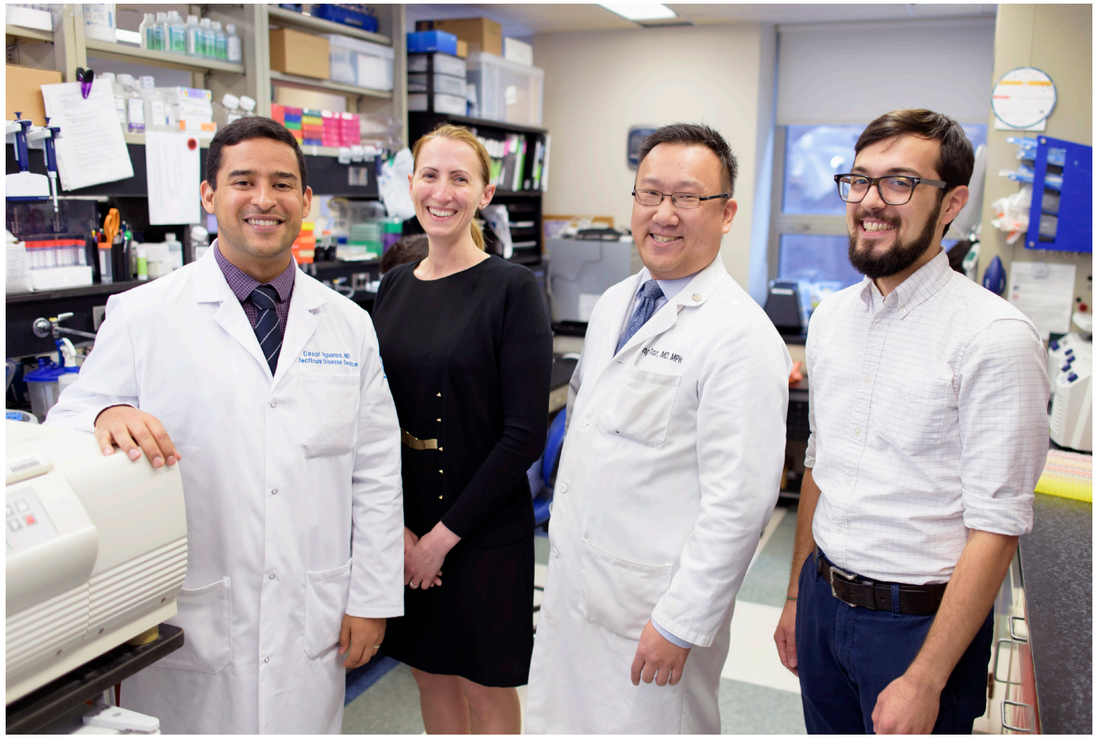
Robert Okolie
Nurse Practitioner
(Nutrition)

"I am passionate about caring for our adult patients and working to optimize their liver health before, during, and after cancer therapy to allow them to have the best quality of life possible."

— JACLYN NEWFIELD
NURSE PRACTITIONER
GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION SERVICE

"Within the practice I work, we now have SMOFlipid, an alternative to standard fat emulsion. This allows for safe administration of lipids in most pts with abnormal liver enzymes."

— ROBERT OKOLIE
NURSE PRACTITIONER
GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION SERVICE



Some of the FMT Team — From left: Cesar Figueroa Ortiz, Elizabeth Robilotti, Ying Taur, and research study assistant Mergim Gjonbalaj in the Schwartz 5 Laboratory.

Research Focuses on Helping People with Cancer Rebuild Their Immune Systems after Treatment

OUR BODIES ARE HOMES to trillions of tiny microorganisms, collectively called the microbiota. In recent years, advances in gene sequencing and computational biology have made it possible to begin to quantify and study these microbes by sequencing their combined DNA — what's known as the microbiome.

This research is important for protecting the well-being of people with cancer, especially those undergoing intensive chemotherapy for leukemia or stem cell or bone marrow transplants (BMTs) for a variety of blood cancers. It's long been known that the antibiotics used to prevent or treat infection in immunocompromised people can have a detrimental effect on the microbiome, especially in the gastrointestinal tract.

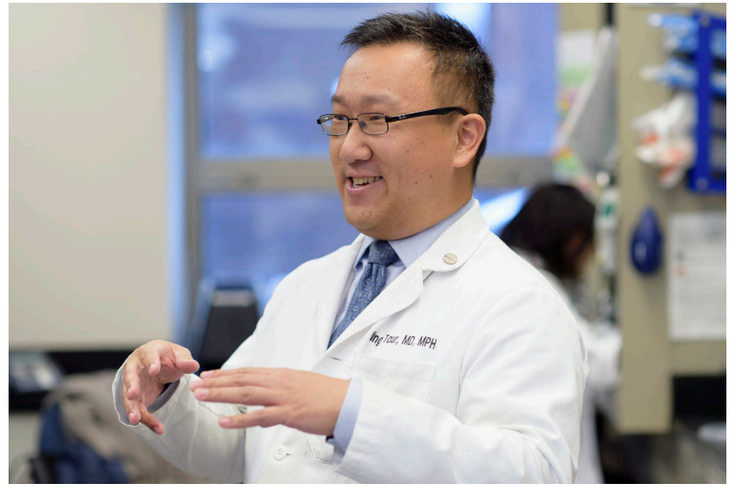
"Some antibiotics are more harmful than others," says Dr. Ying Taur, an infectious diseases physician-scientist at Memorial Sloan Kettering. "The friendliest and most beneficial bacteria are anaerobic, which means they prefer to live in low oxygen environments, such as the colon." These microbes are extremely well suited for residence in the gut and provide a wide variety of benefits to their host.

"Antibiotics that kill anaerobes can be like setting off a nuclear bomb in the gut," he adds. "They can cause widespread damage." Combining these antibiotics with chemotherapy, which has the side effect of damaging the lining of the GI tract, can make the effects even worse..

Previous research from Dr. Taur has looked at the role of antibiotics in people with cancer, especially those undergoing BMTs. Some of his findings have suggested that the best way to fight the dangerous bacteria that can take over the body after cancer treatment may be to maintain a healthy balance of microorganisms and protect those that are known to be healthy. These beneficial bacterial — commensal microorganisms — seem to help the body fight off dangerous infections.

Much of his current work is focused on what is called autologous fecal microbiota transplant (FMT). Dr. Taur is currently leading a clinical trial for people undergoing BMT in which their fecal microbiota are collected and stored before they begin their transplant, then infused back into their bodies after the BMT — once their new immune systems begin to grow.

> **"If there is any chance we can help the new immune system – 'grow up' – more quickly by exposing it to a diverse microbiome, previous studies suggest we'll be able to improve the outcome of transplants."**
>
> **— YING TAUR, PHYSICIAN-SCIENTIST**

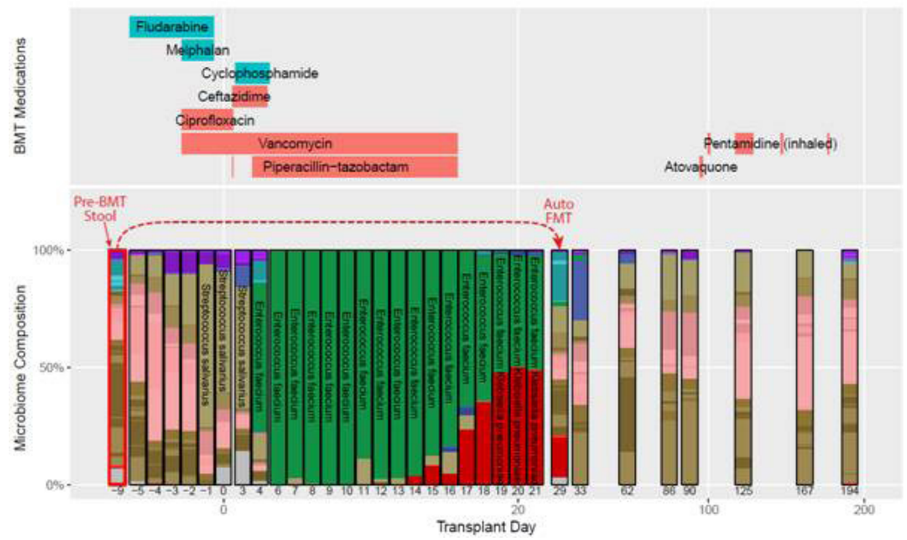


The trial was originally designed to look at whether FMT can treat or prevent a particularly harmful infection caused by a bacterium called *Clostridium difficile (C. diff)*. But Dr. Taur and his co-investigators expect the beneficial effects may be much more wide-ranging than just preventing *C. diff* infections. "When someone gets a BMT, their newly transplanted immune system doesn't always know how to do its job," he says. This can often lead to potentially lethal side effects such as graft-versus-host disease, in which the immune cells from the donor attack the recipient's organs and tissues.

"If there is any chance we can help the new immune system –'grow up'– more quickly by exposing it to a diverse microbiome, previous studies suggest we'll be able to improve the outcome of transplants," he notes. He adds that providing patients with a diverse microbiota may also help protect them from other infectious agents, such as viruses. Cytomegalovirus is known to be especially dangerous in people who have undergone BMTs.

The first phase of this research is using a patient's own microbiota, which their bodies are more likely to recognize and which is less likely to contain dangerous microbes. Eventually, though, the investigators may evaluate the benefits of using an FMT from a healthy donor. This procedure is increasingly being used for people who don't have cancer but are affected by *C. diff*.

In addition to his clinical research, Dr. Taur also has a busy clinical practice in which he sees patients at MSK who are coping with all kinds of infections. The Infectious Diseases Service has two clinics — one for people who are immunocompromised (including those with HIV infections and blood cancers) and one for those who are not. ■



Mohit Chawla reviewing a lung bronchoscopy with physician assistant Sally Sa and nurse Catherine Bautista.

The Interventional Pulmonology Section Uses Technology to Provide Minimally Invasive Procedures to Patients

TECHNOLOGICAL ADVANCES have improved many aspects of cancer care over the past few decades. One area that has made large strides is developing procedures that are less invasive, particularly in the field of interventional pulmonology (IP).

Interventional pulmonology uses flexible scopes and other tools to diagnose, stage, and treat diseases of the airway, including the lungs, and other parts of the chest. At Memorial Sloan Kettering, the program was started in 2008 by Mohit Chawla, who is board certified in IP. In 2010, he was joined by Robert Lee, also a board-certified interventional pulmonologist.

"Our program offers a broad range of procedures, both diagnostic and therapeutic," Dr. Chawla explains. "Many of these are offered through bronchoscopy, which involves working with a small camera inside the airway. We can use this procedure to access the lungs as well as the mediastinum, the area between the heart and lungs."

Bronchoscopy can be used to obtain biopsy samples from masses and nodules in the lungs, as well as to biopsy lymph nodes in the mediastinum. "This used to be done with two separate procedures, a needle biopsy in the lung and either a separate bronchoscopy or a surgical procedure to remove the lymph nodes," Dr. Chawla says. "Now we can do it all with one low-risk procedure, which makes it much easier for patients." In addition, the advent of endobronchial ultrasound (EBUS) allows IP specialists to combine the standard bronchoscope with an ultrasound probe to more safely and accurately sample lymph nodes in the mediastinum.

> **"Our program offers a broad range of procedures, both diagnostic and therapeutic. Many of these are offered through bronchoscopy, which involves working with a small camera inside the airway. We can use this procedure to access the lungs as well as the mediastinum, the area between the heart and lungs."**
>
> **— MOHIT CHAWLA, INTERVENTIONAL PULMONOLOGIST**

He adds that the volume of lung biopsies has increased since the introduction several years ago of low-dose CT screening for lung cancer, which often reveals nodules, enlarged lymph nodes, or other findings that require biopsies to diagnose or rule out cancer.

Another technology that has improved these biopsy procedures is navigational bronchoscopy. This GPS-like system helps doctors localize lung masses or nodules. It can be combined with a different type of EBUS. This method uses an ultrasound probe to visualize lung masses prior to biopsy, after they have been localized by navigation. IP procedures can also take advantage of the ultrathin bronchoscope, which allows better navigation inside the chest and more detailed imaging of the area in and around lung masses.

"Another area where the IP team can offer exceptional care is through our Complex Airways Program," Dr. Lee says. "We are able to offer a number of therapeutic procedures to people who have cancer that is making breathing difficult." Both primary cancers or metastatic tumors that have spread to the lungs, trachea, and adjacent areas from other parts of the body and are blocking a person's airway. The IP team can open up the airway with different bronchoscopy techniques, such as stenting or laser.

"Breathing problems often make it difficult for people to get the therapies they need to treat their cancers," Dr. Chawla says. These problems may be caused by cancer as well as benign conditions, such as tracheal stenosis (a narrowing of the trachea that can occur after radiation therapy or a breathing tube) and tracheomalacia (in which the trachea collapses, which can happen in people with chronic obstructive pulmonary disease).

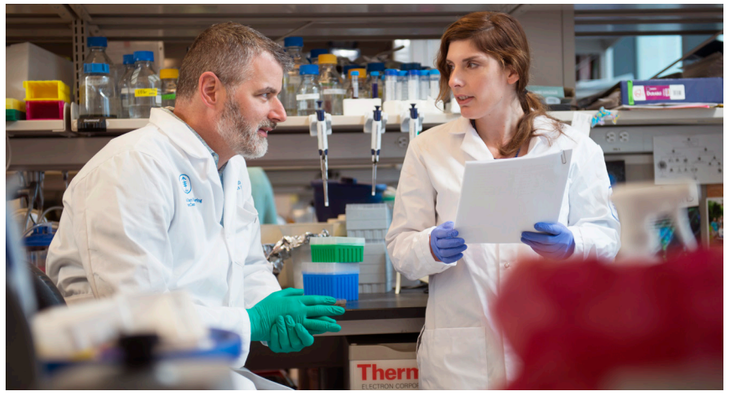
Robert Lee points to a CT scan of abnormalities.

> **"Another area where the IP team can offer exceptional care is through our Complex Airways Program. We are able to offer a number of therapeutic procedures to people who have cancer that is making breathing difficult."**
>
> **— ROBERT LEE, INTERVENTIONAL PULMONOLOGIST**

"We can use stents or lasers to open up the airways," Dr. Lee adds. "People feel much better, and this may enable them to go home from the hospital or to continue their chemotherapy."

All of the procedures offered by the IP team require advanced training and multidisciplinary care, including collaborations with the critical care, anesthesiology, interventional radiology, and head and neck and thoracic surgical teams. MSK places a strong emphasis on education and training, offering one of the few IP fellowships in the country. These fellowships, which were the first in New York State and were started in 2014, are open to doctors who have already trained in internal medicine, pulmonology, and critical care. They enable an increased level of specialization for those interested in IP.

In addition, MSK offers yearly continuing medical education programs for members of the academic and medical communities. These programs are available to physician assistants and nurse practitioners in addition to thoracic surgeons, pulmonologists, and other doctors. "We do these classes to educate the community about the standard of care, and so that they know when patients should be sent to MSK for specialized treatment," Dr. Chawla concludes. ■



Tobias Hohl reviews the results of an experiment with Neta Shlezinger in the Hohl Laboratory.

The Infectious Diseases Service Focuses on Research to Bring the Best Care to People with Cancer

ONE OF THE most serious complications that people with cancer face beyond the disease itself is the threat of infections. Treatments such as chemotherapy can weaken the immune system, making it more difficult for the body to fight infections. In addition, some cancers, especially blood cancers, affect the body's production of immune cells, making it harder to recognize and fight off microbes.

Memorial Sloan Kettering's Infectious Diseases Service is made up of experts who are dedicated to preventing, diagnosing, and treating infections, so that people with cancer and their oncologists can concentrate on the ultimate goal: bringing the disease under control.

Physician-scientist Dr. Tobias Hohl, who leads the service, focuses his research on fungal infections in people with cancer. "Fungal infections are very common worldwide, and in healthy people they are usually considered to be nothing more than a nuisance," he says. "But they can be serious problem in people with cancer, especially infections in the lungs or those that can spread through the bloodstream and reach deep organs."

The people with cancer who are most at risk of developing fungal infections are those with leukemia or lymphoma, especially those who are undergoing stem cell or bone marrow transplants (BMTs) in which they receive new blood cells from a donor. "The transplant process requires doctors to ablate the patient's immune system, which means they will not have a functioning system for weeks or even months," Dr. Hohl explains. "These patients lack the immune cells that defend them against fungi."

Two of the most important types of immune cells for defense against fungi are called neutrophils and monocytes. Both are part of the innate immune system, which involves defense mechanisms that come into play immediately after a foreign invader is detected. A recent paper from Dr. Hohl's laboratory, published in *Science*, looked at the innate immune response to a fungal infection by *aspergillus*.

Aspergillus is a type of fungus that forms filaments when it grows — it's commonly found as fuzzy growth on food. And because it's ubiquitous, it's difficult to avoid breathing in its spores. In a healthy person with a functioning immune system, neutrophils and monocytes quickly eliminate the spores in the lungs. In people with cancer who are lacking those cells, especially those who have undergone BMTs, the fungus can form filaments in the lungs, a life-threatening infection.

"The goal of our research is to understand the mechanism by which the host's immune system kills these fungal spores," Dr. Hohl says. "We found that it does so by engulfing the fungal spores — a process called phagocytosis — inducing them to kill themselves through inducing programmed cell death, or apoptosis. The discovery that apoptosis is involved is something that wasn't previously known."

Dr. Hohl's team is studying the mechanism by which immune cells induce this programmed cell death with the hopes of eventually developing drug interventions that could induce the same effect in the absence of a working immune system.

The investigators used mouse models and human cells to study ways to intervene in this process. "We found that when we made the fungal cells more resistant to cell death, they became more virulent," he says. "Conversely, if we made them more sensitive to cell death, they became less virulent. We think the players in the molecular mechanisms of this process are potentially druggable targets.

"Fungal infections ... can be a serious problem in people with cancer, especially infections in the lungs or those that can spread through the bloodstream and reach deep organs."

— TOBIAS HOHL, PHYSICIAN-SCIENTIST

"What we're trying to do now is to identify which part of the protein is critical for this function," he adds. "We also plan to study this more broadly to find out if the same players are at work in other types of fungal infections." The investigators hope that if they further develop the concept of manipulating programmed cell death as a therapeutic strategy, they would ultimately like to be able to apply it to many types of fungal pathogens.

"The Infectious Diseases Service focuses on a wide range of research," Dr. Hohl concludes. "Some of it is very clinical, and some of it is focused on the very basic mechanisms of pathogenesis and virulence. To provide the best care, it's important to seek knowledge in both of these areas." ■

The Endocrinology Service Makes Important Contributions to the Treatment of Pituitary Tumors

From left: Neurosurgeon Viviane Tabar, head & neck surgeon, Marc Cohen, and endocrinologist Eliza Geer.

TREATING TUMORS of the pituitary gland — often referred to as the "master gland" because it controls the release of many different hormones in the body — requires highly specialized care. For this reason, Memorial Sloan Kettering established the Multidisciplinary Pituitary and Skull Base Tumor Center in 2015. The center offers coordinated care from experts in a number of different specialties, providing patients with the opportunity to see multiple specialists on the same day.

Last year, endocrinologist Eliza Geer joined the center as its medical director. Her level of expertise in the medical treatment of these rare tumors added a critical level of expertise to MSK's team.

"The best treatment for most of these tumors is surgery, but not everyone is able to have surgery because of the location of the tumor," Dr. Geer says. The pituitary gland is located in an important area underneath the brain, behind the eyes and also close to the carotid artery in the cavernous sinus, where important cranial nerves are located. In addition, these tumors can be invasive, making it too risky to remove them entirely.

"Even if surgeons are able to completely remove the tumors, they may come back," Dr. Geer adds. "And people who have had a successful surgical procedure may still have a number of symptoms that need to be managed due to the nature of these tumors and the fact that some types produce hormones."

Dr. Geer specializes in the treatment of Cushing's disease, which results from tumors in the pituitary. These tumors cause the pituitary to release high levels of adrenocorticotropic hormone (ACTH). ACTH, in turn, stimulates the production of cortisol, a stress hormone made by the adrenal glands. These excess hormone levels can lead to wide-ranging symptoms, including excessive weight gain, diabetes, high blood pressure, and psychiatric problems like depression.

Cushing's disease is difficult to diagnose in large part because it's so rare. "Most endocrinologists see only a few cases in their entire careers, if any," Dr. Geer says.

"The best treatment for most of these tumors is surgery, but not everyone is able to have surgery because of the location of the tumor."

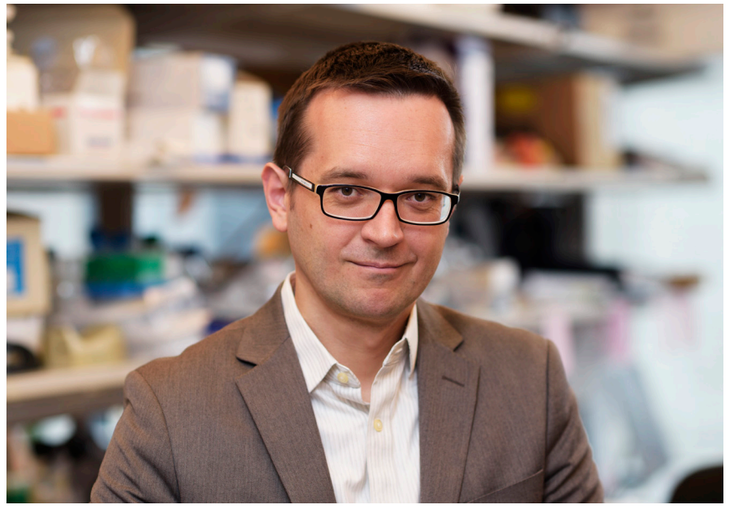
— ELIZA GEER, ENDOCRINOLOGIST

Diagnosis is also complex. There are many different tests that need to be run, and the findings don't always line up with one another. And some tumors may be so small that they aren't visible on an MRI, another aspect that makes them challenging to localize and remove.

In addition to treating Cushing's, Dr. Geer has expertise in acromegaly, which results from an overproduction of a growth hormone that's induced by a different type of pituitary tumor.

Follow-up care is an important aspect of the standard of care for these tumors, and one that is provided by Dr. Geer and the Endocrinology Service. "There are very few medical therapies to treat elevated levels of cortisol, making research into developing new drugs crucial," she concludes. "It's important to continue monitoring patients for recurrence as well. These tumors can sometimes come back 10 or 20 years after treatment." ■

The Renal Service Trial Will Investigate Electronic Cigarette Safety and Develop New Tools for Studying Vascular Health



Roman Shingarev researches the health risks of vaping.

MANY PEOPLE CONSIDER electronic cigarettes to be a safer alternative to traditional cigarettes, but little research has been done on how safe they really are. Although electronic cigarettes don't contain tar, a known carcinogen, the addictive component — nicotine — is the same. And nicotine is known to have detrimental effects on vascular health.

For this reason, Memorial Sloan Kettering investigators Dr. Roman Shingarev and Dr. Edgar Jaimes have undertaken research to study the potential downsides of vaping. They have received funding from the National Institutes of Health and the Food and Drug Administration to conduct a randomized, controlled clinical trial that will analyze both the short- and long-term influence of electronic cigarettes on vascular function.

"This research has two goals," says Dr. Shingarev, a member of MSK's Renal Service. "It will help to establish the biological effects of electronic cigarettes with potential implications for the safety of their use as a smoking cessation tool. It also will help us to create a new working methodology for studying vascular dysfunction overall and investigating the vascular system in greater detail."

In the trial, investigators will collect baseline samples of blood and urine from the volunteers. The participants will then be exposed to traditional cigarettes, electronic cigarettes, or sham electronic cigarettes (for the control group), and changes in the blood and urine will be studied. A number of measures will be analyzed, including oxidative stress, endothelial cell integrity, and the functionality of the endothelial cells collected from the veins of the participants.

"These techniques have been used before, but we're trying to bring them all together to create one powerful tool," Dr. Shingarev says. The researchers will also use an instrument called an EndoPAT machine to measure the overall vascular functionality before and after exposure to nicotine.

> **"These techniques have been used before, but we're trying to bring them all together to create one powerful tool."**
>
> **ROMAN SHINGAREV, PHYSICIAN-SCIENTIST**

Because the vascular system plays an essential role in how cancer spreads or metastasizes — providing rogue cancer cells with a route for traveling through the body — learning more about how it functions can also provide significant insight into some of the fundamental processes of cancer. "In addition to aiding in metastasis, the vascular system also contributes to the formation of new blood vessels, which are required for tumors to get the nutrients they need to grow," Dr. Shingarev says.

There is yet another reason to study the functioning of the vascular system at a cancer center: Vascular condition is often a limiting factor on how much treatment people with cancer can tolerate. But until now there have been few good ways to evaluate the health of people with cancer's vascular system.

MSK's Renal Service plays a crucial role in caring for patients — not only those with kidney cancer, but all people who are at risk of developing kidney problems because of their cancer or its treatment, as well as those who have existing kidney disease.

"With intravenous chemotherapy, the endothelial cell layer, the lining inside the blood vessel, is where the drug first comes in contact with the body," Dr. Shingarev says. Because the kidneys are a very vascular organ, with a filtration system that is essentially a specialized blood vessel for filtering out toxins, they are often where the first negative effects of treatment are detected. The kidneys are also an important mode of eliminating drugs from the body.

"For these reasons it's vital to monitor the kidneys during cancer treatment," Dr. Shingarev concludes. "For a lot of cancer drugs, reduced kidney function limits how much treatment people with cancer can receive, or whether they can receive chemotherapy at all. The more we can learn about these processes, the more effectively we can optimize and personalize cancer treatment for our patients. We hope our electronic cigarettes trial, which we expect to complete in 2018, will help to shed important light on this issue." ■

Decoding the Genetics of Thyroid Cancer Leads to New Treatment Approaches

NEARLY 57,000 new cases of thyroid cancer are expected to be diagnosed in the United States this year. The reported incidence of this cancer is growing, due in large part to detection of small tumors through imaging studies. Because many of these thyroid cancers do not cause clinically significant disease, the Thyroid Cancer Disease Management team at Memorial Sloan Kettering has been a leader in advocating for a conservative management of these incidentally discovered tumors.

The majority of clinically significant thyroid cancers are caught at an early stage when they can be cured with surgery alone. However, additional treatments are needed to cure or control the disease in patients with locally invasive tumors or with distant metastases.

Radioactive iodine (RAI) therapy takes advantage of the fact that thyroid cells concentrate the majority of the iodine ingested in the diet. When iodine is made radioactive, it can home in on normal thyroid cells as well as thyroid cancer cells. However, not all thyroid cancers retain the ability to take up iodine, and therefore some thyroid cancers do not respond to RAI therapy and continue to progress.

MSK endocrinologist and scientist Dr. James Fagin has discovered that some of the common genetic changes that cause thyroid cancer disable the mechanisms that control iodine transport into thyroid cells. He showed this in cultured thyroid cells and in mouse models of the disease created in his laboratory, and that RAI effectiveness could be restored by treating the mice with drugs targeting a signaling pathway called MAP kinase (MAPK). This prompted the design of a landmark clinical trial reported in 2013, which found that an investigational drug called selumetinib, which works by blocking MAPK signaling, could re-sensitize cancer cells to RAI.

However, not all thyroid cancers respond to this approach, and MSK researchers are focused on decoding the genomic and biochemical basis for what makes them different. Important insights from this laboratory-based work have allowed the design of novel trials with a combination of targeted drugs that overcome these resistance mechanisms. "These combination therapies have led to remarkable responses in patients with advanced forms of the disease. It is encouraging that what we've observed in the clinic is consistent with the mechanisms we had previously described in the lab," Dr. Fagin says.

Endocrinologist & scientist Dr. James Fagin.

"An important effort by our team is to understand the genetic evolution of human thyroid cancer, and to then recreate the disease by introducing these defects into genetically engineered mice," he adds. "This research provides a blueprint for the events that drive progression to the more virulent forms of the disease, such as poorly differentiated thyroid cancer and anaplastic thyroid cancer." Based on this genomic research, and on functional studies performed in the laboratory, MSK clinicians are undertaking a number of clinical trials designed to exploit the therapeutic vulnerabilities that arise through these genetic alterations.

> **"This research provides a blueprint for the events that drive progression to the more virulent forms of the disease, such as poorly differentiated thyroid cancer and anaplastic thyroid cancer."**
>
> **— JAMES FAGIN, ENDOCRINOLOGIST**

Much of Dr. Fagin's current work is focused on understanding how mutations in genes that encode an important protein complex, called SWI/SNF, affect the biology of thyroid cancer. Research from many other labs has shown that this complex controls the epigenetic state of cells during development and in various cancer types. Epigenetic changes are known to influence the way that genes are expressed. "We have already created three mouse models with mutations of different subunits of the SWI/SNF complex, and they have all shown a similar biology to what we see in patients," Dr. Fagin says. His team is now looking more in depth at these changes to determine, among other things, how they may be best treated with drugs.

"We already have a number of leads for agents that can correct some of these epigenetic changes," he says. "Our hope is that once they are reversed, cells may regain the ability to act like normal thyroid cells and trap iodine, and that we may be able to use combination therapies to develop more effective treatments." ■

Gastroenterologists Play a Growing Role in the Management and Treatment of Cancer

Mark Schattner between endoscopy procedures.

MEMORIAL SLOAN KETTERING'S Gastroenterology Service has two important functions. One is consultative: Any patient treated for cancer at MSK who has underlying gastrointestinal problems — whether or not they are related to cancer and its treatment — may receive treatment from a gastroenterologist to help manage or treat a range of problems. Gastroenterologists also help with specialized nutritional support for patients who need it.

But depending on the type and stage of cancer, gastroenterologists may play a leading role in treatment, either independently managing care in people with early-stage gastrointestinal (GI) cancers or working with colleagues in medical oncology and surgery to diagnose more advanced cancers.

Many of the procedures done by gastroenterologists are possible because of advances in endoscopy, the use of slender, tubular instruments called endoscopes to view the insides of the GI tract and — in many cases — offer minimally invasively procedures through those scopes.

"Starting from the top of the GI tract and moving all the way down, endoscopy can be used to prevent cancer by removing precancerous polyps or lesions," says Dr. Mark Schattner, Chief of MSK's Gastroenterology, Hepatology, and Nutrition Service. "In some cases endoscopy enables people with early-stage cancer to avoid surgery." For patients with stage I tumors of the esophagus, stomach, colon, and rectum, gastroenterologists at MSK can frequently remove these tumors completely with an endoscope, sparing these organs and providing people with the opportunity for a quick and complete recovery.

Dr. Schattner adds that for people with early-stage cancers, gastroenterologists may be their primary doctor at MSK, something that's unusual at a center where most patients are treated by medical and surgical oncologists. Endoscopic procedures are also increasingly used to help people manage complications that result from their disease or as a complication from treatment. For example, patients who undergo surgery for pancreatic tumors. "One of the biggest problems related to these surgeries is that patients develop fluid leaks," Dr. Schattner says. "In the past, these were treated with an external drain that came through the skin. This was difficult for patients. Now we can use endoscopy and ultrasound to identify where fluid is collecting and to enable it to drain directly into the GI tract, which is where it the fluid be going anyway." He says the technique works very well, and that it has changed the care not only for people who undergo pancreas surgery but also those who have pancreatitis.

> **"Starting from the top of the GI tract and moving all the way down, endoscopy can be used to prevent cancer by removing precancerous polyps."**
>
> **— MARK SCHATTNER, GASTROENTEROLOGIST**

Dr. Schattner is also collaborating with bioengineers on MSK's Interventional Radiology Service to develop a new way to deliver irreversible electroporation (IRE), a treatment that uses electrical fields to destroy tumors and to open ducts that are blocked by tumors. Traditionally IRE has been done with rigid probes, but thanks to a flexible device developed at MSK, this procedure may soon be offered via an endoscope. The procedure is still in the testing stage, but investigators hope to soon make it available to patients.

Gastroenterologists also play an important role in screening for a number of GI cancers, especially for people who are at increased risk due to personal or family history.

As a reflection of the increasingly important role that endoscopy plays for many people with cancer, MSK is expanding the availability of its services, which are now available on Saturdays for scheduled, elective outpatient procedures as well as for emergencies. These Saturday appointments, available in Manhattan, offer the full range of endoscopy procedures, including advanced ones that may require hospital facilities as backup.

In addition, for people who want to receive their care closer to home, MSK offers selective procedures at MSK Monmouth in Middletown, New Jersey. The first outpatient facility outside of Manhattan to provide endoscopy to MSK patients, MSK Monmouth focuses on procedures that can be safely done in the outpatient setting.

"We know that nobody likes to wait for procedures," Dr. Schattner says. "They want to get in and get it done, whether it's medically or psychologically urgent. We're pleased to be able to provide this option to our patients." ■

Nurse Mary Vooss preparing for an endoscopy procedure.

Nursing Contributions to Endoscopy and Bronchoscopy

AS ADVANCES ARE MADE in the field of endoscopy, members of the nursing team are tasked with mastering new equipment and techniques. Those efforts are rewarded with positive outcomes, particularly those undergoing minimally invasive procedures.

Endoscopic mucosal resection is a minimally invasive procedure to remove early-stage cancers from the digestive tract. Because these procedures can be curative, they are rewarding cases in which to participate. Years ago, these people would have had to undergo hospitalization and open surgery. Today, many of them are having their cancer removed in a relatively short outpatient visit.

Capsule endoscopy is another procedure that requires nursing support. For this exam, the patient swallows a pill containing a camera that visualizes and photographs the entire digestive tract and allows doctors to detect gastrointestinal anomalies. Nurses play an important role in alleviating the patient's anxieties during this procedure as well as informing them of the steps to follow to achieve a successful evaluation.

Colonoscopy is also performed in the endoscopy unit. During this procedure, nurses are responsible for providing instructions, education, and support to patients during the often-confusing and unpleasant prep process. They also assist in the procedure room, both in the scrub nurse role and by providing another set of eyes to watch the exam on screen. Endoscopists are particularly concerned with flat (also called sessile) polyps. Nurses who work in the endoscopy procedure rooms develop experience detecting these easy-to-miss polyps. Evidence shows that having nurses participate in this procedure improves the outcome for patients.

> **Endoscopists are particularly concerned with flat (also called sessile) polyps. Nurses who work in the endoscopy procedure rooms develop experience detecting these easy-to-miss polyps. Evidence shows that having nurses participate in this procedure improves the outcome for patients.**

Endoscopy nurses also support the Interventional Pulmonary Service and the procedures that this team performs. As with gastroenterology, pulmonary procedure nurses are part of a team delivering care that is at the forefront of modern medicine. Procedures that are rare in community hospitals — for example, endobronchial ultrasounds and placement of fiducial markers to allow for precisely targeted radiotherapy —are commonplace at MSK.

One of the pulmonary procedures that can make a huge difference is the insertion of pleural drainage catheters that drain fluid from around the lung. People often report that they felt like they were drowning prior to the placement of one of these catheters. Their condition is often noticeably improved by the time the procedure is completed.

Endoscopy nurses are also involved in clinical trials. For example, they play a vital role in pre- and postprocedure education and assessment for a recently launched trial from MSK gastroenterologist Hans Gerdes. This phase I clinical trial is evaluating the use of WST 11 (Tookad) vascular-targeted photodynamic therapy to treat severe dysphagia due to esophagogastric cancer. Some nurses also provide care during these complex laser procedures.

Another recent development is an increase in the number of dual-role nurses on the endoscopy unit. To support the approach of relationship-based care, these nurses each work with a single doctor from inpatient endoscopic procedures to the outpatient clinic setting (to maintain continuity of care). They meet patients in the outpatient clinic, provide care to them in the endoscopy procedure room, and follow them through the course of treatment. In this way, they can serve as a liaison and resource to patients as they navigate visits with other healthcare providers and during tests and procedures in other areas of the hospital. This model can provide a sense of comfort and confidence in MSK for our patients. ■

Research Takes Aim at the Cardiac Side Effects of Common Breast Cancer Treatment

TRASTUZUMAB (HERCEPTIN®) has changed the way many breast cancers are treated. For a large number of women, it can contribute toward a cure, and for others, it can help provide long-term control of their disease. But the benefits of this drug come at a cost. Trastuzumab can cause potentially life-threatening damage to the heart.

Investigators on Memorial Sloan Kettering's Cardiology Service are undertaking a number of initiatives to decode the underlying mechanisms that can lead to this potentially severe complication and to find ways to address it — through both prevention and treatment.

"MSK's cardiovascular practice is devoted to the cancer mission," says Cardiology Service Chief Dr. Richard Steingart. "Our task is to minimize the heart damage that may occur as a consequence of treatment for breast cancer to enable patients to receive the best drugs we can offer to control their cancer."

Trastuzumab is monoclonal antibody that works by blocking a protein called HER2, which is amplified in about one-quarter of breast cancers and contributes to cancer growth. Before the drug was developed, HER2-positive breast cancers were considered to be among the most aggressive. Now treatment with trastuzumab in combination with chemotherapy has led to a significant reduction in breast cancer recurrence and improvement in overall survival.

But by unlucky coincidence, heart cells called cardiomyocytes also contain the HER2 protein. (Cardiomyocytes make up the muscle tissue responsible for the heart's beating.) "In the normal heart, HER2 plays a role in helping the heart repair itself from whatever injury may occur over the normal course of life," Dr. Steingart says. This problem may be made worse because the chemotherapy drugs that are used in combination with trastuzumab, such as anthracyclines like doxorubicin can also have a negative effect on the heart.

Several clinical trials are underway at MSK to study these effects. "It's important to develop better ways to monitor the heart for early signs of cardiac impairment due to breast cancer treatment," says cardio-oncologist Anthony Yu, who is leading some of these trials. "We also need to identify factors that suggest who may be at higher risk of developing these impairments, and find ways to manage them."

A new echocardiographic technique that has been developed in recent years, called speckle tracking strain, is being used in people with breast cancer to monitor for early signs of cardiotoxicity. The goal is to identify them early so that medical interventions can prevent these cardiac problems from progressing. "About 15 to 20 percent of patients taking trastuzumab have some degree of impairment in the squeezing function of their hearts, but it really only progresses to severe congestive heart failure in 2 to 4 percent of patients," Dr. Yu explains. "We're trying to treat these heart problems so that we don't have to discontinue potentially lifesaving cancer treatment."

Dr. Yu and his team are also studying people who are several years out from treatment, to learn more about the long-term cardiotoxic effects of trastuzumab and how this may affect exercise capacity.

Important research is going on in the laboratory as well. MSK physician-scientist Angel Chan, in conjunction with cardiology experts at Mount Sinai, is using stem cell techniques to study the molecular mechanisms that lead to heart failure after treatment with trastuzumab and anthracyclines.

She is using pluripotent stem cells derived from the skin cells of people who have suffered adverse cardiac effects— as well as those who haven't — to create heart cells in a dish. "These cells will provide a valuable tool to study how trastuzumab damages the heart at a cellular level and also to study the cellular machinery, including the mitochondria," Dr. Chan says.

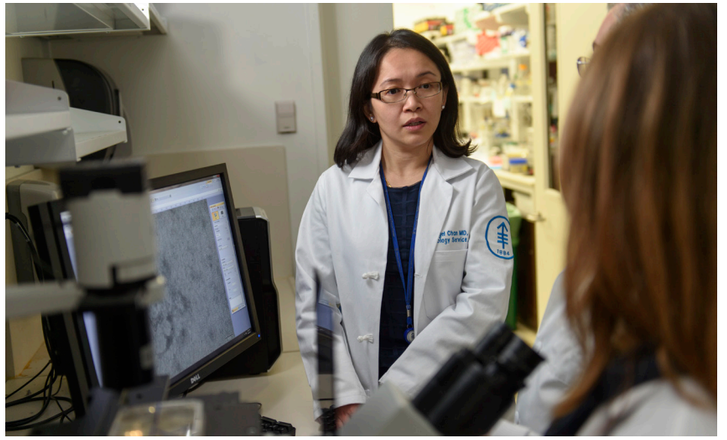
The ultimate goal of her work is to determine why some people are more susceptible to developing heart failure than others on a molecular and genetic level, and to find ways to prevent and treat it.

Through research led by Dr. Yu, Dr. Chan, and many others, experts on the Cardiology Service are tackling the heart complications of cancer treatment on many fronts — with the goal of ultimately improving long-term outcomes for patients at MSK and beyond. ■

Anthony Yu leads several clinical trials in the Cardiology Service.

> **"It's important to develop better ways to monitor the heart for early signs of cardiac impairment due to breast cancer treatment."**
>
> **— ANTHONY YU, CARDIO-ONCOLOGIST**

> **"(Pluripotent stem cells) will provide a valuable tool to study how trastuzumab damages the heart at a cellular level and also to study the cellular machinery, including the mitochondria."**
>
> **— ANGEL CHAN, PHYSICIAN-SCIENTIST**



Physician-scientist Angel Chan studies cardiotoxicity and stem cells.

Antibiotic Management Program Seeks to Reduce Dangerous Infections

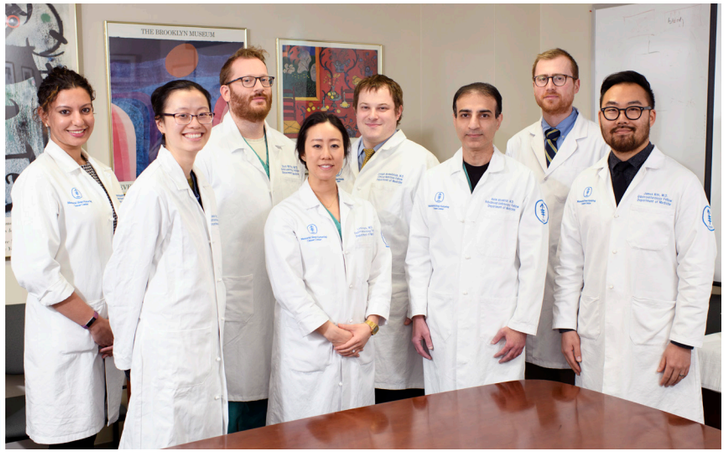
Antibiotic overuse is for a major cause of antibiotic resistance and *Clostridium difficile* infections. Additionally, many emergency room visits are due to adverse drug events related to antibiotics. Optimizing antibiotic use is particularly important for people with cancer, who have an increased risk of infection while undergoing treatment. When someone with a suspected infection is admitted to the hospital, MSK's Antibiotic Management Program (AMP) provides advice to clinicians on the most effective and safe antibiotic treatments. Conversely, when there is no longer evidence of an infection, the AMP team reminds clinicians to discontinue unnecessary antibiotic use.

THE AMP TEAM is led by Susan Seo, an infectious diseases (ID) physician. It also consists of a team of three clinical pharmacy specialists and a data manager, who work together with multiple departments to improve the quality of antimicrobial prescribing and advance patient outcomes. The program has been a local and national model for implementing antimicrobial stewardship programs at institutions serving immunocompromised patients.

ID pharmacists play an important role in antimicrobial stewardship: The knowledge of medications, dosing, pharmacokinetics, drug interactions, and toxicities is invaluable. "We are involved in day-to-day stewardship operations such as assisting prescribers via antibiotic approvals, educating staff and trainees about rational antimicrobial use, identifying areas for improvement, implementing changes, and measuring outcomes to help our patients," says pharmacy specialist, Nina Cohen. Multidisciplinary collaborations with hospital administration, clinical care services, infection control, information technology, microbiology, and pharmacy among other services are crucial. By working together, streamlining antibiotic use can combat the growing problem of antibiotic resistance and *C. difficile* infections, and can improve patient outcomes. ■

Above, left to right: Data coordinator Zivile Gedrimaite, Antibiotic Management Program Director Susan Seo, clinical pharmacy specialist, Marco Scipone. Below from left to right: Clinical pharmacy specialists Alla Paskovaty and Nina Cohen.

GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION

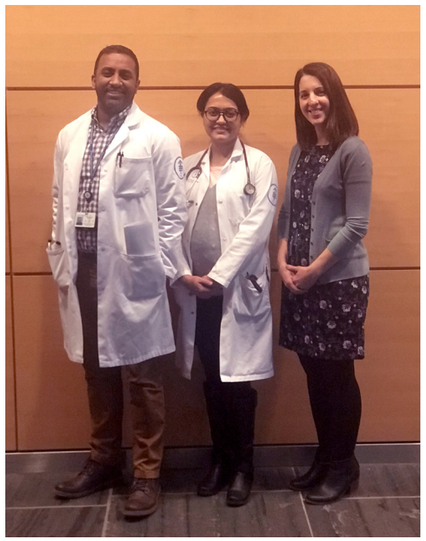


From left to right: Priya Simoes, Janie Yang, Elliott Birnstein, Leslie Park, Joseph Mermelstein, Asim Khokhar, Brett Van Leer-Greenberg, and James Kim.

PULMONARY

From left to right: David Eshak, Saira Imran, Priyanka Makkar, and Karan Gupta.

INFECTIOUS DISEASES



From left to right: Shane Alexander, Ritu Kathuria, and Fellowship Director Anna Kaltsas.

Subspecialty Medicine Fellowships

THE GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION SERVICE offers three fellowship training programs in gastroenterology, advanced gastrointestinal endoscopy, and clinical nutrition. The program offers education and training in the full range of gastrointestinal (GI) endoscopic procedures in a state-of-the-art endoscopy unit, located within MSK's Surgical Day Hospital. These fellows develop expertise in performing upper gastrointestinal endoscopy, hemostasis, polypectomy, small bowel enteroscopy, video capsule endoscopy, and enteral stent insertion. They will also gain exposure to endoscopic ultrasound and endoscopic retrograde cholangiopancreatography procedures.

Under the leadership of gastroenterologist Robin Mendelsohn, Nutrition Fellowship Training Program Director, the nutrition fellowship offers one position each year. The program provides training in inpatient and outpatient GI consultation, covering the full spectrum of nutritional disorders, including supplemental enteral and parental nutrition, short bowel syndrome, malabsorption, malnutrition, gastroparesis, and vitamin and mineral deficiencies. In addition to the Gastroenterology, Hepatology, and Nutrition faculty, additional members of the nutrition team include specialized nutrition nurses, dieticians, and pharmacists. ■

THE INFECTIOUS DISEASES (ID) fellowship at MSK is the only Infectious Diseases training program in the United States based at a cancer treatment center. Trainees become experts in the management of infections associated with cancer treatments such as allogeneic hematopoietic stem cell transplantation, checkpoint blockade treatment to enhance T cell-mediated clearance of tumors, and treatments that employ T cells expressing tumor-specific chimeric antigen receptors (CARs). A number of former ID fellowship trainees hold career development awards from the National Institutes of Health (NIH) and oversee NIH-funded laboratory research programs.

Broadly speaking, clinical investigators within the Infectious Diseases Service focus on diagnosis and therapy of infections in the compromised host as well as hospital infection control. Collaborative clinical research projects between the Infectious Diseases Service and other services within MSK focus on monitoring and augmenting antiviral immunity in transplant patients and people receiving other forms of cancer therapy.

Our ID research laboratories study the immune response to infection with bacterial, fungal, and viral pathogens. We also are actively investigating the pathogenesis of mycobacterial infections. Our ID fellows are on the forefront of research to learn more about cancer patients' unique risk factors for developing infections and also how to best treat such infections and prevent them from occurring in the first place. ■

PULMONARY TRAINING at MSK provides fellows with experience in managing patients who have any type of lung disease. Our outpatient pulmonary clinics are open to all people with pulmonary disease, not just those being treated for cancer or cancer-related pulmonary disease. This two-year fellowship also offers unique and extensive exposure to people who are immunocompromised.

Procedure training in diagnostic bronchoscopy includes gaining experience with endobronchial ultrasound and transbronchial needle aspiration. Interventional pulmonary attending doctors give trainees exposure to advanced diagnostic and therapeutic techniques. Our fellows gain extensive experience in the management of pleural disease, including thoracic ultrasound, chest tubes, and tunneled pleural catheters. ■

Standing on the Shoulders of Giants

DIANE STOVER

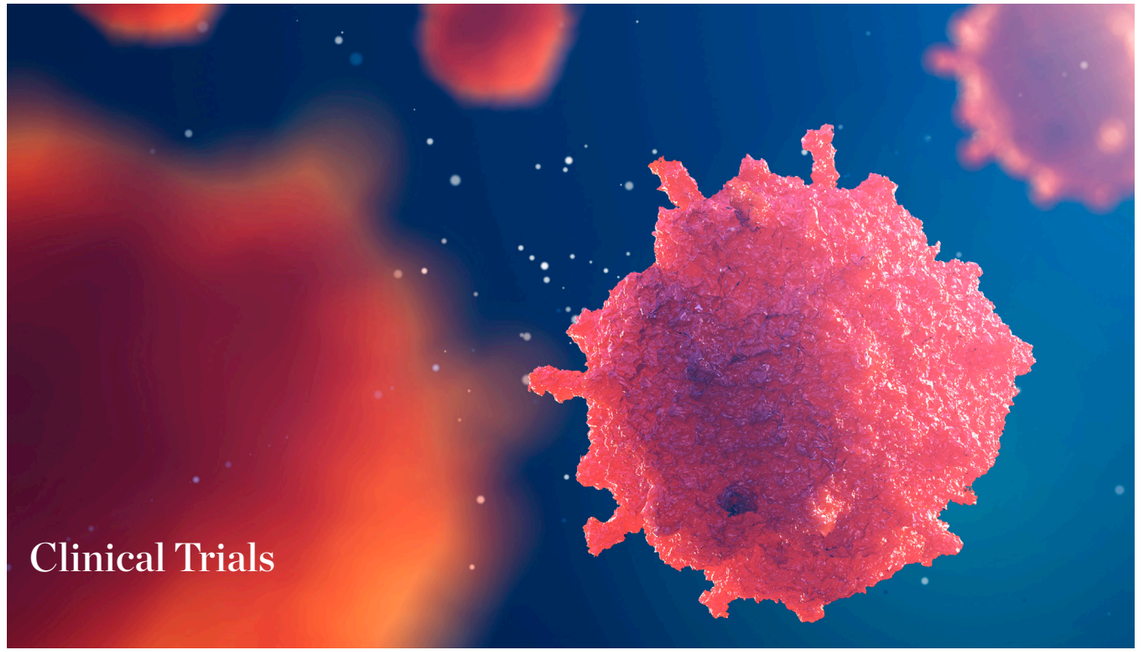
CARLOS FLOMBAUM

ROBERT C. KURTZ

DIANE STOVER joined the Cardiopulmonary Service at Memorial Sloan Kettering in 1977. In 1986, she was appointed Chief of the Pulmonary Service; she was named Head of the Division of General Medicine in 1991. Dr. Stover served as Division Head for 20 years and maintained the title of Pulmonary Service Chief for 31 years. During her time at MSK, Dr. Stover has lectured, published, and focused her research primarily on pulmonary disorders in people with cancer. Her avocation has been to develop ways to help children and young adults to make the decision not to smoke. Dr. Stover is continuing to work closely with her colleague, Mohit Chawla, as he assumes the role of Pulmonary Service Chief. She will continue to care for patients and focus on her passion for teaching students, house staff, and pulmonary fellows.

ROBERT C. KURTZ started his career as an internal medicine house officer in the combined New York Hospital–Memorial Sloan-Kettering residency program in 1968. He did his gastroenterology fellowship in the same program and was a chief resident in MSK's Department of Medicine from 1972 to 1973. He joined the Gastroenterology Service faculty in 1975. He was named Chief of the Gastroenterology and Nutrition Service in 1998. His clinical and research interests over the last two decades have been in familial pancreatic cancer. After 19 years leading the Gastroenterology, Hepatology, and Nutrition Service, Dr. Kurtz stepped down as Chief in January 2017, passing the title on to Mark Schattner. Dr. Kurtz continues as a faculty member on the service, seeing patients, teaching, and leading his research program.

CARLOS FLOMBAUM began at MSK as an assistant attending Physician in the Clinical Physiology and Renal Service in July 1978. Dr. Flombaum served as Acting Chief of the Renal Service in 1989 before being appointed Chief the following year. He oversaw the service for 24 years, until Edgar Jaimes stepped in to that role in 2014. Dr. Flombaum continues to serve as a member of the Renal Service, while devoting time to teaching, mentoring, and carrying on his collaborative efforts with the Nutrition Service.



Clinical Trials

Following is a list of clinical trials that were in development or open to accrual at the time of publication.

INFECTIOUS DISEASES SERVICE

- **A Randomized Controlled Trial of Autologous Fecal Microbiota Transplantation (auto-FMT) for Prophylaxis of *Clostridium Difficile* Infection in Recipients of Allogeneic Hematopoietic Stem Cell Transplantation**

  IRB #: 14-025; PI: Ying Taur, MD

  For *Clostridium difficile* infection (CDI), fecal microbiota transplantation (FMT) has been shown to be a highly effective treatment, with cure rates far exceeding those of conventional therapy with antibiotics. This study aims to explore the full potential of FMT as a treatment in immunocompromised recipients of an allogeneic hematopoietic stem cell transplant who are at high risk of CDI and other intestinal microbiota-related diseases.

- **An Intermediate-Size, Expanded Access Protocol to Provide Brincidofovir for the Treatment of Serious Adenovirus Infection or Disease**

  IRB #: 16-044; PI: Genovefa Papanicolaou, MD

  Severe adenovirus (ADV) is an imminently life-threatening infection, but there is currently no approved drug for ADV infection in the allogeneic hematopoietic stem cell transplant setting. This expanded-access protocol enables same-day administration of brincidofovir to patients with newly diagnosed ADV who do not have any safe, nontoxic alternative treatment options.

- **A Single Center, Open-Label Trial of Isavuconazole Prophylaxis Against Invasive Fungal Infection in Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplant [open to accrual]**

  IRB #: 17-112; PI: Genovefa Papanicolaou, MD

  Allogeneic hematopoietic stem cell transplant patients are at risk of invasive fungal infections secondary to neutropenia, respiratory viral infection, and corticosteroid use for graft-versus-host disease. Isavuconazole is a broad-spectrum azole approved by the Food and Drug Administration in 2015 for treatment of aspergillus and mucor infections, and has a more favorable safety profile than other antifungal prophylaxis currently available.

- **SHP620-303: A Phase III, Multicenter, Randomized, Open-label, Active-Controlled Study to Assess the Efficacy and Safety of Maribavir Treatment Compared to Investigator-Assigned Treatment in Transplant Recipients with Cytomegalovirus (CMV) Infections that Are Refractory or Resistant to Treatment with Ganciclovir, Valganciclovir, Foscarnet, or Cidofovir**

  IRB #: 17-140; PI: Genovefa Papanicolaou, MD

  Cytomegalovirus (CMV) is the most common clinically significant viral infection after allogeneic hematopoietic stem cell transplant and, if left untreated, may progress to multiorgan disease. Current antivirals are largely effective, but their use is limited by toxicity and the emergence of resistant CMV (R-CMV). Maribavir is a potent and selective antiviral and because of its novel mechanism of action, there is no cross-resistance with other antivirals.

- **A Phase III, Multicenter, Randomized, Double-Blind, Double-Dummy, Active-Controlled Study to Assess the Efficacy and Safety of Maribavir Compared to Valganciclovir for the Treatment of Cytomegalovirus (CMV) Infection in Hematopoietic Stem Cell Transplant Recipients (Am 1.0, 02 March 2017)**

  IRB #: 17-232; PI: Genovefa Papanicolaou, MD

  In a Phase II study comparing maribavir versus valganciclovir for preemptive treatment of cytomegalovirus (CMV) viremia in allogeneic hematopoietic stem cell transplant 80 percent of patients on maribavir and 66 percent of patients on valganciclovir achieved undetectable CMV viral load by week six. Maribavir appears to be a suitable alternative to valganciclovir for preemptive treatment of CMV particularly in patients with inadequate counts or tenuous grafts where myelosuppression is a concern.

- **AIC316-03-II-01: A Randomized, Open-Label, Multi-Center, Comparative Trial to Assess the Efficacy and Safety of Pritelivir Versus Foscarnet for the Treatment of Acyclovir-Resistant Mucocutaneous HSV Infections in Immunocompromised Adults (PRIOH-1)**

  PI: Yeon Joo Lee, MD

  Mucocutaneous acyclovir (ACV)-resistant herpes simplex virus (HSV) often manifests itself as severe disease with extensive ulceration, pain, and risk of dissemination, and is associated with substantial morbidity in heavily immunocompromised patients. Pritelivir is a helicase-primase inhibitor with a distinct mode of action from antivirals currently in clinical use, is active against HSV1/2 strains resistant to ACV, and is given orally, thus offering an advantage over IV foscarnet.

ENDOCRINOLOGY SERVICE

- **CLCI699C2302: A Phase III, Multi-Center, Randomized, Double-Blind, 48-Week Study with an Initial 12-Week Placebo-Controlled Period to Evaluate the Safety and Efficacy of Osilodrostat in Patients with Cushing's Disease**

  IRB #: 17-351; PI: Eliza Geer, MD

  There is a growing need to develop and study new treatments for patients whose Cushing's disease is not cured by surgery alone, since persistent and recurrent Cushing's disease is common and associated with high morbidity and mortality. This investigation focuses on novel approaches for the management of Cushing's disease. Osilodrostat is a promising new cortisol biosynthesis inhibitor that in a proof of concept study normalized 24-hour urinary-free cortisol in 11 out of 12 patients.

- **OOC-ACM-303:A Phase III, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate Efficacy and Safety of Octreotide Capsules in Patients Who Previously Tolerated and Demonstrated Biochemical Control on Injectable Somatostatin Receptor Ligands (SRL) Treatment**

  PI: Eliza Geer, MD

  Recently a new transient permeability enhancer formulation of octreotide was developed. It allows for oral administration, thus avoiding invasive intramuscular or deep subcutaneous injections. Previously a Phase III study with 155 acromegaly patients showed 65 percent maintenance of response with 86 percent of patients electing to enroll in the extension phase. Now the Food and Drug Administration is requiring additional Phase III data for potential approval.

- **COR-2017-01: A Double-Blind, Placebo-Controlled, Randomized Withdrawal Following Open-Label Therapy Study to Assess the Safety and Efficacy of Levoketoconazole (2S,4R-ketoconazole) in the Treatment of Endogenous Cushing's Syndrome**

  PI: Eliza Geer, MD

  There are only two Food and Drug Administration approved medical therapies currently available to treat Cushing's disease, and neither are cortisol biosynthesis inhibitors. Ketoconazole has been widely used off-label for the treatment of Cushing's, however, recently the FDA released warnings regarding the risk of hepatotoxicity associated with its use. The 2S,4R enantiomer of ketoconazole has higher potency on key cortisol synthesis enzyme targets and lower interaction with CYP7A1, which may be relevant for hepatotoxicity risk.

- **Genomic Predictors of Papillary Microcarcinoma Disease Progression**

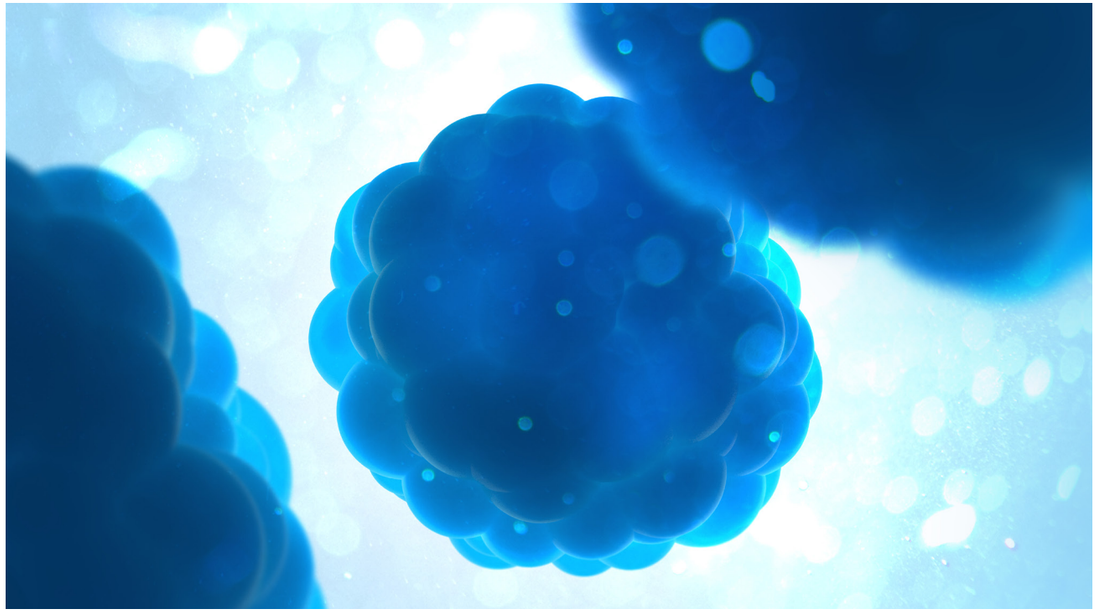
  IRB #: 14-277; PI: Michael Tuttle, MD

  This protocol continues the MSK Thyroid Cancer Disease Management team's long history of pioneering, implementing, and validating a risk-adapted approach to the treatment and follow-up of thyroid cancer. By identifying molecular alterations that are predictive of disease progression in papillary microcarcinoma, we can significantly improve our risk stratification abilities and more reliably identify individual patients who would benefit from early surgical intervention versus active surveillance.

- **HRP-503-001: Psychological Adjustment to Initial Treatment for Low-Risk Thyroid Cancer**

  PI: Michael Tuttle, MD

  For the first time, in 2016, the American Thyroid Association clinical thyroid cancer management guidelines endorsed active surveillance as an alternative to immediate surgery in very low risk thyroid cancer. However, no studies to date have compared the psychological adjustment and quality of life in low-risk patients based on their initial management decision (active surveillance versus immediate surgery). A prospective evaluation of the patient experience in the first year following these important initial management decisions will allow us to better understand how these patients are dealing and coping with their initial management decisions.



GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION SERVICE

- **A Phase I Trial of Vascular-Targeted Photodynamic Therapy in Esophagogastric Cancer Patients with Moderate to Severe Dysphagia**

  IRB #: 15-319; PI: Hans Gerdes, MD

  Most patients with esophagogastric cancer present with or experience dysphagia, which can lead to malnutrition, aspiration, and impaired quality of life. Available therapies do not give substantive nor durable relief, and there is a pressing need for more effective methods of palliation. In collaboration with urologist Jonathan Coleman, we are investigating a new light activating agent WST-11. Part one of the study will establish the maximum tolerated dose (MTD) for palliation of dysphagia in up to 36 patients. Part two of this study will investigate WST-11 plus immunotherapy to treat both the obstructing primary tumor as well as metastatic disease in an additional ten patients.

- **Safety of Fecal Microbiota Transplantation (FMT) for Recurrent or Refractory *C. Difficile* Infection in Patients with Solid Tumors**

  IRB #: 15-337; PI: Robin Mendelsohn, MD

  Clostridium difficile infection (CDI) is the most frequent cause of healthcare-associated diarrhea and is a significant cause of morbidity and mortality. Immunocompromised cancer patients undergoing chemotherapy are at particular risk of CDI, not only due to disruptions in their immune responses but also because of increased frequency and duration of hospitalizations as well as recurrent exposures to broad-spectrum antibiotics. To date there have been no prospective studies on fecal microbiota transplant (FMT) for recurrent CDI in cancer patients.

- **Next-Generation Sequencing to Evaluate Transcriptomic Changes Associated with *H. Pylori* Infection and Gastric Cancer Carcinogenesis**

  IRB #: 15-182; PI: Mark Schattner, MD

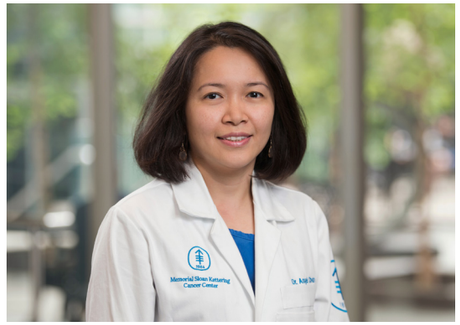
  This a multicenter collaborative project supported by the Starr Cancer Consortium that includes collaborators from MSK's Infectious Diseases and Gastroenterology, Hepatology, and Nutrition Services. Our hypothesis is that, as a result of chronic *H. pylori* infection, both the microbiome and the host mucosal and adaptive immune systems are altered, creating an inflammatory environment that promotes malignancy. With current next-generation sequencing technology and an improved ability to interrogate small tissue samples, our uniquely positioned multidisciplinary team is well equipped to study the development of *H. pylori*-associated gastric cancer.

RENAL SERVICE

- **IIT: Investigation of the Effects of Electronic Cigarettes on Vascular Health**

  IRB #: 17-071; PI: Roman Shingarev, MD

  Tobacco use is the most significant modifiable risk factor for adverse health outcomes and is regarded as the most important determinant of preventable morbidity and mortality in the United States. Cigarette smoking is a major risk factor for different types of cancer, atherosclerotic vascular disease, and lung disease including emphysema and lung cancer.



ANGEL CHAN

MOHIT CHAWLA

EMMY LUDWIG

LENA HEUNG

ELVINA KHUSAINOVA

SUSAN SEO

Appointments in the Division of Subspecialty Medicine

ANGEL CHAN, MD, PHD, JOINED THE CARDIOLOGY SERVICE

Angel Chan joined the Cardiology Service as an instructor. Dr. Chan previously served as a clinical/research cardio-oncology fellow, beginning in July of 2015. After a year in that position, she assumed the role of the advanced cardiac imaging fellow at MSK. She continues her career as a translational researcher in cardio-oncology.

ELVINA KHUSAINOVA, MD, JOINED THE PULMONARY SERVICE

Elvina Khusainova joined the Pulmonary Service as an instructor. Dr. Khusainova first came to MSK in July of 2012 to do her pulmonary critical care training. After finishing her training in July 2015, she practiced at Milford Memorial Hospital in Delaware, focusing her attention in the intensive care unit. She returned to MSK in August 2017.

Promotions in the Division of Subspecialty Medicine

LENA HEUNG, MD, PHD, PROMOTED TO ASSISTANT ATTENDING PHYSICIAN

Lena Heung was promoted to Assistant Attending Physician at Memorial Hospital, Assistant Member at MSK, and Instructor in medicine at the Weill Cornell Medical College. Lena obtained her BS in biology from the University of North Carolina at Chapel Hill and her MD and PhD degrees from the Medical University of South Carolina. She completed her internal medicine/pediatrics residency at Baystate Medical Center/Tufts University School of Medicine and her Infectious Diseases fellowship training at the University of Washington and MSK. In 2017, she was the recipient of an NIH/NIAID Mentored Clinical Scientist Research Career Development (K08) Award. Her research is currently focused on dissecting the role of monocytes in the innate immune response to infection by the opportunistic fungus *Cryptococcus neoformans*. The goal of her work is to identify host immune mechanisms that can be harnessed to develop novel antifungal therapies.

EMMY LUDWIG, MD, PROMOTED TO ASSOCIATE CLINICAL MEMBER AND ASSOCIATE ATTENDING PHYSICIAN

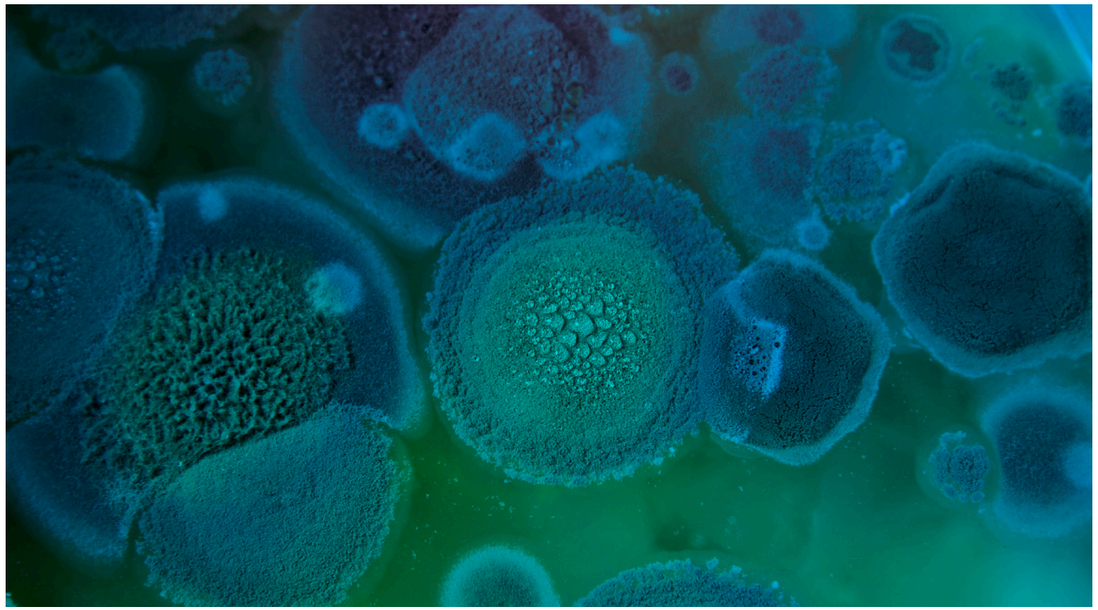
Emmy Ludwig was promoted to Associate Clinical Member at MSK and Associate Attending Physician at Memorial Hospital. Dr. Ludwig is a gastroenterologist. She received her MD degree from Columbia University in 2000, receiving honors in all of her major clinical clerkships and was elected to Alpha Omega Alpha (medical school honor society). She completed a residency in internal medicine at New York Presbyterian Medical Center Columbia Campus and a three-year fellowship in gastroenterology and nutrition at MSK in 2006. She has served and continues to serve as the Associate Program Director of that fellowship program for the last ten years. She is also a member of the MSK ethics committee. She has particular interest in palliation of gastrointestinal (GI) manifestations of cancer and cancer treatment and GI issues specific to women. Dr. Ludwig is a member of the New York Society for Gastrointestinal Endoscopy, the American Society for Gastrointestinal Endoscopy, and the American Gastroenterological Association.

MOHIT CHAWLA, MD, PROMOTED TO CHIEF, PULMONARY SERVICE

Mohit Chawla was promoted to the Chief Attending of the Pulmonary Service at Memorial Hospital. Dr. Chawla received his MD degree from New York Medical College in Valhalla, New York. He went on to complete an Internal Medicine Residency Training at Saint Vincent's Hospital in Manhattan, followed by fellowships in Pulmonary Medicine and Critical Care Medicine at MSK and in Interventional Pulmonology at Henry Ford Hospital in Detroit. Dr. Chawla founded the Section of Interventional Pulmonology at MSK in 2008 and the first Interventional Pulmonology fellowship in New York State in 2014. During the course of his time at MSK, he has introduced various novel devices for minimally invasive diagnostics and therapeutic interventions, including endobronchial valves to control prolonged air leaks and various stents for malignant airway obstruction. Dr. Chawla also served as President of the New York State Thoracic Society and has led eight annual continuing medical education courses on Interventional Pulmonology to date.

SUSAN SEO, MD, PROMOTED TO CLINICAL MEMBER AND ATTENDING PHYSICIAN

Susan Seo was promoted to Clinical Member at MSK and Attending Physician at Memorial Hospital. Dr. Seo received her MD degree from the University of North Carolina at Chapel Hill, and she completed her residency and training in internal medicine at Beth Israel Deaconess Hospital in Boston. Dr. Seo founded the multidisciplinary Antibiotic Management Program (AMP) at MSK, which is one of New York City's first antimicrobial stewardship programs and is routinely recognized as a model for developing a stewardship program.



Publications

CARDIOLOGY SERVICE

- **Prognostic Utility of Differential Tissue Characterization of Cardiac Neoplasm and Thrombus via Late Gadolinium Enhancement Cardiovascular Magnetic Resonance among Patients with Advanced Systemic Cancer.**
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- **Cardiac Safety of Paclitaxel Plus Trastuzumab and Pertuzumab in Patients With HER2-Positive Metastatic Breast Cancer.**
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ENDOCRINOLOGY SERVICE

- **Selumetinib-Enhanced Radioiodine Uptake in Advanced Thyroid Cancer**
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- **Transposon mutagenesis identifies chromatin modifiers cooperating with Ras in thyroid tumorigenesis and detects ATXN7 as a cancer gene.**
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GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION SERVICE

- **Adenoma Prevalence in Blacks and Whites Having Equal Adherence To Screening Colonoscopy: The National Colonoscopy Study.**
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INFECTIOUS DISEASES SERVICE:

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PULMONARY SERVICE

- **Diagnostic Evaluation of Pulmonary Abnormalities in Patients with Hematologic Malignancies and Hematopoietic Cell Transplantation.**
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RENAL SERVICE

- **Hypophosphatemia after Hepatectomy or Pancreatectomy: Role of the Nicotinamide Phosphoribosyltransferase.**
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