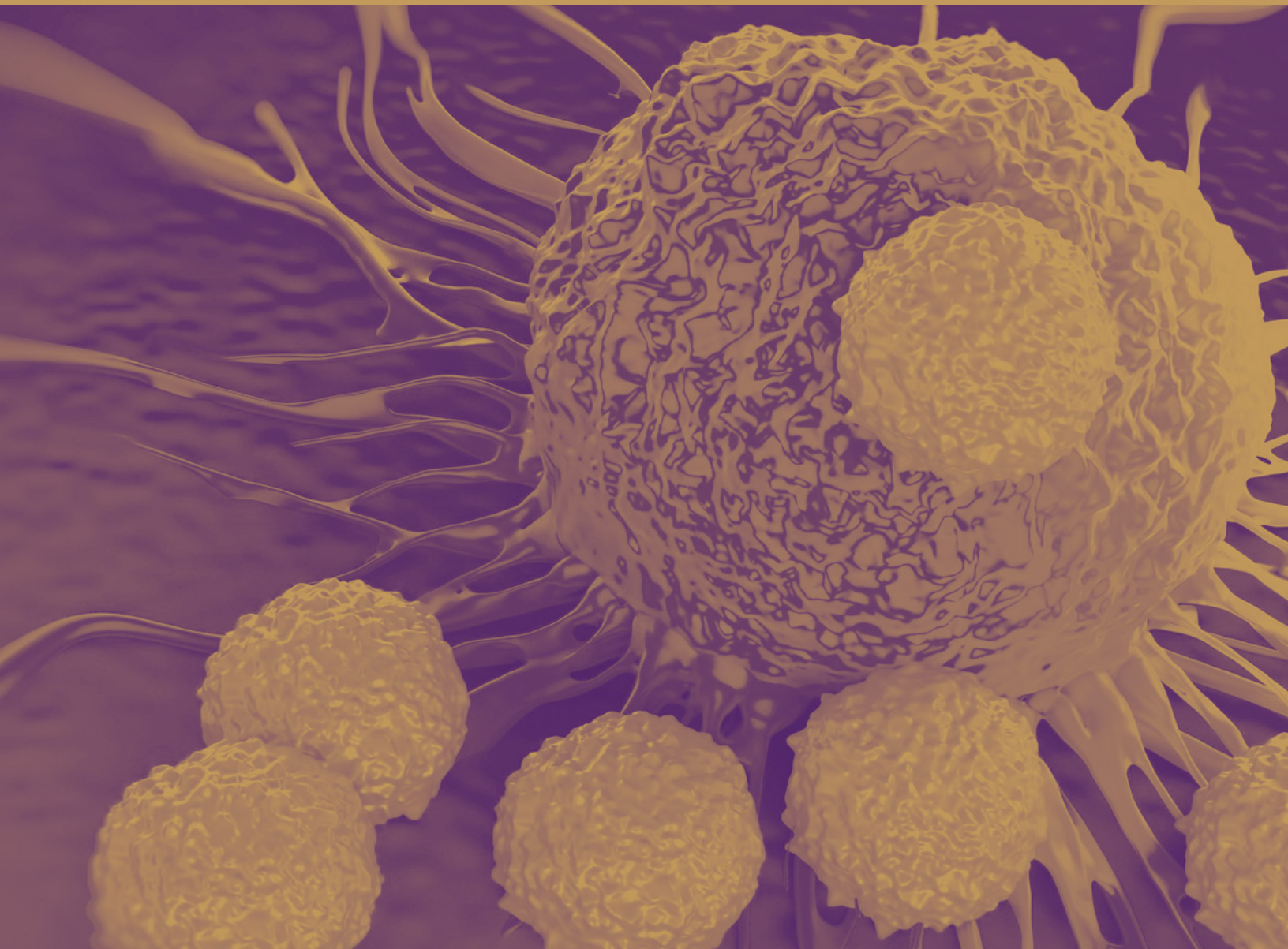




Perlmutter Cancer Center

2017 YEAR IN REVIEW



2

NEW
MULTIDISCIPLINARY
CENTERS

\$105M+

IN TOTAL
RESEARCH
FUNDING

Pioneering

PRACTICE-CHANGING
ADVANCES IN
IMMUNOTHERAPY

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MESSAGE FROM THE DIRECTOR

Dear Colleagues:

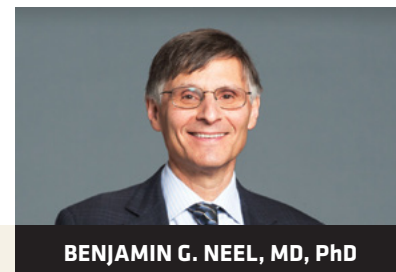
With every passing year, we collectively move closer to our goal of conquering cancer. Our recent strides in marshaling the immune system against this disease have fundamentally shifted the balance toward eradication of many previously intractable cancers. At Laura and Isaac Perlmutter Cancer Center, we are proud of the leadership role our physician-scientists, research staff, and clinicians have played in pioneering immunotherapy.

This year, the U.S. Food and Drug Administration approved two novel immunotherapy-based treatments for advanced bladder cancer—the first effective new treatments in three decades—due in no small part to the success of clinical trials led by Arjun V. Balar, MD, at our institution. Similar achievements in melanoma, lung cancer, breast cancer, and others are testaments to the power of this immune-based approach.

Side by side with these clinical successes, we have continued to invest in our infrastructure and our people, initiating and expanding cancer services for patients. Robert J. Cerfolio, MD, MBA, who has performed more robotic thoracic procedures than any other surgeon worldwide, joined Perlmutter Cancer Center in 2017 to lead our new, comprehensive Lung Cancer Center. Separately, in response to the growing need for multidisciplinary clinical and research expertise in pancreatic cancer, we established the Pancreatic Cancer Center and welcomed renowned surgical oncologist Diane M. Simeone, MD, as its leader. The center's launch bolsters a year of groundbreaking pancreatic

cancer findings published by our physician-scientists and researchers in *Cell*, *Nature Medicine*, *Nature Communications*, and *Cancer Immunology Research*. To help pioneer new treatment approaches for blood cancers, Samer Al-Homsi, MD, MBA, joined as director of the Blood and Marrow Transplant Program, followed by Raoul Tibes, MD, PhD, who joined as director of the Clinical Leukemia Program. Together, they will seamlessly connect patients with a pipeline of enhanced, state-of-the-art treatment options, including a new haploidentical transplantation program built in collaboration with Johns Hopkins School of Medicine.

Our multidisciplinary teams have continued to produce noteworthy research with potentially practice-changing implications. Over the past year, our researchers have created a blood test to accurately detect metastatic melanoma and a method to identify a brain tumor subtype with a standard MRI. Amid a bounty of advanced therapies, we've discovered that high doses of vitamin C could be a viable treatment option for certain types of



BENJAMIN G. NEEL, MD, PhD



Professor of Medicine

Laura and Isaac Perlmutter
Director

Laura and Isaac Perlmutter
Cancer Center at NYU Langone

leukemia and pre-leukemia. By studying how different types of lung cancer cells utilize fuel, we've identified a potential vulnerability that can be targeted by a drug in clinical trials. And, by observing its genetic landscape for the very first time, our researchers have gained valuable insight into the underpinnings of uterine carcinosarcoma, a notoriously treatment-resistant cancer.

As part of these advances in research and clinical care, we have established and expanded patient-navigator-guided programs to connect at-risk, medically underserved populations with affordable, accessible breast and colorectal cancer screenings, care, and cutting-edge clinical trials. With the recruitment of Ophira M. Ginsburg, MD, as director, our new High-Risk Cancer Genetics Program will also provide genetic counseling to at-risk individuals identified through these community programs.

As we turn the page to a new year, we remain optimistic that the future of cancer prevention, research, and clinical care will be borne out through the efforts of our committed team.

FACTS & FIGURES

Perlmutter Cancer Center

CLINICAL

382,000+

PATIENT ENCOUNTERS
at outpatient locations

5,800+

NEW PATIENTS
across all network
locations¹

121

**CLINICAL TRIALS
OPENED**

534

PATIENTS ACCRUED
to interventional
treatment
clinical trials

31

**PHASE I CLINICAL
TRIALS OPENED**

RESEARCH &

180

MEMBERS
in the cancer center

\$105M+

TOTAL FUNDING
in cancer-related
extramural research

151

**HIGH IMPACT (IF ≥ 10)
PUBLICATIONS**
by Perlmutter Cancer
Center members²

133

OUTREACH EVENTS

6,500+

ATTENDEES
at in-person lectures,
screenings, health fairs,
and speakers
bureau events

ACCOLADES

Nationally Ranked

FOR CANCER
in *U.S. News and World Report's*
"Best Hospitals"



1 of 69

National Cancer Institute–designated
cancer centers



Magnet®

RECOGNITION

for nursing excellence for NYU Langone's
Tisch Hospital, Rusk Rehabilitation,
and NYU Langone Orthopedic Hospital



Commission on Cancer

ACCREDITATION

by the American College of Surgeons

QOPI®

QUALITY ONCOLOGY PRACTICE INITIATIVE CERTIFIED
through the QOPI Certification Program (QCP™),
an affiliate of the American Society of Clinical Oncology

FACT®

ACCREDITATION FOR AUTOLOGOUS TRANSPLANTATION

Foundation for the Accreditation of Cellular Therapy
certified by University of Nebraska Medical Center

Unless otherwise noted, all data is FY 2017 (September 2016–August 2017).

¹ January–December, 2016

² January–December, 2017

NYU Langone Health

View of NYU Langone Health's main Manhattan campus, including renderings of the new Science Building (left) and the Helen L. and Martin S. Kimmel Pavilion (right), both set to open in 2018.
(Image credit: Ennead Architects)



#19

IN THE NATION

and nationally ranked in 12 specialties: Rehabilitation, Orthopedics, Rheumatology, Neurology & Neurosurgery, Geriatrics, Urology, Cardiology & Heart Surgery, Gastroenterology & GI Surgery, Diabetes & Endocrinology, Pulmonology, Cancer, and Nephrology



#12

IN THE NATION BEST MEDICAL SCHOOLS FOR RESEARCH

and a leader in innovation in medical education, including accelerated pathways to the MD degree



Leader

IN QUALITY CARE AND PATIENT SAFETY

For the past four years, NYU Langone has received top rankings for overall patient safety and quality of care from Vizient, Inc., formerly the University HealthSystem Consortium. In 2017, NYU Langone received two significant awards from Vizient—the Bernard A. Birnbaum, MD, Quality Leadership Award and the Ambulatory Care Quality and Accountability Award for demonstrated excellence in delivering high-quality, patient-centered outpatient care.

5 Star Rating

FROM CMS HOSPITAL COMPARE

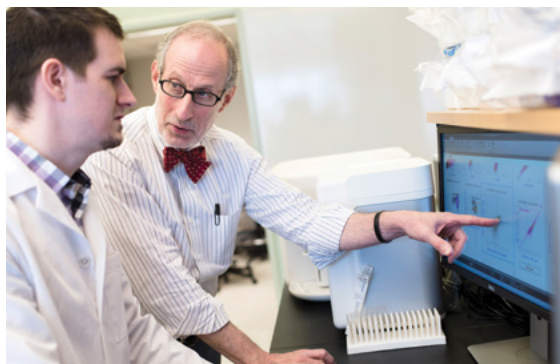
NYU Langone Health is the only full service hospital in New York State and one of 9 percent of hospitals nationwide to receive a five-star rating from the Centers for Medicare and Medicaid Services (CMS). The rating reflects overall safety, quality, and patient experience.

New Programs, Recruits, and Practice-Changing Discoveries Define Banner Year

Immunotherapy Findings Redefine Standard of Care for Advanced Cancers

As recently as 2016, when patients with advanced bladder cancer were too medically frail to take the standard-of-care chemotherapy agent cisplatin, physicians had no other effective treatments to offer. Now, oncologists have two new FDA-approved immunotherapies to choose from, thanks to findings from key clinical trials led by Perlmutter Cancer Center. The center's researchers have also driven remission-achieving advances in immunotherapy for patients with triple-negative breast cancer, recurrent Hodgkin lymphoma, advanced melanoma (Jeffrey S. Weber, MD, PhD, *below*), and advanced non-small cell lung cancer.

➔ [Read more on](#)
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↑ Jeffrey S. Weber, MD, PhD

The new Liver Tumor Program brings together expertise from across the medical center, from the Department of Hepatology to the Transplant Institute.



↑ Theodore H. Welling, MD

Multidisciplinary Liver Tumor Program Launched

Innovation and a patient-centered approach characterize the new multidisciplinary Liver Tumor Program, launched in 2017 at Perlmutter Cancer Center and directed by Theodore H. Welling, MD, associate professor of surgery.

Nationally recognized for his advances in liver transplantation, laparoscopic liver surgery, and surgery requiring expertise in bile-duct and hepatic-vascular resection and reconstruction, Dr. Welling joined NYU Langone in early 2017. Previously he served as co-director of the multidisciplinary liver tumor program at the University of Michigan Health System. At NYU Langone, Ira M. Jacobson, MD, professor of medicine, will collaborate closely with Dr. Welling on the Liver Tumor Program as the medical center's new director of hepatology.

The program brings together the expertise of many specialists—hepatologists, oncologists, surgeons, interventional radiologists, radiation oncologists, researchers, nurses, and others—with the goals of delivering evidence-based medicine and providing access to the program's clinical trials, while simultaneously researching the origins of and new treatments for liver and biliary cancers. The program will also work in close partnership with NYU Langone's Transplant Institute for those patients in need of transplantation.

International Collaborative Grant Program Tackles Cancer Metabolism

A new discovery by Perlmutter Cancer Center researchers is spurring a series of advanced metabolomic investigations halfway across the world, thanks to the Perlmutter Cancer Center–Technion-Israel Institute of Technology Collaborative Oncology Research Grant Program, generously supported by the Laura and Isaac Perlmutter Foundation.

Through the program, Mark R. Philips, MD, professor of medicine, cell biology, and biochemistry and molecular pharmacology, and Alec Kimmelman, MD, PhD, professor of radiation oncology, the Anita Steckler and Joseph Steckler Chair of Radiation Oncology, and co-leader of the Cancer Cell Biology Research Program, have teamed up with Eyal Gottlieb, PhD, and Hossam Haick, PhD, of Technion to explore a new metabolic vulnerability of cancer first identified in the Philips laboratory. The team's study involves *KRAS*, which when mutated drives abnormal growth in more than 90 percent of pancreatic cancers, as well as in many lung and colorectal tumors. Because of this, *KRAS* mutations are among the most attractive targets for anti-cancer drug discovery.

The team's collaborative inquiry builds off Dr. Philips's recent work that uncovered an elusive molecular mechanism responsible for altered sugar (glucose) metabolism in cancers caused by *KRAS* mutations. Dr. Philips's laboratory discovered that only one of the two forms of *KRAS* interact with hexokinase, increasing the enzyme's efficiency in initiating cellular glucose utilization. The finding suggests that, in

addition to driving uncontrolled cell growth, *KRAS* might alter cell metabolism directly. Furthermore, interfering with this *KRAS*-hexokinase interaction could interrupt the full function of *KRAS*, thereby blocking tumor progression. These results were presented by Dr. Philips at the National Cancer Institute's Second RAS Initiative Symposium in December 2017.

The Perlmutter Cancer Center–Technion team is currently conducting additional investigations into tumor metabolism to assess the clinical applications of this finding. At Technion, sophisticated metabolomic analyses are under way in Dr. Gottlieb's laboratory, using cell lines with and without the hexokinase-interacting form of *KRAS* that were created by Dr. Philips's group through CRISPR-Cas9 gene editing. Using tumors established in mice with the same cell lines, Dr. Kimmelman is comparing the metabolic differences of these two forms of *KRAS*-driven tumors and will soon extend this inquiry to mouse models of pancreatic cancer. Once a metabolic pattern has been established, Dr. Haick's laboratory at Technion will use nanoarray technology in an attempt to develop a biomarker that detects this metabolic profile in patients.

"Our international team is in a unique position to potentially impact basic and translational research by both deepening the field's understanding of *KRAS* biology and producing a clinically useful biomarker," says Dr. Philips.

New Pancreatic Cancer Center Focuses on Research, Early Detection

Building on a strong framework of collaboration, Perlmutter Cancer Center created a new multi-disciplinary Pancreatic Cancer Center in July 2017. Renowned pancreatic cancer surgeon and researcher Diane M. Simeone, MD, the Laura and Isaac Perlmutter Professor of Surgery, professor of pathology, and associate director of translational research, leads the combined effort, which leverages insights and expertise from across the institution. The center will tackle long-standing questions about pancreatic cancer's diagnosis, treatment, and prevention, and further expand on recent research insights—and potential solutions—to target pancreatic cancer's impressive ability to evade the immune system.

"Advances in many areas of cancer biology and genomics have created an unprecedented opportunity to drive discoveries that have real impact on patients, especially those with lethal diseases like pancreatic cancer. It is our obligation to step up to this challenge."

—Diane M. Simeone, MD

 [Read more on](#)
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Additions to Clinical Team Boost Strong Research in Blood Cancers

Hematologist-oncologist Samer Al-Homsi, MD, MBA, joined Perlmutter Cancer Center in June 2017 to lead the bone marrow transplantation program. Dr. Al-Homsi will facilitate NYU Langone's collaboration with Johns Hopkins School of Medicine to inaugurate the haploidentical transplantation program at Perlmutter Cancer Center.

In another appointment, Raoul Tibes, MD, PhD, was named director of Perlmutter Cancer Center's Clinical Leukemia Program in October 2017. Dr. Tibes will build a translational leukemia program that will bring novel therapeutic combinations to patients through investigator-initiated trials. In their respective programs, Dr. Tibes and Dr. Al-Homsi will work together closely to bring multiple treatment options to patients.

These faculty will complement a robust hematology research team at Perlmutter Cancer Center. Among their discoveries: An investigation earlier this year by Benjamin G. Neel, MD, PhD, professor of medicine and director of Perlmutter Cancer Center, and Iannis Aifantis, PhD, professor of pathology and chair of the Department of Pathology, discovered that high-dose vitamin C might benefit some blood cancer patients by revving up an enzyme that encourages bone marrow stem cells to mature and die. The research was published online in August 2017 in *Cell*.

[→ Read more on](#)
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Researchers have found that

high-dose vitamin C

might benefit some
blood cancer patients

Clinical Trials Enterprise Makes Strides

In recognition of its significant contributions to the advancement of cancer care by maintaining high-quality clinical trials, the National Cancer Institute has selected Perlmutter Cancer Center to participate in its High Performing Site Initiative (HPSI). The NCI selection was based on patient recruitment and maintenance of high-level-data quality scores, among other factors. In addition, Perlmutter Cancer Center has joined the GlaxoSmithKline (GSK) Oncology Clinical and Translational Consortium, a group of clinical sites that have preferred access to GSK's first-in-human and phase I/early phase II studies. These two developments are expected to rapidly expand the number and quality of advanced treatments available to cancer patients at the center.

New Multidisciplinary Center Aims to Outpace Lung Cancer

Perlmutter Cancer Center has dedicated itself to taking on the nation's leading cause of cancer-related deaths with the launch of its new Lung Cancer Center, led by internationally renowned thoracic surgeon Robert J. Cerfolio, MD, MBA. The center will employ cutting-edge robot-assisted surgery techniques, telemedicine, and genomic research to study, diagnose, treat, and ultimately prevent lung cancer.

The center's clinical offerings are bolstered by its underpinnings in basic and translational research across the medical center. Using the revolutionary CRISPR-Cas9 system, Thales Y. Papagiannakopoulos, PhD, assistant professor of pathology, identified resource vulnerabilities that could be exploited for treatment, as recently reported in *Nature Medicine*.

[→ Read more on](#)
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Robert J. Cerfolio, MD, MBA, director of the Lung Cancer Center, has performed

more robotic thoracic surgeries

than any other surgeon in the world

Melanoma Metastasis: Sugar Fuels It, and a New Diagnostic Test Finds It

Samples from a well-curated melanoma tissue repository have helped Perlmutter Cancer Center scientists track down a key contributor to melanoma's metastasis. Comparing the presence of certain sugars in tissue samples from primary and metastatic melanoma patients, Eva M. Hernando-Monge, PhD, associate professor of pathology and associate director of basic research, and colleagues showed for the first time that FUT8, an enzyme involved in the transfer of sugars to proteins (glycosylation), plays a role in melanoma metastasis in human cancer cells. The results were published in June in *Cancer Cell*.

In a separate study, senior study investigator and dermatologist David Polsky, MD, PhD, the Alfred W. Kopf, MD, Professor of Dermatologic Oncology, and his researchers have created and verified a blood test that can identify metastasis in melanoma patients who lack mutations in *BRAF* or *NRAS* genes. This quick, accurate monitoring tool might enable earlier detection of cancer recurrence and faster treatment adjustments.

→ [Read more on](#)
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↑ Eva M. Hernando-Monge, PhD



Active Surveillance a Safe Option for Men with Low-Risk Prostate Cancer

Active surveillance (AS) is gaining momentum among Swedish men with low- and very-low-risk prostate cancer, according to a new study of one of the world's few national prostate cancer databases by Stacy Loeb, MD, assistant professor of urology and population health. The findings may prompt more physicians and patients to consider AS in their treatment plan.

In collaboration with an international research team from Sweden and England, Dr. Loeb evaluated data from Sweden's National Prostate Cancer Registry, finding that when Swedish men with very-low-risk cancer are presented with the option, they are more likely to choose AS over immediate treatment, which has greater side-effect risks. The study, published online in *JAMA Oncology* in October 2016, reported an increase from 57 percent of Swedish men with very-low-risk prostate cancer choosing AS in 2009 to 91 percent choosing AS in 2014. For Swedish men with low-risk prostate cancer choosing AS, the figures increased from 40 percent to 74 percent during the same period. The oncological outcomes for recently diagnosed Swedish men choosing AS or immediate treatment have not yet been published.

Previous research, including work published by NYU Langone researchers, has shown that carefully selected patients who remain on AS for low- or very-low-risk prostate cancer have a very low risk of dying from the disease. Among American men with low-risk prostate cancer, the AS rate is 40 to 50 percent in most studies. According to Dr. Loeb, although this percentage is increasing, it remains lower than it could be. "American men should be informed that AS is a safe option that is recommended by the guidelines and be given a solid understanding of the extent of their cancer so that more men with low-risk disease might opt for surveillance," she says.

Dr. Loeb's research has been made possible in part by generous support from the Edward Blank and Sharon Cosloy-Blank Family Foundation and the Gertrude and Louis Feil family.

MRI Biomarker Discovery Enables Noninvasive Diagnosis of Glioma Subtype

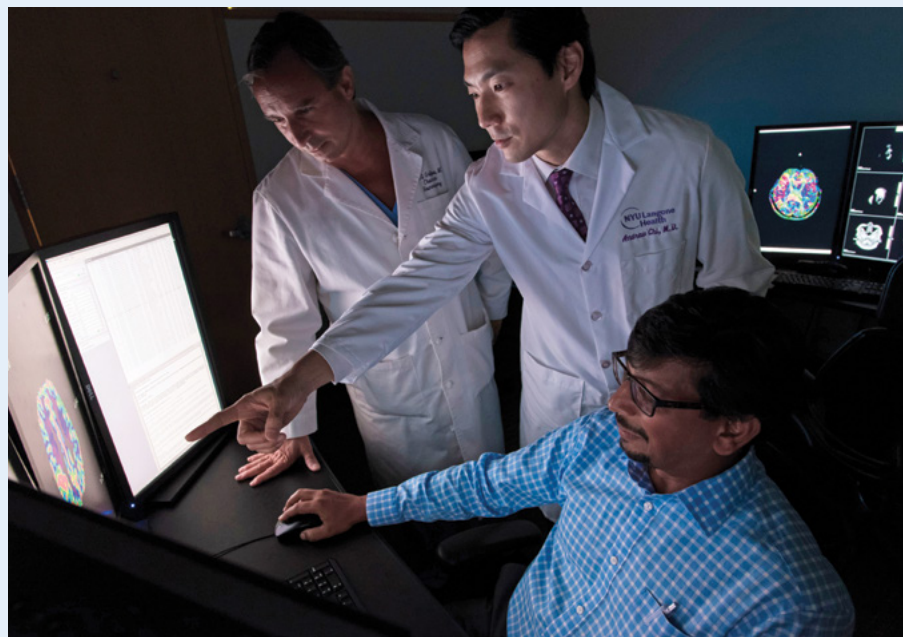
As scientists are gaining increasing knowledge of the many molecular subtypes that make up various cancers, determining which subtype a patient has typically requires genetic testing of a tumor tissue sample. In the case of gliomas and other brain malignancies, this means entering the brain surgically through the skull to obtain tumor cells—an invasive procedure at best, and one that might be unavailable in certain settings.

However, thanks to a recent discovery by the NYU Langone Brain Tumor Center, it is now possible to identify one subtype of lower-grade glioma, defined by *IDH* gene mutation, simply by looking at a routine MRI scan of the brain—without any additional research equipment or software.

This promising new diagnostic protocol hinges on a novel structural biomarker known as a T2-FLAIR mismatch, identified and validated by Rajan Jain, MD, associate professor of radiology and neurosurgery, and his Brain Tumor Center colleagues. The biomarker, described in the July 2017 issue of *Clinical Cancer Research*, is 100 percent indicative of the subtype of *IDH*-mutant gliomas that lack codeletion of chromosomes 1p and 19q, and can be easily recognized by comparing standard T2-weighted and fluid-attenuated inversion recovery (FLAIR) MRI sequences. To confirm the biomarker's specificity, two independent neuroradiologists retrospectively analyzed the MRI scans and other medical

records of hundreds of glioma patients from a publicly available database—The Cancer Genome Atlas/The Cancer Imagine Archive (TCGA/TCIA)—and from NYU Langone's own patient archives. The analysis found that although not all patients with *IDH*-mutant, non-codeleted gliomas showed a T2-FLAIR mismatch in their brain scans, every patient who did have that imaging biomarker had the specified *IDH*-mutant molecular subtype.

"It's what we're all looking for—a noninvasive way to diagnose a tumor's molecular subtype without obtaining brain tissue," says Andrew S. Chi, MD, PhD, assistant professor of medicine, neurology and neurosurgery, director of the Neuro-Oncology Program at Perlmutter Cancer Center, and co-director of the Brain Tumor Center at NYU Langone. Because each glioma's molecular subtype is increasingly being used to target optimal treatment, adds Dr. Chi, the subtype should be determined for every patient, underscoring the need for a noninvasive approach. "This discovery goes beyond gliomas," he says. "With advances in radiology and the increasing sensitivity of DNA detection methods, one day we will simply perform an MRI scan—or even blood tests—to diagnose any brain cancer's molecular subtype, without ever opening the skull."



↑ John G. Golfinos, MD; Andrew S. Chi, MD, PhD; and Rajan Jain, MD

"This discovery goes beyond gliomas. One day, we will simply perform an MRI scan—or even blood tests—to diagnose any brain cancer's molecular subtype, without ever opening the skull."

—Andrew S. Chi, MD, PhD

Molecular Details Underscore Challenges of Treating Gynecologic Cancers

Investigations into the genetic profiles of ovarian cancer and uterine carcinosarcoma (UCS), a rare and aggressive gynecologic cancer, by Douglas A. Levine, MD, professor of obstetrics and gynecology and director of the Division of Gynecologic Oncology, and his Perlmutter Cancer Center colleagues have shed light on these tumors' tenacity.

In March 2017, Dr. Levine, his Perlmutter Cancer Center team, and an international group of researchers published a new "genetic atlas" for UCS in *Cancer Cell*, revealing a complex array of mutations that might explain why these tumors have been

notoriously difficult to treat. Of note: One gene that normally protects against cancer, *TP53*, was mutated in 91 percent of the tumors in the study.

Similarly, molecular studies conducted by Dr. Levine and his colleagues and published in *Nature Communications* provided strong evidence for most, if not all, ovarian cancers starting in the fallopian tubes rather than the ovaries. This new understanding could lead to earlier detection of a cancer that is often diagnosed too late, which reduces survival.

➔ [Read more on](#)
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Bringing Health to Beauty Salons and Barbershops—and Smoking Cessation to Hospitals

Programs established by Joseph E. Ravenell, MD, associate professor of population health and medicine, director of diversity in research, and associate dean for diversity affairs and inclusion; Gbenga G. Ogedegbe, MD, MPH, the Dr. Adolph and Margaret Berger Professor of Population Health and Medicine and director of the Center for Healthful Behavior Change; and Kathie-Ann Joseph, MD, MPH, associate professor of surgery and population health and chief of Breast Surgery Services at NYC Health + Hospitals/Bellevue, are bringing valuable breast and colorectal cancer education beyond clinic walls and into medically underserved communities across New York City.

With the help of trusted patient navigators recruited from local communities, the programs meet individuals in settings where they're more likely to be receptive to medical advice, such as barbershops, beauty salons, and places of worship. Over the past year, more than 5,000 at-risk women have been educated on the importance of breast cancer screening through the Beatrice W. Walters Breast Health Outreach and Navigation Program. Some programs are now being expanded to include a genetic counseling component, a critical offering for higher-risk individuals. Similarly, in its continuing effort to address health equity, the cancer center launched its High-Risk Cancer Genetics Program in 2017, directed by Ophira M. Ginsburg, MD, associate professor of population health and medicine.

Within clinic walls, researchers are bringing effective smoking cessation approaches bedside.



↑ Joseph E. Ravenell, MD, speaks about colorectal health at a Harlem barbershop


With the support of a new grant from the National Cancer Institute's Cancer Center Cessation Initiative, Donna Shelley, MD, MPH, associate professor of population health and medicine and co-leader of the Epidemiology and Cancer Control Research Program, and Scott E. Sherman, MD, MPH, associate professor of population health, medicine, and psychiatry, will integrate a new, evidence-based smoking cessation treatment program into the clinical care at Perlmutter Cancer Center.

➔ [Read more on](#)
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2017 IN DEPTH

A Year of Practice-Changing Research and Clinical Trials



 Arjun V. Balar, MD

Immunotherapy Provides New Options for Patients with Advanced Cancers

As recently as 2016, when patients with advanced bladder cancer were too medically frail to take the standard-of-care chemotherapy agent cisplatin, oncologists had no other effective alternatives to offer. Today, the field of immunotherapy is expanding the options for these patients—and for those with triple-negative breast cancer, recurrent Hodgkin lymphoma, melanoma, and lung cancer. In clinical trials led by Perlmutter Cancer Center physicians, a significant portion of patients with these refractory cancers were able to achieve lasting remission—providing key evidence that could swiftly change practice patterns.

FIRST EFFECTIVE TREATMENTS FOR ADVANCED BLADDER CANCER IN THREE DECADES

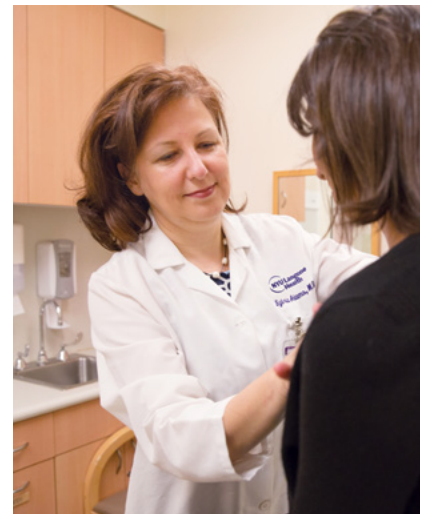
By harnessing the immune system to target bladder cancer, researchers have yielded two discrete new treatment agents. Based primarily on clinical trials led by Arjun V. Balar, MD, assistant professor of medicine and director of the Genitourinary Medical Oncology Program, the FDA approved atezolizumab (Tecentriq®) and pembrolizumab (Keytruda®) as first-line treatments for these particularly frail patients with advanced bladder cancer in early 2017. These immune system-boosting agents are the first-ever FDA-approved treatments for cisplatin-ineligible bladder cancer.

In the clinical evaluation of atezolizumab, published in *The Lancet* in January 2017, bladder tumors shrank by at least 30 percent, and new tumor growth stalled in 28 (24 percent) of 119 patients. All study participants received the medication as their initial therapy for the disease. Similarly, pembrolizumab shrank tumors by at least a third in 24 percent of patients. Of those, 6 percent saw their tumor lesions disappear. The pembrolizumab study was published in *The Lancet Oncology* in November 2017. All patients enrolled in the study were ineligible for cisplatin because of medical frailty.

“Responses with non-cisplatin chemotherapy, the previous standard, are short-lived and patients die within 10 months, on average,” says Dr. Balar. “Immunotherapy harnesses the immune system to generate durable responses and is better tolerated than chemotherapy. Immunotherapy is the most important advancement in bladder cancer therapy in more than 30 years, and it has charted a new path in how we will approach understanding and treating this cancer moving forward.”

A POSITIVE FOR TRIPLE-NEGATIVE BREAST CANCER

Pembrolizumab has also shown promise for patients with metastatic triple-negative breast cancer (mTNBC). According to an international clinical trial led by Sylvia Adams, MD, associate professor of medicine, breast tumors shrank by more than 30 percent in 12 (23 percent) of 52 patients who received pembrolizumab as first-line therapy, and the disease stabilized in 9 additional patients (17 percent). By contrast, breast tumors shrank by more than 30 percent in just 8 (5 percent) of the 170 patients who had been previously treated with other agents; each of these 8 patients lived at least another year. In addition, the disease stabilized in 35 (21 percent) of the 170 patients. These findings were presented at the June 2017 annual meeting of the American Society of Clinical Oncology.



↑ Sylvia Adams, MD

“The more robust response rates of first-line therapy, compared with second or later lines, suggest that immunotherapy administered earlier in the disease course is more beneficial,” says Dr. Adams.

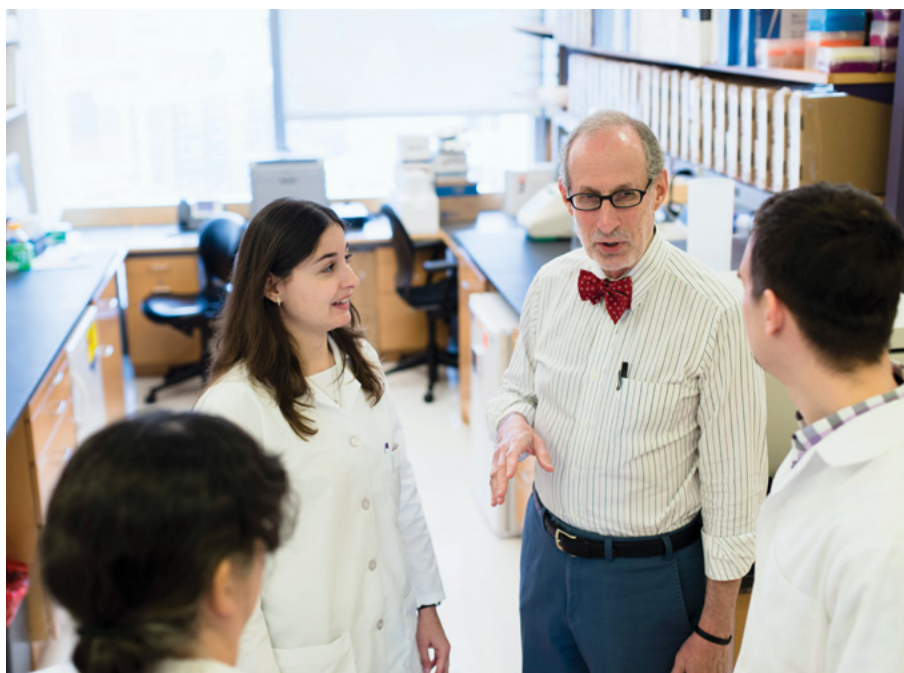
“Although only a small subset of women responded to the drug, pembrolizumab worked extremely well in that subset and responses were durable,” Dr. Adams adds. “By causing fewer side effects and promoting longer life expectancy, pembrolizumab could help change the outcome of mTNBC.”

ACHIEVING REMISSION FOR RELAPSED HODGKIN LYMPHOMA

A combination of complementary immunotherapy drugs brentuximab vedotin (Adcetris®) and nivolumab (Opdivo®) destroyed most cancer cells in 64 percent of patients with recurrent Hodgkin lymphoma, according to the results of an early-phase clinical trial led by Catherine M. Diefenbach, MD, assistant professor of medicine and director of the Clinical Lymphoma Program.

All 19 patients in the study achieved some degree of remission after three months of treatment. Dr. Diefenbach initiated the trial after her research revealed that immune dysfunction in patients with Hodgkin lymphoma could indicate that some standard treatments were less likely to work. These observations led her and her colleagues to test whether drugs that spur the immune system to attack cancer cells, such as checkpoint inhibitors like nivolumab, would work well with the targeted chemotherapy agent brentuximab vedotin. The findings were presented at the December 2016 annual meeting of the American Society of Hematology.

“If further testing proves successful, such dual therapies could become an alternative curative regimen for relapsed Hodgkin lymphoma,” says Dr. Diefenbach.



 Jeffrey S. Weber, MD, PhD

NIVOLUMAB SAFER AND MORE EFFECTIVE FOR ADVANCED MELANOMA

The second-generation immune checkpoint inhibitor nivolumab is proving safer and less toxic for patients whose advanced melanoma has a high risk of recurrence after initial resection and therapy.

A head-to-head comparison of nivolumab and ipilimumab, both FDA-approved medications for metastatic melanoma, was conducted with 906 patients with high-risk stage IIIB, IIIC, and IV melanoma. At 18 months, the relapse-free survival rate for nivolumab was 66 percent, compared with 53 percent for ipilimumab. Results of the international trial, led by principal investigator Jeffrey S. Weber, MD, PhD, the Laura and Isaac Perlmutter Professor of Oncology, deputy director of Perlmutter Cancer Center, and co-leader of its Melanoma Research Program,

were published in November 2017 in *The New England Journal of Medicine*.

“Our results demonstrate that nivolumab is more effective in treating patients with stage III and IV resected melanoma, cutting the risk of relapse by a third,” says Dr. Weber. “Results like this will change how we practice medicine. Hopefully, physicians will embrace the use of nivolumab as adjuvant therapy in these high-risk patients.”

“Our results demonstrate that nivolumab is more effective in treating patients with stage III and IV resected melanoma, cutting the risk of relapse by a third.”

—Jeffrey S. Weber, MD, PhD

COMBINATION THERAPY MIGHT BE MORE EFFECTIVE THAN CHEMOTHERAPY ALONE AS FIRST-LINE TREATMENT OF ADVANCED LUNG CANCER

Pembrolizumab, which has already been shown safe and effective as monotherapy for advanced, non-squamous non-small cell lung cancer (NSCLC), might also be an effective component in combination therapy for the disease.

Led by Leena Gandhi, MD, PhD, associate professor of medicine and director of thoracic medical oncology, researchers from the KEYNOTE-021 study demonstrated for the first time that combining an immune checkpoint inhibitor—in this case, pembrolizumab—with a platinum-doublet chemotherapy regimen might be more effective than chemotherapy alone as first-line treatment for advanced, non-squamous NSCLC. Currently, platinum-doublet chemotherapy is the standard of care for patients without a targetable gene mutation.

The study, published in November 2016 in *The Lancet Oncology* and presented with updated outcomes at the October 2017 World Conference on Lung Cancer in Yokohama, Japan, reported that 57 percent of patients receiving the combination therapy responded to treatment, whereas only 31 percent responded to chemotherapy alone. The results also showed that the combination therapy significantly prolonged progression-free survival, with a median of 19 months for the combination versus 9 months for the chemotherapy group. In addition, although a survival benefit was not observed upon initial data analysis, results presented at the conference showed that those treated with the combination therapy appeared to live longer than those treated with chemotherapy alone.

Previously, most studies had shown that adding any other agent to platinum-doublet chemotherapy resulted in increased side effects that outweighed additional benefits. However, in this study, researchers found the side effects were comparable in both groups.

Based on the results of this small-scale study, in May 2017, the U.S. Food and Drug Administration granted accelerated approval to this combination regimen. Dr. Gandhi is now leading a larger, confirmatory phase III trial for this therapy (KEYNOTE-189), with preliminary results to be reported in April 2018.



↑ Leena Gandhi, MD, PhD

Immunological and Molecular Clues Reveal New Insights to Pancreatic Cancer

From revealing genetic underpinnings to testing new clinical protocols, Perlmutter Cancer Center research teams are targeting pancreatic cancers in innovative ways.

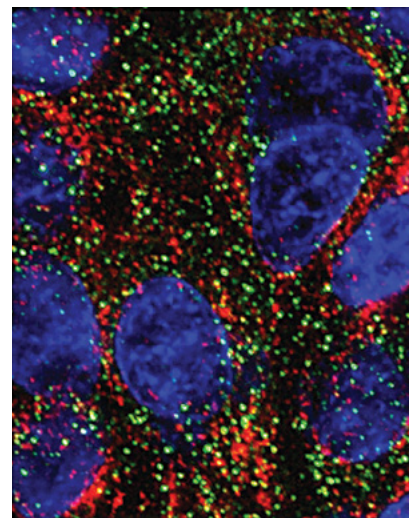
Building on its robust research and strong clinical framework, Perlmutter Cancer Center launched its new, multidisciplinary Pancreatic Cancer Center in July 2017. Renowned pancreatic cancer surgeon and researcher Diane M. Simeone, MD, the Laura and Isaac Perlmutter Professor of Surgery, professor of pathology, and associate director of translational research, directs this combined clinical and research effort, leveraging insights and expertise from across the institution. The center will tackle long-standing questions about pancreatic cancer's diagnosis, treatment, and prevention, and further expand upon recent research findings described below.

STRESS GRANULES PROTECT PANCREATIC CANCER CELLS

Pancreatic cancer cells protect themselves by producing stress granules that lessen the effects of chemotherapy, according to research from the laboratory of

Perlmutter Cancer Center investigator Dafna Bar-Sagi, PhD, professor of biochemistry and molecular pharmacology and medicine, senior vice president and vice dean for science, and chief scientific officer. Dr. Bar-Sagi and collaborators reported in the December 2016 issue of *Cell* that cancer cells with mutations in the *KRAS* gene make six times more stress granules than cells without the mutations when exposed to radiation or the chemotherapy agent oxaliplatin. The team also produced the first-ever images of stress granules inside human pancreatic tumors.

"Our results explain why *KRAS* mutant cells are so good at resisting treatment and suggest a way to make them many times more vulnerable to existing chemotherapies," says Dr. Bar-Sagi. "Given the lack of good treatments for these patients, the ability to interfere with this coping mechanism would be revolutionary."



↑ Pancreatic cancer cells (red) form stress granules (green) near their nuclei (blue) to protect their genetic messages and resist chemotherapy



↑ Diane M. Simeone, MD

Perlmutter Cancer Center is

1 of 12 national sites

participating in the Pancreatic Cancer Action Network's Precision Promise, a large-scale precision medicine trial led by Diane M. Simeone, MD



IMMUNE ACTION REVEALED IN EXISTING THERAPY

Researchers have revealed a second, previously unappreciated mechanism of action for a decades-old cancer drug. Initially designed to prevent cancer cells from multiplying, nab-paclitaxel (Abraxane®) can also stimulate the immune system to attack pancreatic tumors, according to research in Dr. Bar-Sagi's laboratory.

By studying a mouse model of pancreatic cancer and laboratory-grown macrophage cells, the research team showed that the drug causes macrophages in the tumor microenvironment to transition to an immune-activating state. The team reported their findings in February 2017 in *Cancer Immunology Research*.

"Our study reveals a previously unappreciated role for Abraxane® in tumor immunology," says Dr. Bar-Sagi. "In doing so, it suggests ways to improve the drug and argues for its inclusion in new kinds of combination treatments."

TWO PROTEINS HELP PANCREATIC CANCER EVADE IMMUNE SYSTEM

In complementary research, George Miller, MD, the H. Leon Pachter, MD Professor of Surgery, professor of cell biology, and co-leader of the Tumor Immunology Research Program, and his team revealed molecular interactions that can prevent the immune system from attacking pancreatic tumors. High levels of two proteins—Dectin-1 and Galectin-9—in pancreatic tumors and surrounding immune cells, were found to prevent macrophages from triggering reactions that kill cancer cells. The research team compared mice with pancreatic cancer that made Dectin-1 to a group of mice engineered not to make the protein and found that the mice without Dectin-1 lived longer. The team also found that treating mice with an antibody that blocked Galectin-9 from interacting with Dectin-1 dramatically reduced tumor size and increased survival. Dr. Miller's team reported their findings in *Nature Medicine* in May 2017.

"Our results have potentially broad implications because macrophages with Dectin-1 on their surfaces, and cells expressing Galectin-9, infiltrate many cancer types," says Donnele A. Daley, MD, chief resident in the Department of Surgery and former postdoctoral fellow in Dr. Miller's laboratory.

PIONEERS IN PANCREATIC CANCER RESEARCH

Dafna Bar-Sagi, PhD, Named NCI Outstanding Investigator

The National Cancer Institute has recognized Dr. Bar-Sagi for her fundamental contributions to uncovering the mechanisms that drive cancer, as well as for her stellar record of scientific productivity.

George Miller, MD, Receives Ruth Leff Siegel Award for Excellence in Pancreatic Cancer Research

Dr. Miller received the 2017 Ruth Leff Siegel Award for Excellence in Pancreatic Cancer Research for his groundbreaking research on immune suppression of pancreatic cancer. Dr. Miller's Perlmutter Cancer Center colleague Dr. Kimmelman received the Ruth Leff Siegel Award in 2014.

Alec Kimmelman, MD, PhD, Delivers Honorary Lecture

Dr. Kimmelman delivered the 2017 Lori Groetken Memorial Lecture "Identifying Metabolic Dependencies in Pancreatic Cancer" at Washington University School of Medicine in St. Louis, Missouri.

SEVERING PANCREATIC CANCER'S FUEL LINES

Pancreatic cancers are known to have adaptive metabolic networks that sustain their proliferation, and exploiting this difference from normal cells could reveal new therapeutic targets, according to a collaborative study led by Alec Kimmelman, MD, PhD, professor of radiation oncology, the Anita Steckler and Joseph Steckler Chair of Radiation Oncology, and co-leader of the Cancer Cell Biology Research Program.

The researchers, whose results were published in July 2017 in *Nature Communications*, found that simply shutting down a novel metabolic pathway they had previously identified causes pancreatic ductal adenocarcinoma cells to shift their metabolic networks to sustain themselves with available nutrients. Building on this discovery, the team conducted a series of proteomic and metabolomic analyses to identify promising combination therapies that can target more than one metabolic pathway.

"This work highlights how metabolically adaptive pancreatic cancers are, offering us the opportunity to understand these adaptations and hopefully develop effective therapeutic combinations," says Dr. Kimmelman.

RESEARCHERS SELECTED TO CO-LEAD AND COLLABORATE IN PANCREATIC CANCER TRANSLATIONAL RESEARCH TEAM

Nine pancreatic cancer researchers from Perlmutter Cancer Center have been selected to lead and collaborate in a Cancer Interception Translational Research Team by Stand Up To Cancer (SU2C) and the Lustgarten Foundation for Pancreatic Cancer Research.

The team, co-led by Dr. Kimmelman and David P. Ryan, MD, of Massachusetts General Hospital, was awarded \$2.6 million to develop novel approaches to treat and evaluate early pancreatic cancer. In particular, they will assess the benefits of adding certain drugs to chemotherapy treatments with the hope of minimizing disease recurrence.

"Not only do we believe that this clinical trial has the potential to change the standard of care in how we approach this deadly disease, the analysis of clinical specimens collected from the initiative will be quite powerful in informing future trials and further improving patient outcomes," says Dr. Kimmelman.

"For example, our group will look at how tumor cell metabolism is impacted by treatment using our newly created metabolomics core facility, led by Drew Jones, PhD, and Michael E. Pacold, MD, PhD."

In addition to Dr. Kimmelman, the Perlmutter Cancer Center team includes:

- ➔ **Dafna Bar-Sagi, PhD**
- ➔ **Pratip Chattopadhyay, PhD**, associate professor of pathology and director of the Precision Immunology Laboratory in the Division of Advanced Research Technologies
- ➔ **Deirdre J. Cohen, MD**, assistant professor of medicine
- ➔ **Kevin L. Du, MD, PhD**, assistant professor of radiation oncology and director of the Radiation Oncology Residency Program
- ➔ **George Miller, MD**
- ➔ **Michael E. Pacold, MD, PhD**, assistant professor of radiation oncology and chair of the faculty advisory committee for the Metabolomics Core Resource Laboratory
- ➔ **Diane M. Simeone, MD**
- ➔ **Kwok-Kin Wong, MD, PhD**, the Anne Murnick Cogan and David H. Cogan Professor of Oncology and director of the Division of Hematology and Medical Oncology

"The selection of our group as a Cancer Interception Translational Research Team by SU2C and the Lustgarten Foundation is a tremendous honor. It underscores our commitment to push the boundaries of pancreatic cancer research so that we can provide patients with this relentless disease access to the most innovative treatments and world-class care."

—Dafna Bar-Sagi, PhD

Outpacing Lung Cancer

A new, multidisciplinary center aims to accelerate and streamline the translation of potential therapeutic targets into novel treatment options.

CLINICAL COLLABORATION, SURGICAL ADVANCES BOOST LUNG CANCER PREVENTION AND TREATMENT

Robot-assisted surgery, telemedicine, and the latest in genomic research will anchor Perlmutter Cancer Center's new multidisciplinary Lung Cancer Center. The center brings together new and existing programs to study, diagnose, treat, and ultimately prevent the nation's leading cause of cancer-related deaths.

Robert J. Cerfolio, MD, MBA, who has performed more robotic thoracic procedures than any other surgeon worldwide and developed innovations that have given rise to global changes in lung cancer surgery, joined Perlmutter Cancer Center in 2017 to lead the team. The mission of the Lung Cancer Center is twofold: to bring new discoveries to the

clinical setting more rapidly and efficiently, and to improve clinical collaboration and community outreach. Dr. Cerfolio, professor of cardiothoracic surgery and director of clinical thoracic surgery, has trained many practicing thoracic surgeons and will continue this emphasis at the new center.

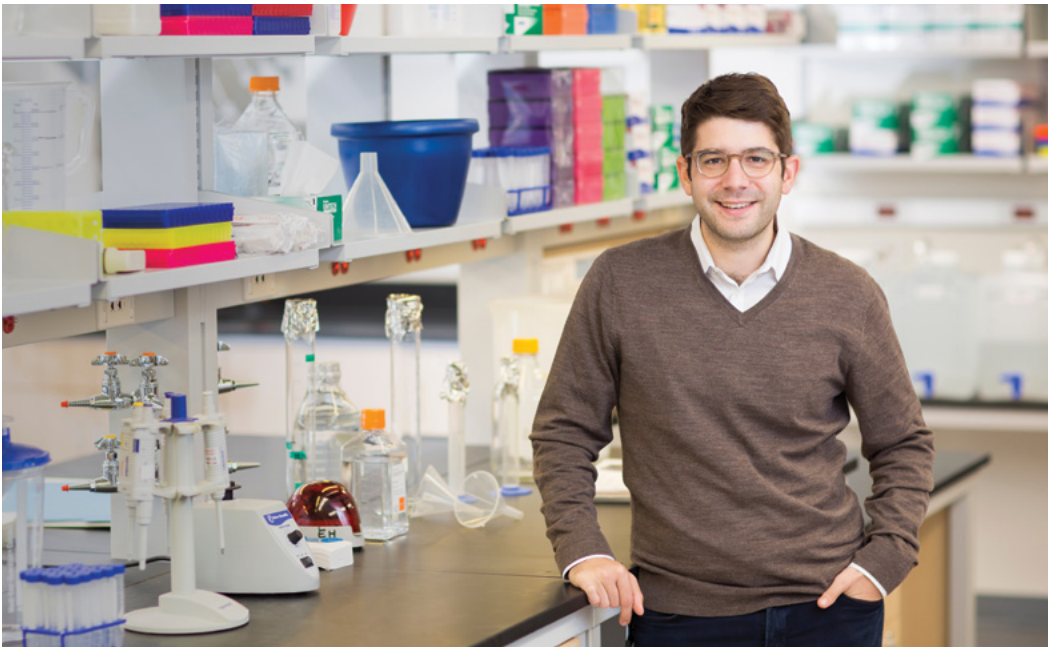
In parallel with promoting surgical advances, the multidisciplinary nature of the center will strengthen researchers' existing inquiries into disease progress and novel therapies, such as the immunotherapy studies under way by Leena Gandhi, MD, PhD, associate professor of medicine and director of thoracic medical oncology. *(See page 13 to read about Dr. Gandhi's research on pembrolizumab combination therapy in non-small cell lung cancer, recently published in The Lancet Oncology.)*

In addition to Dr. Cerfolio and Dr. Gandhi, the new center includes, among others:

- **Abraham Chachoua, MD**, the Jay and Isabel Fine Professor of Oncology, professor of urology, and associate director for cancer services
- **Harvey I. Pass, MD**, the Stephen E. Banner Professor of Thoracic Oncology, professor of cardiothoracic surgery, director of thoracic oncology, and director of the Division of Thoracic Surgery
- **Peter B. Schiff, MD, PhD**, professor of radiation oncology, director of faculty affairs, and vice chair of the Department of Radiation Oncology
- **Benjamin Cooper, MD**, assistant professor of radiation oncology
- **Daniel H. Sterman, MD**, the Thomas and Suzanne Murphy Professor of Pulmonary and Critical Care Medicine, professor of cardiothoracic surgery, director of the Multidisciplinary Pulmonary Oncology Program, and director of the Division of Pulmonary, Critical Care, and Sleep Medicine
- **Kwok-Kin Wong, MD, PhD**, the Anne Murnick Cogan and David H. Cogan Professor of Oncology and director of the Division of Hematology and Medical Oncology

↓ Robert J. Cerfolio, MD, MBA





↑ Thales Y. Papagiannakopoulos, PhD

GENETIC RESEARCH IDENTIFIES GROWING PAINS, NEW THERAPEUTIC VULNERABILITY IN LUNG CANCER CELLS

Genetic changes that help non-small cell lung cancer thrive also make it vulnerable to a promising experimental drug, according to a study led by Thales Y. Papagiannakopoulos, PhD, assistant professor of pathology. The research was published online in October 2017 in *Nature Medicine*.

Using the CRISPR-Cas9 gene editing system to make changes in *KEAPI* similar to those in about 10 percent of lung cancers, researchers found that weakening the gene's function increased the production of antioxidants that help cancer cells thrive despite oxidative stress—a damaging by-product of their *KRAS*-mutation-driven, energy-intensive growth. Because lung cancer cells with co-occurring mutations in *KEAPI* and *KRAS* must use large amounts of glutamate to keep oxidative stress at bay, they become highly dependent on this amino acid.

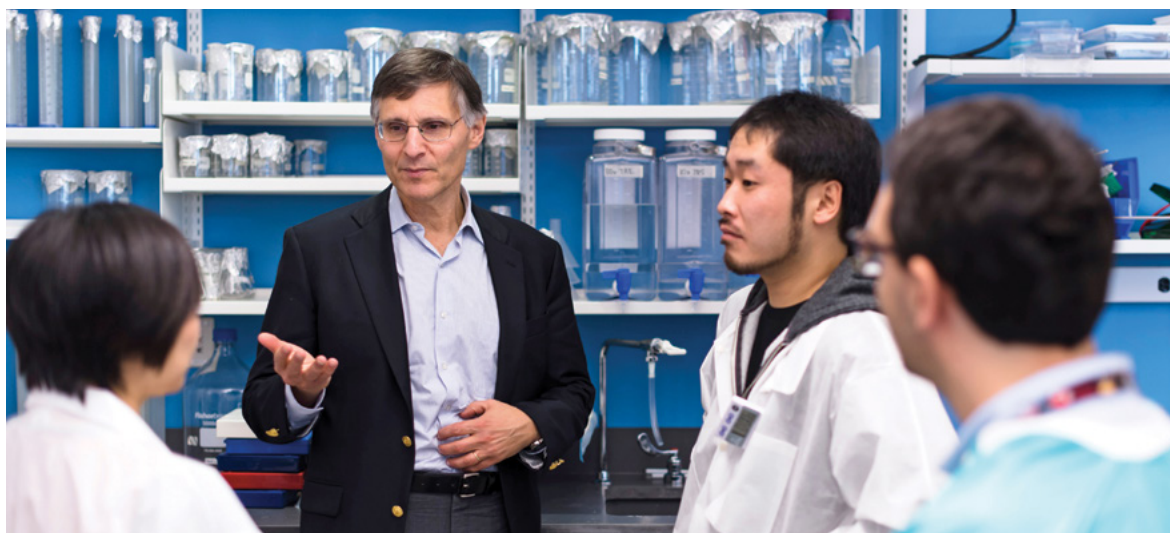
Recognizing this “competition” for glutamate as a weakness, the researchers showed that the experimental drug CB-839 stopped tumor growth in mice with *KRAS* and *KEAPI* mutations by cutting off the cells’ glutamate supply. Because adenocarcinoma cells with mutations used up so much glutamate to enable antioxidant production, they did not have enough to fuel aggressive, *KRAS*-driven growth. Consequently, the cancer cells starved.

“Our study results suggest that a drug currently in clinical trials might be more effective against cancers with combined *KRAS* and *KEAPI* mutations, which represent perhaps 10 percent of patients diagnosed with lung adenocarcinoma, or 9,000 patients per year,” says Dr. Papagiannakopoulos.

Beyond lung cancer, a second study published in October 2017 in *eLife* by the same team reported that *KEAPI* mutations might also make glutaminase inhibitors such as CB-839 more effective against melanoma, bone cancer, kidney cancer, urinary tract cancer, and colon cancer, among others.

Two Promising New Approaches to Eliminating Blood Cancer Stem Cells

New research from Perlmutter Cancer Center investigators reveals insights about the biological miscues that allow blood cancer cells to propagate. The studies provide a basis for novel therapeutic approaches that marshal the body's own stem cells to stave off cancer.



↑ Benjamin G. Neel, MD, PhD

VITAMIN C HELPS CANCER DRUGS PACK A MORE POTENT PUNCH

High-dose vitamin C could offer a new treatment pathway for some patients with blood cancer, according to findings from a study published in August 2017 in *Cell* by Benjamin G. Neel, MD, PhD, professor of medicine and Laura and Isaac Perlmutter director of Perlmutter Cancer Center, and Iannis Aifantis, PhD, professor of pathology and chair of the Department of Pathology. In mice studies, the researchers found that vitamin C effectively “told” faulty bone marrow stem cells to mature and die, rather than multiply to cause certain types of leukemia.

In these cancers, changes in one copy of an enzyme—TET2—disrupts its normal role in regulating blood stem cell turnover. The research found that vitamin C, by

activating the remaining normal copy of TET2 or the related TET3 enzyme, restored TET function in mice genetically engineered to mimic the loss of function seen in cancer cells. Likewise, vitamin C suppressed the growth of human leukemic cells from a small number of patients when those cells were implanted in mice. Detailed analysis of how vitamin C affects these malignancies suggested that vitamin C-treated cells might also become extra susceptible to drugs called PARP inhibitors, which are already approved for some ovarian cancer patients. Indeed, early studies suggested that this drug combination further shifted leukemia cells from self-renewal to maturity and cell death.

TET2 mutations are found in 10 percent of patients with acute myeloid leukemia, 30 percent of those with myelodysplastic

syndrome, and nearly half of patients with chronic myelomonocytic leukemia. New tests suggest that about 2.5 percent of all cancer patients—or about 42,500 new patients each year in the United States, including some with lymphomas and solid tumors—might develop TET2 mutations.

“We’re excited by the prospect that high-dose vitamin C might become a safe treatment for blood diseases caused by TET2-deficient leukemia stem cells, most likely in combination with other targeted therapies,” says Dr. Neel. Based on this work, Perlmutter Cancer Center is currently enrolling eligible patients in a phase Ib/IIa clinical trial to evaluate high-dose vitamin C as treatment for myelodysplastic syndrome.

NOVEL ANTIBODY TARGETS LEUKEMIC STEM CELLS

A team of researchers from Perlmutter Cancer Center and Memorial Sloan Kettering Cancer Center has developed an antibody that selectively causes leukemia stem cells to die. The antibody targets a protein-sugar molecule called CD99 that is present at high levels on the surface of stem cells responsible for blood cancers, including acute myeloid leukemia (AML) and the related myelodysplastic syndromes (MDS).

While the team is working on why the binding of their antibody to CD99 causes leukemia stem cells to die, they speculate that CD99 promotes the growth and survival of leukemic cells. The antibody appears to reverse both of these effects. Experiments in both human cells and in mice with AML confirmed the finding, published online in January 2017 in *Science Translational Medicine*.

“Our findings not only identify a new molecule expressed on AML and MDS stem cells that is responsible for the initiation and maintenance of these human malignancies, but we show that antibodies against this target can directly kill them,” says corresponding study author Christopher Y. Park, MD, PhD, associate professor of pathology.

“The Clinical Leukemia and Blood and Marrow Transplant Programs really go hand-in-hand, and we care for the same patients. It will be a very close collaboration. In a way, you can’t imagine one without the other.”

—Raoul Tibes, MD, PhD

NEW LEADERSHIP BOOSTS CLINICAL BLOOD CANCER PROGRAMS

In October 2017, Raoul Tibes, MD, PhD, was named director of Perlmutter Cancer Center’s Clinical Leukemia Program and associate professor of medicine. Dr. Tibes will focus on building a translational leukemia program that will bring novel therapeutic combinations into the clinic through investigator-initiated trials. Prior to joining NYU Langone, Dr. Tibes’s clinical trials and laboratory work led to the development of a pivotal trial of a first-of-its-kind inhibitor of the B-cell lymphoma 2 protein/gene, which helps acute leukemia and many other cancers evade cell death (apoptosis). Based on the results of this foundational study, Dr. Tibes is investigating the combination of this inhibitor with a current standard-of-care treatment in AML, and preliminary results of this trial have been highly promising. Several other novel concepts arising from his laboratory are also being investigated in the clinical setting. Dr. Tibes was most recently an assistant professor of medicine and the director of the leukemia program at Mayo Clinic in Scottsdale, Arizona.

In another appointment, hematologist-oncologist Samer Al-Homsi, MD, MBA, joined Perlmutter Cancer Center in June 2017 to lead the Blood and Marrow Transplant Program. Dr. Al-Homsi, a clinical professor of medicine, will facilitate NYU Langone’s collaboration with Johns Hopkins School of Medicine on haploidentical transplantation, which increases the donor pool available to patients requiring transplantation. Despite having just arrived, Dr. Al-Homsi has already performed 16 allogeneic transplants, which enables the cancer center to apply for accreditation through the Foundation for the Accreditation of Cellular Therapy (FACT) for allogeneic transplants; the cancer center is currently accredited by FACT to perform autologous transplants in adults and children.

In their new roles, Dr. Tibes and Dr. Al-Homsi are working together to provide multiple treatment options to patients, especially those with AML and myelodysplastic syndromes. Many of these patients are not ideal candidates for allogeneic stem cell transplants—often the only curative therapy—because of the procedure’s intensity. In these cases, Dr. Al-Homsi will evaluate patients for transplantation after their initial treatment provided by Dr. Tibes. If the patient does not qualify for a transplant or if the leukemia returns following a transplant, Dr. Tibes can offer these patients options to participate in clinical trials and access to other novel treatments.



↑ Raoul Tibes, MD, PhD



↑ Samer Al-Homsi, MD, MBA

Tracking Melanoma's Transition into Metastasis

In addition to uncovering a key driver of metastasis, researchers have developed a blood test to detect metastasis in more than half of melanoma patients.

SUGARS HELP FEED MELANOMA METASTASIS

Samples from a well-curated melanoma tissue repository have helped Perlmutter Cancer Center scientists track down a key contributor to melanoma's metastasis. Comparing the presence of certain sugars in tissue samples from primary and metastatic melanoma patients, Eva M. Hernando-Monge, PhD, associate professor of pathology and associate director of basic research, and colleagues in the NYU Department of Chemistry's Biomedical Chemistry Institute homed in on a mechanism by which melanoma might spread to the brain and other organs. Their research, published in June 2017 in *Cancer Cell*, shows for the first time that the process called glycosylation, in which an enzyme triggers the transfer of sugars to proteins, plays a role in melanoma metastasis in human cancer cells.

"Our study shows that sugars are active components of cancer and cancer development," says senior co-author Lara K. Mahal, PhD, professor of chemistry at the Biomedical Chemistry Institute. "From this understanding, we can now target enzymes involved in glycosylation as potential therapeutic targets."

In the case of metastatic melanoma, an enzyme called FUT8, which controls transfer of the sugar fucose, might be a key target. The researchers found that adding fucose to a protein called L1CAM protects it from cleavage by proteases, enabling it to promote melanoma cells' growth around blood vessels and thus colonization of distal organs. Other studies have also pointed to L1CAM as a promoter of brain metastasis in cancers, suggesting a possible mechanism by which fucose can act.



↑ Eva M. Hernando-Monge, PhD

Identifying FUT8's role in melanoma metastasis is only the tip of the iceberg, Dr. Mahal says. The researchers are currently expanding their studies to investigate how alterations in genes and proteins involved in glycosylation might influence brain metastasis.

"We believe ours is one of the first studies examining clinical samples of primary and metastatic cells taken from the same patient," says Dr. Hernando-Monge. "This was only possible due to our extraordinary access to well-annotated human tumor samples through our colleagues in Perlmutter Cancer Center's Melanoma Research Program."

JEFFREY S. WEBER, MD, PHD: GIANTS OF CANCER CARE AWARD RECIPIENT

Jeffrey S. Weber, MD, PhD, the Laura and Isaac Perlmutter Professor of Oncology and deputy director of Perlmutter Cancer Center, was named a 2016 Giants of Cancer Care award recipient. Presented by OncLive, the awards are given to researchers whose work has profoundly impacted the field.

In addition to co-directing Perlmutter Cancer Center's Melanoma Research Program with Iman Osman, MD, professor of dermatology, medicine, and urology, Dr. Weber oversees the center's development of experimental therapeutics. Continuously funded by the National Cancer Institute for more than 20 years, Dr. Weber's research focuses on harnessing the immune system to fight cancer. Dr. Weber has led many clinical trials using checkpoint inhibitors, tumor-infiltrating lymphocytes, and other agents to boost cancer immunity.

Read more about Dr. Weber's recent research uncovering nivolumab's superiority in late-stage melanoma and as adjuvant therapy on page 12.



Jeffrey S. Weber, MD, PhD

NEW BLOOD-BASED GENETIC TEST DETECTS MELANOMA METASTASIS

Gene-based testing of blood samples can quickly and accurately detect metastasis in nearly all types of metastatic melanoma, according to a Perlmutter Cancer Center clinical study of a new diagnostic tool, presented at the April 2017 annual meeting of the American Association for Cancer Research.

This new test will be the latest addition to a suite of melanoma metastasis monitoring tools developed and validated by David Polsky, MD, PhD, the Alfred W. Kopf, MD, Professor of Dermatologic Oncology, professor of pathology, and director of the Pigmented Lesion Section, and his researchers in conjunction with Bio-Rad Laboratories. In 2016, the team evaluated two novel tests to detect *BRAF* or *NRAF* mutations, which are known to drive cancer growth and account for more than half of the 73,000 cases of melanoma diagnosed each year in the United States.

Following this, the team turned their attention to the large population of patients with melanoma who lack *BRAF* or *NRAF* mutations, and subsequently, any disease activity monitoring tools.

The new test identifies two mutations in telomerase reverse transcriptase (TERT)—the most commonly mutated gene in melanoma—in the blood of patients with metastasizing cancer. The team's initial investigation evaluated tumor and blood plasma samples from a small group of patients diagnosed with metastasizing melanoma. The genetic test developed by the research team correctly identified all tumor samples that contained the TERT mutation. The test also detected the TERT mutation in the plasma of 75 percent of the cases with the mutation, and did not generate any false positives from plasma samples or any of the tumor samples lacking the mutation.

As of October 2017, Dr. Polsky and his research team have expanded their sample collection to 31 patients as part

of their ongoing studies. The team is using these samples to monitor progression of aggressive cancer, and to determine whether the test can be used to detect other types of cancer containing TERT mutations.

The research team estimates that the disease activity of nearly all melanomas will be detectable once the new TERT test and the existing *BRAF* and *NRAF* tests become widely available. Similarly, such quick, accurate monitoring tools for melanoma metastasis might enable earlier detection of cancer recurrence—and faster treatment adjustment—than is currently possible. "Our goal is to use this suite of tests to make more informed treatment decisions—including identifying more immediately when a treatment has stopped working, cancer growth has resumed, and the patient needs to switch therapy," says Dr. Polsky.

New Molecular Insights and Established Therapies Help Unravel Gynecologic Cancers

Genetic clues and therapeutic mechanisms uncovered by Perlmutter Cancer Center physician-researchers are reshaping the field's knowledge of ovarian cancer, uterine carcinosarcoma, and fertility preservation.



 Douglas A. Levine, MD

OVARIAN CANCERS MIGHT START IN THE FALLOPIAN TUBES

Most, if not all, ovarian cancers might start in the fallopian tubes instead of the ovaries—a shift in understanding that could help identify these cancers earlier, when they are more treatable—according to a study by Perlmutter Cancer Center researchers published in October 2017 in *Nature Communications*. The discovery hinges on analysis of the genetic signatures of ovarian cancer cells. The research team compared the genetic profiles of ovarian cancer cells from 96 women with high-grade carcinoma in the pelvis and found that they match those of the fallopian tubes, not the ovaries themselves.

Past studies in several cancer types have shown that cancer cells with different origins have different genetic profiles. “We found no differences in the 20,000 genes that we can identify,” says senior study author Douglas A. Levine, MD, professor of obstetrics and gynecology and director of the Division of Gynecologic Oncology. “This leads us to believe that these ovarian cancers all originate in the fallopian tubes.”

The new findings suggest that in women at high risk for ovarian cancer, including those with genetic mutations known to increase risk, such as *BRCA*, removing the fallopian tubes—but not the ovaries—might reduce the risk of ovarian

cancer. Dr. Levine and his research team are on the forefront of efforts to assess this option. “We are one of several centers taking part in Women Choosing Surgical Prevention, or the WISP trial, which seeks to determine whether removing the tubes alone improves quality of life, compared with removing both the tubes and ovaries,” he says.

Furthermore, if biomarkers can be found for these tubal cells, future diagnostic tests on blood samples, cervical cells, and tubal tissue might be able to detect ovarian cancer earlier. Although the team plans to conduct studies to apply these findings to clinical practice, Dr. Levine cautions that it might take years to prove that these approaches detect ovarian cancer earlier, prevent its spread, or extend survival in patients with the disease.

This research result has created the foundation for additional inquiries into ovarian cancer. “Now that we have a better understanding of its origins, we can investigate ovarian cancer prevention, diagnosis, and treatment with greater precision,” says Dr. Levine.

WIDE GENETIC VARIETY IN RARE UTERINE CANCER ELUCIDATES TREATMENT CHALLENGES AND POTENTIAL THERAPEUTIC TARGETS

In their March 2017 publication in *Cancer Cell*, Dr. Levine, his Perlmutter Cancer Center colleagues, and an international group of researchers unveiled a new “genetic atlas” for uterine carcinosarcoma (UCS), revealing a complex array of mutations that might explain why these rare, aggressive gynecologic tumors have been especially difficult to treat.

Supported by the Cancer Genome Atlas Research Network, the findings also point toward possible treatments, with some already approved and others currently in clinical studies. New treatment options are urgent, adds Dr. Levine, because only about one of every three women survives longer than five years after UCS diagnosis.

Investigators sampled tissue from 57 women with confirmed cases of UCS. Of these, 64 percent had the cancer recur within the study follow-up period, and 58 percent died. The average follow-up period was 25.7 months. Analysis of the 57 samples yielded 9,149 genetic mutations, and of these, 14 genes were identified as commonly mutated in UCS. One gene that normally protects against cancer, *TP53*, was mutated in 91 percent of the tumors in the study.

Because of the mix of mutations, drugs aimed at specific genetic targets are more likely to be effective against certain UCS tumors but not others, suggesting that personalized treatment might be necessary to achieve better outcomes. "Using this new collection of genomic information, physicians will be better able to determine the specific genetic fingerprint of each patient's tumor and to find treatment options that better suit them," Dr. Levine says.

EVEROLIMUS COULD HELP PRESERVE FERTILITY IN WOMEN UNDERGOING CANCER TREATMENT

New research suggests that everolimus, a drug used to slow tumor growth, might protect ovaries from the depletion of viable eggs caused by cyclophosphamide, a standard treatment for breast cancer and other malignancies. The findings, led by investigators from Perlmutter Cancer Center and NYU Langone's Fertility Center, suggest new options for patients trying to balance cancer treatment with their ability to have children in the future.

"Our results argue that everolimus, an mTOR inhibitor, might represent a fertility-sparing drug treatment to complement the freezing of eggs and embryos, which are valued methods, but can be time-consuming, costly, less effective with age, and not protective of long-term ovarian function," says study first-author Kara N. Goldman, MD, assistant professor of obstetrics and gynecology.

The study, conducted in mice, compared fertility after treatment with cyclophosphamide alone, in combination with everolimus, or in combination with another experimental mTOR inhibitor. The mice treated with cyclophosphamide

alone had 64 percent fewer primordial follicles, which contain immature egg cells, and half as many pups per litter, representing a significant impact on fertility potential, when compared with control mice. Combination treatment with everolimus or the experimental mTOR inhibitor alongside cyclophosphamide preserved primordial follicles and normal litter sizes. The study was published in March 2017 in the *Proceedings of the National Academy of Sciences*.

"Only clinical trial results will tell us whether these drugs can protect fertility and counter hormonal deficits naturally by preserving follicles," says senior study author Robert J. Schneider, PhD, the Albert B. Sabin Professor of Microbiology and Molecular Pathogenesis, professor of radiation oncology, and associate dean for Technology Ventures and Partnerships. "Our goal is to complete studies to identify the best dose for ovarian preservation and then to get everolimus into a trial."

DOUGLAS A. LEVINE, MD, DELIVERS PRESIDENTIAL PLENARY LECTURE AT INTERNATIONAL CANCER MEETING

The International Gynecologic Cancer Society invited Dr. Levine to deliver its presidential plenary lecture at the organization's biennial meeting in Lisbon, Portugal, on October 29, 2016. His talk, titled "Incorporating Precision Medicine into Clinical Practice," addressed the current state of precision medicine in treating solid tumors, including ovarian cancer dynamics and endometrial cancer biomarker advancements, and the residual unmet needs in identifying therapeutic targets.

Connecting Medically Underserved Patients with Accessible, Affordable Cancer Resources

It has long been recognized that health happens outside the clinic walls. In partnership with NYU Langone's Department of Population Health, Perlmutter Cancer Center is bridging the gap between medicine and public health in New York City's underserved communities, with innovative cancer programs and practice-changing initiatives.

BARBERSHOPS CONNECT PATRONS WITH COLORECTAL CANCER CARE

African American men are at a higher risk of death from colorectal cancer—yet they have lower rates of preventive colonoscopies due to poor access and uneven experience within the healthcare system.

In their effort to address this problem, Joseph E. Ravenell, MD, associate professor of population health and medicine, director of diversity in research, and associate dean for diversity affairs and inclusion, and

Gbenga G. Ogedegbe, MD, MPH, the Dr. Adolph and Margaret Berger Professor of Population Health and Medicine and director of the Department of Population Health's Division of Health and Behavior, realized that they needed to meet these men in their community, where they might be more receptive to discussing their health. "If we rely on a traditional clinical approach to improving outcomes for a population known to be less likely to seek healthcare, we're going to miss those who most need our help," notes Dr. Ravenell.

The resulting, groundbreaking Men's Health Initiative, created with funding from the National Institutes of Health and the Centers for Disease Control and Prevention, applies a culturally tailored strategy: Trusted members of the community are recruited, trained as patient navigators, and placed in barbershops and churches. There, they identify men who haven't had colonoscopies and guide—and, in some cases, accompany—those men to screenings and follow-up care.

↓ Joseph E. Ravenell, MD, speaks to a Harlem barbershop patron about colorectal health



Recently, Dr. Ravenell and his research team completed a randomized trial to investigate the impact of patient navigators in barbershops on the colorectal cancer (CRC) screening rates among 731 low-income African American men age 50 or older in New York City. Patient navigators recruited participants who were then assigned to receive either patient navigation or a more standard screening referral.

Participants in the patient navigator groups received counseling, advice on logistical and psychosocial barriers, and screening appointment reminders. Those in the standard referral group received only printed CRC screening education and a list of screening facilities.

After six months, nearly 18 percent of patients in patient navigator groups—even those with limited health literacy or no insurance—had undergone screening for CRC, compared with only 8.4 percent in the standard referral arm. The results were published in the August 2017 issue of the *American Journal of Public Health*.

“Barbershops hold special appeal for community-based intervention trials, as they are cultural institutions that draw large and loyal male clienteles and provide an open forum for discussion of numerous topics, including health,” Dr. Ravenell says. “Our results emphasize the importance of basing screening interventions in nonclinical settings.”

“If we rely on a traditional clinical approach to improve outcomes for a population known to be less likely to seek healthcare, we’re going to miss those who most need our help.”

—Joseph E. Ravenell, MD

WELTERS BREAST HEALTH OUTREACH AND NAVIGATION PROGRAM CELEBRATES ONE-YEAR ANNIVERSARY, 5,000 WOMEN SERVED

One short year after launching, the Beatrice W. Welters Breast Health Outreach and Navigation Program has educated more than 5,000 women in all five New York City boroughs about maintaining breast health through screening services. Since 2016, the program has hosted 94 outreach events at churches, beauty salons, and health fairs. As a result, 531 people, many of them uninsured women, subsequently enrolled in its navigation services, which include free or low-cost mammograms as well as active breast cancer support for women—from diagnosis, through treatment, and to survivorship.

Co-directors Dr. Ravenell and Dr. Joseph attribute the program’s success to their prior work building community partnerships and their ability to leverage existing relationships within the NYU Langone network, such as NYC Health + Hospitals/Bellevue and NYU Langone Family Health Centers in Flatbush and Sunset Park, to reach patients.

The Welters Program is made possible by generous support from Beatrice W. Welters and her family, and the Laura and Isaac Perlmutter Foundation.

The success of the Men’s Health Initiative in promoting colorectal cancer screenings is now being applied to breast cancer through the Beatrice W. Welters Breast Health Outreach and Navigation Program (see box on this page).

GENETIC COUNSELING AND PATIENT NAVIGATION PROGRAMS TO HELP HIGH-RISK PATIENTS

Medical oncologist Ophira M. Ginsburg, MD, has joined Perlmutter Cancer Center as director of its new High-Risk Cancer Genetics Program, which identifies, studies, and cares for patients with hereditary syndromes that increase cancer risk. In addition to the Department of Medicine, Dr. Ginsburg also holds a faculty appointment in the Department of Population Health, where she is continuing her global cancer control research to improve cancer outcomes in underserved populations.

“We have an underserved population within the New York area in terms of cancer care provision,” says Dr. Ginsburg. “A big part of that is risk reduction and genetic counseling for higher-risk individuals.”



↑ Kathie-Ann Joseph, MD, MPH, speaks at Perlmutter Cancer Center’s annual Breast Cancer in Women of Color event

Working together, Dr. Ginsburg, Dr. Ravenell, and Kathie-Ann Joseph, MD, MPH, associate professor of surgery and population health and director of Breast Surgery Services at NYC Health + Hospitals/Bellevue, are implementing initiatives to improve equitable access to clinical cancer genetics services for underserved men and women. In January 2018, Dr. Joseph will launch a cancer genetics component within the Beatrice W. Welters Breast Health

Outreach and Navigation Program, which just celebrated its one-year anniversary (*see box at left*). Similar to Dr. Ravenell's barbershop model, the Welters Program uses a patient navigator approach in local salons, churches, and community-based organizations to educate medically underserved women about breast cancer and the critical importance of screening.

This new genetic counseling component will allow Dr. Joseph to identify and refer high-risk individuals to the program's dedicated genetic counselor at NYC Health + Hospitals/Bellevue—an enhanced offering made possible through a grant from the Greater New York City affiliate of the Susan G. Komen Foundation. These high-risk individuals might also be paired with a patient navigator who will help them move through the health system should follow-up care be necessary.

Concurrent with these community efforts, the cancer center recently received a \$4 million grant from the New York City Department of Health and Mental Hygiene to build on the success of these barbershop and beauty salon programs by launching the Communities Partnering in Navigation in New York City Program. Its goal is to refer 6,500 patients to colorectal cancer screening and 3,500 to breast cancer screening by mid-2019. In addition to screening, the program's patient navigation component is currently being implemented at NYU Langone's Family Health Centers (Federally Qualified

Health Centers) in Brooklyn to serve its target community.

With this momentum, Dr. Ginsburg and her colleagues will lead a symposium, "Global Cancer Research: Addressing Disparities, Locally and Globally," on March 15, 2018, co-sponsored by the National Cancer Institute Center for Global Health and in partnership with six area cancer centers. Taking place immediately prior to the Consortium of Universities for Global Health's annual meeting, this symposium will help draw attention to healthcare disparities across the city, the country, and the world.

INCORPORATING SMOKING CESSATION INTO HOSPITAL CARE

Perlmutter Cancer Center is connecting more of its patients with evidence-based treatment for smoking through a new program supported by a \$329,000 grant from the Cancer Center Cessation Initiative, part of the National Cancer Institute's Cancer Moonshot program. Using an innovative opt-out approach, the program will refer all patients who identify as smokers—regardless of their readiness to quit—for treatment with a nurse practitioner, who will integrate smoking cessation treatment into their routine services at the center. The new grant, one of 22 funded at university-based hospitals, will be led by the co-directors of the Department of Population Health's Section on

\$329K+

GRANT FROM THE NATIONAL CANCER INSTITUTE

was awarded to researchers to integrate evidence-based smoking cessation strategies at Perlmutter Cancer Center

Tobacco, Alcohol, and Drug Use: Donna Shelley, MD, MPH, associate professor of population health and medicine and co-leader of the Epidemiology and Cancer Control Research Program, and Scott E. Sherman, MD, MPH, professor of population health, medicine, and psychiatry.

The grant follows a successful comparative effectiveness trial that used evidence-based smoking cessation treatment at Bellevue Hospital and the Veterans Affairs New York Harbor Healthcare System. The study, led by Dr. Sherman with help from Dr. Shelley and NYU Langone colleagues, took the unusual step of offering cessation help to all patients who reported smoking upon hospital admission.

The research team identified 18,797 patients between July 2011 and April 2014. Of these, 1,618 enrolled in the study, which compared multisession telephone counseling to referral to a state-run quit-line. The researchers reported in the October 2016 issue of the *American Journal of Preventive Medicine* that 37.4 percent of the patients who received counseling reported smoking abstinence after six months, compared with 31.5 percent who had been referred to the quit-line.

This quit rate was very high, given that a quarter of participants were homeless or in unstable housing, 60 percent had a history of substance abuse, 43 percent reported current hazardous drinking, and half had a psychiatric diagnosis. The investigators concluded that if one in three of these smokers could be encouraged to quit through this relatively simple intervention, it should be feasible to replicate the program in more resource-rich hospital settings.

In 2012, Freya R. Schnabel, MD, professor of surgery and director of breast surgery, co-founded the International Society for Cancer Risk Assessment and Management:

the first

international, multidisciplinary, multi-institutional collaborative effort to address

breast cancer risk assessment

and promote effective strategies for education, surveillance, and risk reduction.

Academic Activities

SELECT PUBLICATIONS

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AWARDS AND HONORS

Jeffrey C. Allen, MD, received Lifetime Achievement Award at International CNS Germ Cell Tumor Symposium, Columbus, Ohio

Russell S. Berman, MD, elected Director of the American Board of Surgery; appointed Editorial Board Member of *Annals of Surgical Oncology*

Pratip Chattopadhyay, PhD, elected Chair of the International Society for the Advancement of Cytometry's 2019 Annual Congress

Andrew S. Chi, MD, PhD, appointed Senior Editor of *Clinical Cancer Research*

Luisa Cimmino, PhD, named St. Baldrick's Scholar by the St. Baldrick's Foundation

Babak Givi, MD, appointed to the American Head and Neck Society's Reconstruction Committee and Constitution and Bylaws Committee

Heather T. Gold, PhD, named President-elect of the Society for Medical Decision Making

Kenneth S. Hu, MD, named ASTRO Fellow by the American Society for Radiation Oncology

Alec Kimmelman, MD, PhD, named Lori Groetken Memorial Lecturer at Washington University School of Medicine

Douglas A. Levine, MD, named Presidential Plenary Speaker at the Biennial Meeting of the International Gynecologic Cancer Society in Lisbon, Portugal

Dan R. Littman, MD, PhD, named Innovation Fund Investigator by the Pew Charitable Trusts

George Miller, MD, received the Ruth Leff Siegel Award for Excellence in Pancreatic Cancer Research; appointed Editor-in-Chief of *Oncogene*

Harvey I. Pass, MD, named Clifton F. Mountain Distinguished Lecturer for Thoracic and Cardiovascular Surgery Department at MD Anderson Cancer Center; delivered inaugural Michael J. Hasson Annual Lecture in

Mesothelioma at Oregon Health and Science University Knight Cancer Institute

Mark S. Persky, MD, appointed President of the American Laryngological, Rhinological and Otological Society (the Triological Society)

Dimitris G. Placantonakis, MD, PhD, appointed Associate Editor of *Oncogene*

Mark B. Pochapin, MD, named Vice President of the American College of Gastroenterology

Diane M. Simeone, MD, appointed National Chair of the Pancreatic Cancer Action Network's Scientific and Medical Advisory Board

Jeffrey S. Weber, MD, PhD, received a 2016 Giants of Cancer Care Award from OncLive

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5,104
Nurses

516
MD
Candidates

85
MD/PhD
Candidates

263
PhD
Candidates

418
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