NCI-Designated
CANCER CENTER

International
RESEARCH COLLABORATION

Multiphase
CLINICAL TRIAL PROGRAM

Multidisciplinary
PATIENT-CENTERED CARE

Magnet®
RECOGNITION FOR NURSING EXCELLENCE

NYU Langone MEDICAL CENTER

Perlmutter Cancer Center

2015
YEAR IN REVIEW

Contents

Dear Colleagues and Friends:

Bold. Pioneering. Innovative.

These three words characterize a new era at the Laura and Isaac Perlmutter Cancer Center, renamed in honor of NYU Langone trustees Laura and Isaac Perlmutter, the generous donors of a gift exceeding $50 million. With this gift, we have entered into a new phase of expansion, aimed at ushering in transformative research that translates into innovative patient care and better outcomes. This new funding will allow us to foster new synergies between laboratory scientists, clinical investigators, clinicians, and educators, all with the goals of improved prevention, detection, and treatment of cancer and, ultimately, curing many more cancer patients.

BENJAMIN G. NEEL, MD, PhD

Professor of Medicine

Laura and Isaac Perlmutter Director

Laura and Isaac Perlmutter Cancer Center at NYU Langone Medical Center

We have already added faculty who are among the most distinguished and promising in their fields and who are greatly increasing the breadth and depth of our expertise. In the pages that follow, we share with you the efforts and achievements of Perlmutter Cancer Center's clinicians and scientists in increasing our understanding about how cancer develops and progresses, always with an eye toward its ultimate defeat.

Immunotherapy, highlighted throughout this report, has emerged as one of the most promising therapeutic interventions against a variety of cancers. By enlisting the body's own defenses in the fight against this disease, we are now able to circumvent the resistance mechanisms that often develop to more conventional anticancer drugs.

Many immunotherapies and other exciting targeted treatments remain experimental and are available to patients only through clinical trials. To bring the most promising of these up-and-coming treatments to our patients, we have made a major commitment to bolster our clinical trials capacity. We have recruited new leadership for our clinical trials operation, we are recruiting new clinician-scientists who specialize in clinical trials development and implementation, and we are developing the capacity, through a new Biologics Program and the Office for Therapeutics Alliances, to speed the development of potential new therapies from the discoveries of our laboratory investigators.

With innovative clinical research, top-quality patient care, and world-class medical education, we are boldly moving forward on our mission to advance and shape the future of cancer care.

Perlmutter Cancer Center

1 of 69
NCI-designated cancer centers

Commission on Cancer
accredited

by the American College of Surgeons

53 outreach events
2,800+ attendees

includes in-person lectures, screenings, health fairs, and speakers bureau events in fiscal year 2015

708
publications

by Perlmutter Cancer Center members in fiscal year 2015

1 of 13

centers in the Neurofibromatosis Clinical Trials Consortium

274,700+
patient encounters

fiscal year 2015 total at the center's major outpatient sites

Magnet® recognition
for nursing excellence

NYU Langone's Tisch Hospital, Rusk Rehabilitation, and Hospital for Joint Diseases

159
researchers

as aligned members on NCI cancer center support grant

Nationally Ranked
for Cancer

in *U.S. News & World Report*'s 2015–16 "Best Hospitals"

NYU Langone Medical Center

UHC
Bernard A Birnbaum, MD,
Quality
Leadership Award
2015 WINNER

#1

overall patient safety & quality for three years in a row

AND

ambulatory care quality & accountability

among leading academic medical centers across the nation that were included in the University HealthSystem Consortium 2015 Quality and Accountability Study

Top 15

in *U.S. News & World Report*

BEST HOSPITALS
U.S.News
HONOR ROLL
2015–16

#12

BEST HOSPITALS HONOR ROLL

BEST GRAD SCHOOLS
U.S.News
MEDICAL
RESEARCH
2016

#14

BEST MEDICAL SCHOOLS FOR RESEARCH

and nationally ranked in 12 specialties, including top 10 rankings in Orthopedics (#5), Geriatrics (#6), Neurology & Neurosurgery (#9), Rheumatology (#9), and Rehabilitation (#10)

TRANSFORMATIVE COLLABORATIONS

Strong New Leadership Injects Energy into Clinical Enterprise, Trials Expansion

Innovative therapies and opportunities for participation in clinical trials at NYU Langone Medical Center have received a significant boost with several additions to faculty and Perlmutter Cancer Center leadership. Experimental therapeutics and the phase I clinical trials program are growing rapidly, with the assistance of a reinvigorated clinical trials office.

- Brain tumor specialist **Andrew S. Chi, MD, PhD,** is the new chief of Neuro-Oncology and co-director of the NYU Langone Brain Tumor Center in partnership with John G. Golfinos, MD, chair of the Department of Neurosurgery. Dr. Chi is assistant professor of medicine, neurology, and neurosurgery. In his new role, Dr. Chi leads all neuro-oncologic related programs, working with the Perlmutter Cancer Center's other highly respected neuro-oncology experts. His investigative work focuses on the characterization of the molecular genetic alterations that underlie treatment-resistant brain tumors. In addition to receiving more than a dozen scientific honors and awards, Dr. Chi has served as principal investigator or co-investigator for 16 clinical trials.
- Clinician-scientist **Alec Kimmelman, MD, PhD,** has been named the chair of the Department of Radiation Oncology. He assumed his new role on February 1, 2016. Dr. Kimmelman comes to NYU Langone following a distinguished career in the Departments of Radiation Oncology at Harvard Medical School and the Dana-Farber Cancer Institute. His laboratory has made seminal contributions to the biological underpinnings of pancreatic cancer and has set in motion promising new studies and clinical trials. Dr. Kimmelman is also a practicing radiation oncologist specializing in the treatment of gastrointestinal cancers.

- On March 1, 2016, **Shohei Koide, PhD**, an internationally renowned expert in protein engineering, will take the helm of a new Cancer Biologics Program at the Perlmutter Cancer Center. It will be one of the nation's first programs in biologics research to be based at an academic institution. In taking this step, the Perlmutter Cancer Center is creating an opportunity to develop partnerships with biopharmaceutical companies under the auspices of NYU Langone's Office of Therapeutic Alliances and may provide access to a pipeline of biologic agents with considerable clinical and commercial potential.
- Immunotherapy expert **Jeffrey S. Weber, MD, PhD,** whose investigations and research findings have brought innovative advances in melanoma treatment from the laboratory to clinical practice, has joined the senior faculty of Perlmutter Cancer Center as deputy director and as co-director of its clinical melanoma program. He will also oversee the center's work in experimental therapeutics. Dr. Weber's research has been funded by the NCI for more than 20 years. His expertise in melanoma therapeutics will enhance an already strong Melanoma Program that has been a consistent national leader in research and cutting-edge treatments.

▲ Dafna Bar-Sagi, PhD

New Research Partnership

In a groundbreaking step forward to advance global collaboration in the fight against cancer, two of the world's preeminent academic and research institutions—NYU Langone Medical Center and the Technion–Israel Institute of Technology—formally announced bestowal of a $9 million gift from philanthropists Laura and Isaac Perlmutter that will fund major joint research endeavors aimed at advancing cancer research. The program is positioned to attract additional world-class support from institutions and individuals dedicated to eradicating cancer through innovative and cutting-edge research. "We can jointly leverage the talent and creativity of our researchers toward accelerating breakthroughs," says Dafna Bar-Sagi, PhD, senior vice president and vice dean for science and chief science officer.

The first two collaborative grants made possible by the gift have been announced:

- **Melanoma** Eva M. Hernando, PhD, associate professor of pathology and a member of the Helen L. and Martin S. Kimmel Center for Stem Cell Biology at NYU Langone Medical Center, and Marcelle Machluf, PhD, deputy executive vice president for Research for the Pre-Clinical Research Authority, head of the Interdepartmental Program of Biotechnology, and a faculty member in the Department of Biotechnology & Food Engineering at the Technion–Israel Institute of Technology.
- **Mesothelioma** Harvey I. Pass, MD, the Stephen E. Banner Professor of Thoracic Surgery and chief of the Division of Thoracic Surgery, Perlmutter Cancer Center, and Israel Vlodavsky, PhD, associate professor of cancer and vascular biology at the Technion–Israel Institute of Technology.

Unlocking the Mysteries of Human Immunity

Since setting up his laboratory at NYU School of Medicine in 2010, Sergei Koralov, PhD, assistant professor of pathology, has had a number of insights into B-cell development. Recently, his work has taken on a new dimension since he began engaging with NYU Langone Medical Center's vibrant community of experts on the human microbiome, the 100 trillion bacteria that live in and on the body.

"The sheer number of diseases driven by immune dysfunction is astounding," says Dr. Koralov. "A better understanding of how bacterial communities influence immune function can help us develop more effective treatments."

The research of Dr. Koralov and his colleagues is described in detail in Turning Points, NYU Langone Medical Center's 2015 Research Report, at **nyulangone.org/publications**.

▲ Sergei Koralov, PhD

▲ Dan R. Littman, MD, PhD

Novel Therapeutic Approaches to the Management of Lymphoma

Catherine M. Diefenbach, MD, assistant professor of medicine, and colleagues are collaborating with basic scientists to develop the next generation of therapeutic approaches for managing lymphoma. Dr. Diefenbach is leading a national clinical trial for people with relapsed Hodgkin lymphoma; numerous other clinical trials in various stages are open as well.

New Pathway for Stalling BRCA Tumor Growth Revealed

Inhibiting the action of a particular DNA repair enzyme dramatically slows the growth of tumor cells tied to BRCA1 and BRCA2 genetic mutations, according to an NYU Langone study published online in *Nature* on February 2, 2015. The researchers targeted the enzyme, polymerase theta (PolQ), which is known to be active in several tumors, including breast, ovarian, liver, and colon cancers. The study's senior investigator, Agnel Sfeir, PhD, assistant professor of cell biology and researcher in NYU Langone's Skirball Institute of Biomolecular Medicine, says that if further experiments prove successful, these findings could lead to a new class of targeted therapies against cancers that carry BRCA1 and BRCA2 mutations, such as breast and ovarian cancers. Dr. Sfeir's work shows that such tumors rely on a specific pathway that uses PolQ to repair DNA damage.

Awards and Recognition

- **Martin J. Blaser, MD,** keynote speaker, American Society for Microbiology (ASM) Conference on Beneficial Microbes; delivered the Kinyoun Lecture, NIH NIAID; recipient of the Infectious Diseases Society of America Alexander Fleming Award; delivered the Tytgat Lecture, Netherlands Society of Gastroenterology; member of NIH NCCIH Advisory Board; keynote speaker, Gastrointestinal Tract XVI FASEB Science Research Conference; delivered the ASM Lecture, 115th ASM General Meeting.
- **Stacie Grossman Bloom, PhD,** recipient of the Louise Hanson Marshall Special Recognition Award, Society for Neuroscience.
- **Kenneth H. Cadwell, PhD,** recipient of the Burroughs Wellcome Fund Investigators in the Pathogenesis of Infectious Disease (PATH) Award.
- **Eva M. Hernando, PhD,** named a permanent member of the Cancer Molecular Pathobiology (CAMP) Study Section, NIH, Center for Scientific Review.
- **Ruth Lehmann, PhD*,** member of the Scientific Advisory Board, Institute of Molecular Biology; keynote speaker for the Cold Spring Harbor Laboratory Meeting on Translational Control.
- **Dan P. Littman, MD, PhD*,** named president, American Association of Immunologists first Visiting Professor in Lasker Lessons in Leadership program; keynote speaker for the American College of Rheumatology Annual Meeting; delivered the 13th annual Kimishige and Teruko Ishizaka Lecture in Immunology; keynote speaker for the University of Miami Miller School of Medicine 7th Annual M.D./Ph.D. Student Research Symposium; delivered the Dan H. Campbell Memorial Lecture, 54th Midwinter Conference of Immunologists; keynote speaker at the 27th Symposium on Virus-Host Interactions.
- **Benjamin G. Neel, MD, PhD,** elected member, Association of American Physicians.
- **Danny Reinberg, PhD*,** elected to National Academy of Sciences; named a Fellow of the American Association for the Advancement of Science.
- **George D. Thurston, ScD,** appointed chair, Environmental Health Policy Committee of the American Thoracic Society.

* Howard Hughes Medical Institute Investigator

Ambulatory Care Expansion

The Laura and Isaac Perlmutter Cancer Center has increased the options for outpatient services with the opening of a new site in the Midwood section of Brooklyn, NY. Other New York locations include sites in midtown Manhattan; Brooklyn; Rego Park, in Queens; and Lake Success, on Long Island.

▲ Ambulatory Care Long Island, in Lake Success, NY

Global Breast Cancer Immunotherapy Trial

Sylvia Adams, MD, associate professor of medicine, is the global principal investigator for Keynote 086, a phase III international trial of a promising immunotherapy agent, pembrolizumab, for metastatic triple negative breast cancer.

▲ Sylvia Adams, MD

New Radiation Therapy Facility

In 2015, the newly built Energy Building became home to another Department of Radiation Oncology facility. The Energy Building is the centerpiece of NYU Langone's plan to become a leader in sustainability. Radiation therapy is also provided nearby at the Perlmutter Cancer Center.

New Cancer Survivorship CME

In May 2016, the NYU Post-Graduate Medical School will host a new CME course, "Optimizing Outcomes for Cancer Survivorship," led by Deborah Axelrod, MD, the Kanas Family Foundation Associate Professor of Surgical Oncology, and Marleen I. Meyers, MD, assistant professor of medicine. Healthcare professionals, ranging from oncologists to social workers, will learn about strategies for improved quality of life for cancer survivors through lectures and panel discussions. More information is available online at **nyulmc.org/cme**

New T32 Grant Designed to Train Aspiring Physician-Scientists in Gastrointestinal Cancer Research

George Miller, MD, associate professor of surgery and cell biology, is the principal investigator on a new T32 grant from the National Cancer Institute. This grant will provide funding to train four residents or fellows per year in gastrointestinal oncology. Trainees will be selected from NYU Langone Surgery residents, Radiation Oncology residents, Medical Oncology fellows, and Gastroenterology fellows. They will spend two years in laboratory- or population-based cancer research. The grant has a five-year term and is renewable. Dr. Miller is also director of the S. Arthur Localio Laboratory, where he conducts groundbreaking research on tumor immunity and the microbiome.

NYU LANGONE MEDICAL CENTER NEWS

Groundbreaking Face Transplant Exemplifies Expertise and Multidisciplinary Collaboration

In August 2015, surgeons at NYU Langone Medical Center performed the most complex face transplant to date. The patient, former firefighter Patrick Hardison, had lost all of the skin around his entire face, scalp, and neck, including his eyelids, ears, lips, and nose, while trapped in a burning building. Led by Eduardo Rodriguez, MD, DDS, the Helen L. Kimmel Professor of Reconstructive Plastic Surgery and chair of the Hansjörg Wyss Department of Plastic Surgery, the successful 26-hour operation—the first to include transplantation of eyelids capable of blinking as well as functional ears, among other milestones—involved more than 100 physicians, nurses, and technical and support staff. More than a dozen departments contributed to the planning and execution of the procedure, or to postoperative care.

COLLABORATION AND INNOVATION

Permutter Cancer Center experts are improving the care of patients with common and complex cancers through translational research and novel approaches to treatment and rehabilitation.

▲ Eva Hernando, PhD (center)

New Clues to Melanoma Metastasis

How does an isolated tumor that starts in melanocytes, the cells that produce skin pigment, spread so aggressively to other parts of the body? This fundamental question guides Eva Hernando, PhD, as she investigates the molecular basis of metastatic melanoma, the deadliest form of skin cancer.

The search for answers took a critical turn when Dr. Hernando, associate professor of pathology and a member of the Helen L. and Martin S. Kimmel Center for Stem Cell Biology joined the Interdisciplinary Melanoma Cooperative Group (IMCG) at NYU Langone's Laura and Isaac Perlmutter Cancer Center in 2006. The prospect of collaborating with researchers across a broad range of disciplines was a big draw for Dr. Hernando. Although cancer research often begins by studying cancer cells in tissue culture or in mouse models and then progresses to human tissue samples, Dr. Hernando starts with patient specimens. She and her colleagues use the IMCG's bank of 17,000 human tissue specimens to ask the questions most relevant to patients and then they design experiments to obtain answers.

COLLABORATIVE SPIRIT SUPPORTS INNOVATION

"We never work in isolation," says Dr. Hernando. "We focus on different aspects of melanoma biology but with the main goal of understanding what makes tumor cells spread and how we can use that information to identify and treat patients who are at highest risk for aggressive melanoma."

That collaborative spirit has resulted in a series of discoveries centered on rogue cells that fail to differentiate into mature melanocytes. In an article published in 2013, Dr. Hernando and her team described how melanoma cells overexpress BRD4, a protein known to fuel tumor growth. Inhibiting BRD4, the researchers found, inhibited melanoma growth. Last year, the team found that the same protein helps melanoma cells continue to proliferate. In yet another promising discovery, the team found that more aggressive melanomas lose a specific group of microRNAs, a class of molecules that modulate protein levels.

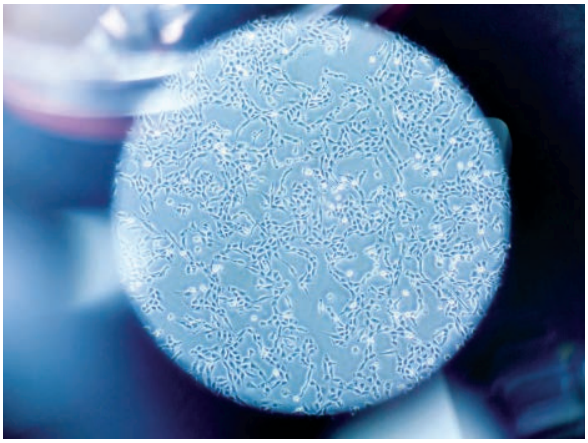
"The same microRNAs that regulate aggressive features of melanoma cells can tell us which patients are at higher risk of developing more metastatic tumors," says Dr. Hernando.

DISCOVERY COULD LEAD TO NEW DIAGNOSTICS

Better diagnostics for melanoma are urgently needed because current methods do not reliably predict which melanoma cells will metastasize. Once melanoma has spread to other parts of the body, it is very difficult to treat: if melanoma is caught early, the survival rate is higher than 92 percent, but when diagnosed at its most advanced stages, life expectancy can be less than a year. A prognostic assay based on an miRNA expression signature, combined with staging criteria, could improve patient prognoses and aid clinical management of patients.

PARTNERSHIP BENEFITS MELANOMA RESEARCH

As part of an exciting new initiative that has taken NYU Langone research to a new continent, Dr. Hernando and colleagues are now collaborating with the Technion–Israel Institute of Technology in the fight against cancer. The partnership, funded by a $9 million gift from philanthropists and NYU Langone trustees Laura and Isaac Perlmutter, bridges two world-class research enterprises and is a milestone in NYU Langone's commitment to international collaboration.



▲ Melanoma cells growing in culture. NYU Langone researchers seek to predict which ones will metastasize.

Melanoma Highlights

TARGETED THERAPY TRIALS MOVING THE BAR FOR MELANOMA PATIENTS

In a presentation at the 2015 ASCO annual meeting in May, Anna C. Pavlick, DO, professor of medicine and the Ronald O. Perelman Department of Dermatology, co-director of the clinical melanoma program, and medical director of the Clinical Trials Office at the Perlmutter Cancer Center presented data from a randomized phase III trial that confirmed clinically meaningful progression-free survival of patients taking a combination of vemurafenib, a BRAF inhibitor, and cobimetinib, a MEK inhibitor. These two treatments target the activity of proteins known to be aberrantly active in about half of melanomas. Median overall survival in BRAF inhibitor-naive patients was greater than two years. Some patients even experienced a complete response, indicating persistent activity with continued therapy.

IMMUNOTHERAPY POISED TO DELIVER

Melanomas are particularly effective at avoiding attack by the immune system. But new treatments that target melanoma's ability to resist immune attack hold promise for melanoma patients. The Cancer Immunology Program at the Perlmutter Cancer Center is taking a multipronged approach to targeting melanoma through the immune system. A team from Permutter Cancer Center reported at the 2015 ASCO annual meeting that in a subset of patients with melanoma brain metastases, radiation therapy induced a prolonged response. The team identified an immunologically distinct subset of tumors with upregulated lymphocyte-activating genes. They concluded that identifying patients with enhanced immunogenicity may predict response to immunotherapy. With access to sophisticated technologies, the Cancer Immunology Program is poised to deliver several promising investigational approaches to melanoma treatment. The arrival of Jeffrey S. Weber, MD, PhD, who as deputy director of the Perlmutter Cancer Center and co-director of the clinical melanoma program, has further boosted the experimental therapeutics program. Dr. Weber is an expert in using immune effector cells called tumor infiltrating lymphocytes and other agents to boost the immune system's response to tumors.

▲ Iman Osman, MD, director of the Interdisciplinary Melanoma Cooperative Group, collaborating with colleagues

NYU Langone's bank of

17,000 specimens

of human melanoma tissue allows researchers to ask the questions most relevant to patients

Techniques, Trials, and New Recruits Enhance Head and Neck Cancer Care

Addressing the complex needs of patients, Mark S. Persky, MD, professor of otolaryngology and director of the Head and Neck Center, continues to build a multidisciplinary team that includes Zujun Li, MD, clinical associate professor of medicine, and Kevin Hu, MD, associate professor of radiation oncology.

Dr. Li and Dr. Hu join existing head and neck surgeons Mark D. DeLacure, MD, the George E. Hall Associate Professor of Head and Neck Cancer Research, associate professor of neurosurgery, and associate professor in the Hansjörg Wyss Department of Plastic Surgery, Babak Givi, MD, clinical assistant professor of otolaryngology and Patient Safety/Quality Improvement Officer, Adam S. Jacobson, MD, associate professor of otolaryngology, David Myssiorek, MD, professor of otolaryngology, and Theresa Tran, MD, assistant professor of otolaryngology. Sungheon Kim, PhD, associate professor of radiology, and Yan Shi, PhD, clinical assistant professor of pathology, are also members of the team. Plans are also under way to launch a new head and neck fellowship under the direction of Dr. Jacobson.

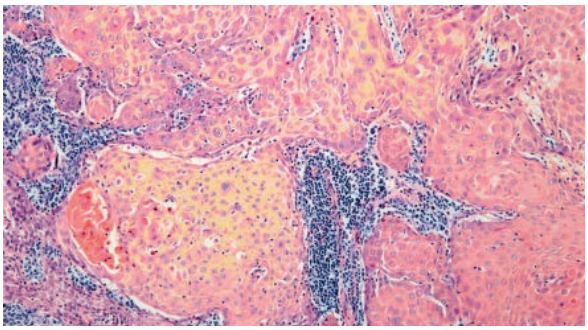
NEW GRANT ADDRESSES CRITICAL ISSUE OF ORAL CANCER PAIN

A new high-priority, one-year grant from the National Institute of Dental and Craniofacial Research (NIDCR) will help address a pressing issue in oral cancer: uncontrolled pain. This funding will allow testing of a novel, nonviral gene delivery method developed at NYU Bluestone Center for Clinical Research and the NYU Oral Cancer Center. The proposed studies will help set the stage for a new class of medications that selectively disrupt local pain signaling, with reduced side effects.

SIMULTANEOUS PET/MRI FOR SURGICAL PLANNING

Dr. Kim is leading a clinical trial to test whether using fludeoxyglucose F 18 injection for PET and MRI to assess lymph nodes prior to surgery can help in the diagnosis of lymph node metastases in patients with head and neck cancers.

▼ Light micrograph of a section through a squamous cell carcinoma of the tongue



EMPHASIS ON PATIENT WELL-BEING

Keenly aware of patient concerns about function and physical appearance, Head and Neck Center experts strive to minimize physical and emotional stress and ease potential side effects through:

- Speech and swallowing rehabilitation
- Occupational and physical therapy
- Social work services
- Support groups
- Integrative health services (massage/acupuncture)
- Specialized nursing

INNOVATIVE TECHNIQUES

Our experts offer:

- Transoral robotic surgery to treat oropharynx cancer
- Endoscopic approaches for skull base tumors
- Organ-sparing, voice-preserving treatments
- Minimally invasive approaches (used whenever possible) to achieve a shorter recovery time and maximize functioning
- Clinical trials and ongoing research in cancer genetics
- Radiation therapy and chemotherapy

Genomics, Animal Modeling Help Identify Aggressive Bladder Cancer Subtypes

The first telltale sign of bladder cancer is usually blood in the urine and perhaps pain upon urination. Here, the parallels among bladder tumors quickly diverge.

Once cancer cells are detected, it can be difficult to differentiate noninvasive tumors from high-grade invasive lesions that have the potential to metastasize. It has been known for some decades that bladder cancers can be divided into two major pathways: low-grade and high-grade. The devil is in the details, says Xue-Ru Wu, MD, the Bruce and Cynthia Sherman Professor in Urological Research and Innovation, professor of pathology, vice chair of Urologic Research, and director of the Goldstein Family Bladder Cancer Research Group. Even among the low-grade and/or noninvasive tumors, a subpopulation will harbor the potential to develop into aggressive and lethal muscle-invasive bladder cancer.

"Recent advances in whole genome sequencing and molecular subtyping have shown that invasive cancers are molecularly quite different from one another. I am still surprised at the complexity of the molecular signatures we are seeing," says Dr. Wu, who is leading an interdisciplinary NCI Program Project (P01) team that is tackling this emerging problem.

bladder cancer is the 4th most commonly diagnosed cancer in men and the

5th most common overall

1 in every 26

men will develop bladder cancer in his lifetime

RISK STRATIFICATION IS KEY

Improving patient outcomes will depend on improved risk stratification, says Dr. Wu. Whole genome sequencing is good at identifying molecular alterations, but it does not tell us what is driving the most aggressive tumors. Animal modeling can help researchers pin down the molecular drivers that are potential therapeutic targets.

"One of our current efforts is to apply genomics to understand why some patients respond better than others to chemotherapy," says Arjun V. Balar, MD, assistant professor of medicine and co-leader of the Genitourinary Cancers Program. For example, NYU Langone is participating in a three-center trial looking at the effect of dose-dense gemcitabine and cisplatin as neoadjuvant chemotherapy prior to surgery for invasive bladder cancer. This study is investigating whether more intense neoadjuvant treatment improves patient response.

Early study results, presented in January at the 2016 Genitourinary Cancers Symposium (ASCO GU) suggest that dose-dense chemotherapy does improve pathological response. But not all patients respond equally well. To help sort out which patients will benefit most from cisplatin therapy, the investigators will sequence more than 400 genes known to be involved in bladder cancer to try to correlate genetic mutations with response to chemotherapy. In particular, says Dr. Balar, the research team will zero in on alterations in DNA-damage repair genes that may correlate with better patient responses to the standard chemotherapy agent cisplatin.

▲ Arjun V. Balar, MD

▲ Xue-Ru Wu, MD

USING THE IMMUNE SYSTEM TO FIGHT BLADDER CANCER

More than a decade ago, NYU Langone radiology researchers pioneered the use of low-dose radiation to prime the immune system against tumors. The abscopal effect is now well established in many radiation treatment regimens for immune sensitive tumors such as melanoma. Taking immune therapy to the next level, NYU Langone investigators are testing this treatment approach in bladder cancer. Specifically, therapeutic antibodies to the programmed cell death pathway (PD)-1 protein and one of its ligands, PD-L1, have shown impressive responses against bladder cancer. Pembrolizumab is among the first of this anti-PD-1 pathway family of checkpoint inhibitors to gain accelerated approval from the FDA. It is currently being used to treat melanomas that have become refractory to standard treatment.

Dr. Balar and his colleagues are among the first in the nation to test the effectiveness of pembrolizumab at augmenting treatment for muscle-invasive bladder cancer. They are leading a phase II trial in which anti-PD-1 treatment (pembrolizumab) is being added to the standard bladder-sparing treatment (radiation given with low-dose chemotherapy, which acts as a radiation sensitizer). "We chose gemcitabine for the low-dose chemotherapy because it is very safe in older people and also because it has been shown to possibly augment the immune system sensitivity of the tumor by depleting certain immunosuppressive cells," says Dr. Balar. "We are adding pembrolizumab with the idea that it may serve as a further immune system stimulant."

Another study, planned for the coming year, innovatively combines an anti-PD-L1 monoclonal antibody (atezolizumab) with the anti-VEGF antibody bevacizumab. The randomized phase II trial in metastatic bladder cancer is being led by Dr. Balar at NYU Langone and Jonathan E. Rosenberg, MD, at Memorial Sloan Kettering Cancer Center. The research team is testing the hypothesis that bevacizumab can promote the maturation and function of dendritic cells and also inhibit the growth of tumor-promoting blood vessels, thereby facilitating a robust immune response boosted by atezolizumab. "A recent phase I trial in advanced melanoma showed promising results with a similar trial design," says Dr. Balar.

Simultaneous PET and MRI Improve Fusion Accuracy for Bladder Cancer

In the first-ever published study of simultaneous MRI and PET image acquisition in bladder cancer patients, researchers in NYU Langone's Departments of Radiology and Urology have shown that this novel technology, which simultaneously acquires FDG-PET and MRI imaging, can greatly improve co-registration accuracy of PET and MRI images. The small investigational study of six patients, published in *Clinical Nuclear Medicine* in August 2015, demonstrated that simultaneous imaging improved the accuracy of co-registration of images of bladder tumors and pelvic lymph nodes. The findings suggest potential utility of PET-MRI for assisting in the diagnostic evaluation of bladder cancer patients. Conventional PET-CT scan imaging, in comparison, performs fusion of PET images acquired in a sequential, rather than a truly simultaneous, fashion. Led by Andrew B. Rosenkrantz, MD, associate professor of radiology and urology, and Dr. Balar, the research team is investigating whether the use of hybrid PET-MRI in a larger series, testing whether it can improve staging of complex bladder cancer, as well as assist in treatment decision making through the development of predictive imaging biomarkers.

▲ Ryan Brown, PhD, and Daniel Sodickson, MD, PhD

Novel Pathways for Treating Pediatric Cancers

Tumor microenvironment provides new childhood leukemia treatment target.

Despite great strides in treating pediatric cancers, doctors have long known that one in four children diagnosed with a devastating form of cancer known as T cell acute lymphoblastic leukemia, or T-ALL, will relapse within five years and face a grim prognosis. Even those who do respond to treatment often suffer serious long-term side effects from the drug and radiation therapies, underscoring the need for more effective and less toxic treatments.

Now, there is fresh hope. Researchers from NYU Langone Medical Center found that a protein on the surface of infection-fighting T cells, named CXCR4, is essential for T-ALL survival. Blocking its activity, they discovered, can halt and even reverse the leukemia's growth and progression in mice. The unexpected finding, if verified in human clinical trials, could point toward a powerful new approach for treating the childhood cancer.

The research, published in June 2015 in *Cancer Cell*, yielded dramatic results in mice that were afflicted with the equivalent of T-ALL and stripped of the CXCR4 protein. "When 100 percent of the mice with the wild-type leukemia had died, every single mouse in which we had deleted CXCR4 in the leukemia cells was alive and running around the cage," says Susan R. Schwab, PhD, assistant professor of pathology and an investigator in the Skirball Institute of Biomolecular Medicine, who co-led the study.

▲ Lauren Pitt, PhD, and Susan R. Schwab, PhD

A second set of experiments, in which the collaborators transplanted leukemia cells from humans into immune-deficient mice, led to similarly surprising effects. Two weeks after some of the mice received a drug designed to block CXCR4, the therapy had effectively halted leukemia progression. Meanwhile, the leukemia continued unabated in the untreated mice.

Co-author Iannis Aifantis, PhD, the Hermann M. Biggs Professor of Pathology and chair of the Department of Pathology at the Laura and Isaac Perlmutter Cancer Center and an Early Career Scientist at the Howard Hughes Medical Institute, says researchers have only begun to explore the microenvironment, or physical niche, of cancer cells.

"It is actually the first study that shows there are specialized microenvironments where leukemia cells reside," Dr. Aifantis says. "We are now able to visualize these microenvironments, even in a living organism, using microscopy." By better understanding these physical niches within the bone marrow, he adds, researchers may be able to target them with antileukemia interventions.

How do cancerous cells co-opt CXCR4? The protein normally acts like a homing beacon to recruit blood cells to the bone marrow and help T cells mature. Among its partners, the protein binds to a signaling molecule named CXCL12, which is secreted by blood vessels and attracts other cells to create T cell–supportive niches in the marrow. The researchers suspect that T-ALL exploits this same signaling pathway to attract blood cells and nutrients to places where it can thrive instead.

Without the guidance of CXCR4, "the leukemia just essentially melts away," Dr. Schwab says. The study showed that depleting CXCL12 itself also stalls T-ALL progression. CXCR4 may play a key role in human development but seems to be less important later in life. In adults, drugs that block the protein's activity in targeting other diseases have been well tolerated, although researchers caution that the medication's safety must be evaluated in children, as well.

The NYU Langone researchers plan to study next-generation inhibitors of CXCR4 that may be even more effective. Some of these drugs are already in clinical trials for other conditions, meaning that tests of their application for T-ALL could proceed quickly. The exciting potential, Dr. Aifantis says, owes much to the multidisciplinary exploration of leukemia's unexplored niches. "We've just approached it from different angles," he says.

Key to runaway cell growth in aggressive pediatric bone cancer revealed.

A particular molecular pathway permits stem cells in pediatric bone cancers to grow rapidly and aggressively, according to researchers at NYU Langone Medical Center and its Laura and Isaac Perlmutter Cancer Center. Results from the study were published online on April 2, 2015, in *Nature Communications*.

In normal cell growth, the Hippo pathway, which controls organ size in animals, works as a dam, regulating cell proliferation. What the researchers found is that the transcription factor—a DNA-binding protein called sex determining region Y box 2, or Sox2 for short—that normally maintains cell self-renewal, actually releases the floodgates in the Hippo pathway in osteosarcomas and other cancers, permitting the growth of highly aggressive, tumor-forming stem cells.

The research team included lead study investigator Upal Basu Roy, PhD, MPH, senior study investigators Claudio Basilico, MD, the Jan T. Vilcek Professor of Molecular Pathogenesis, and Alka Mansukhani, PhD, associate professor of microbiology. Other NYU Langone investigators included N. Sumru Bayin, PhD, Eugenia Han, MD, and Dimitris G. Placantonakis, MD, PhD, assistant professor of neurosurgery.

▲ William L. Carroll, MD

Focusing on Patients and Their Families

NYU Langone fosters a family-centered culture, where children and their families are integral members of the healthcare team. Through this partnership, children are more likely to experience better medical results as a result of improved communications between families and medical staff. To support this partnership, children and families receive comprehensive psychosocial and wellness services through the Sala Institute for Child and Family Centered Care.

"This is especially critical for children diagnosed with cancer," says William L. Carroll, MD, the Julie and Edward J. Minskoff Professor of Pediatrics, professor of pathology, and director of the Division of Pediatric Hematology/Oncology at Stephen D. Hassenfeld Children's Center for Cancer and Blood Disorders, part of Hassenfeld Children's Hospital. "We work to provide the most advanced care appropriate for each child and understand they have needs far beyond a treatment plan."

New research suggests FDA-approved drugs such as verteporfin may prove useful in treating osteosarcoma

Trillions of Reasons Why the Microbiome Matters

Given the crucial digestive roles played by the trillions of microorganisms that inhabit the gut, it might not be surprising if changes in their populations triggered disequilibrium that contributed to several gastrointestinal cancers.

▼ Martin J. Blaser, MD, Lea Ann Chen, MD, and Ilseung Cho, MD

Martin J. Blaser, MD

Newly named chair of the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria

After all, gut function relies on contributions from a variety of microbes whose populations fluctuate with environmental factors such as a changing diet, smoking, and use of antibiotics or other medications. For more than 20 years, NYU Langone has led the nation in research to understand the myriad ways these bacterial inhabitants affect health. Martin J. Blaser, MD, the Muriel G. and George W. Singer Professor of Translational Medicine, professor of microbiology, and director of the Human Microbiome Program at NYU Langone, has pioneered this emerging field and attracted a multidisciplinary team of physicians and scientists to his program.

Emerging research from this initiative is providing evidence that certain bacterial species are indeed associated with the relative risk of developing GI cancers.

THE ORAL MICROBIOME AND PANCREATIC CANCER

The association between periodontal disease and poor health has been understood for some time. Now, Jiyoung Ahn, PhD, RD, associate professor of population health and environmental medicine, and associate director of Population Sciences for the Perlmutter Cancer Center, and colleagues are exploring the association between certain gram-negative oral bacteria and the risk of pancreatic cancer.

By sampling the oral and pancreas microbiome through genomic sequencing in a case-control study, Dr. Ahn and her team have found that these same bacteria are also present in the human pancreatic duct. To establish causality, Dr. Ahn's group is recruiting patients with pancreatic cancer who are having their pancreas removed and taking samples from both the mouth and the pancreas to determine whether the same bacteria are found in both locations. This NIH-supported study will be the first to use genomic sequencing techniques to comprehensively survey the bacteria found in the pancreas and the mouth of patients with pancreatic cancer.

Knowing that smoking is the most tightly linked environmental risk factor for the development of pancreatic cancer, Dr. Ahn established the first survey of the oral microbiome among smokers and nonsmokers. Her group found that smokers have fewer species of bacteria and a lower abundance of proteobacteria.

"Smokers have a very, very different oral microbiome than nonsmokers," says Dr. Ahn. "The next step will be to determine how these changes affect smokers' health."

FIBER, BACTERIA, AND COLON CANCER

The usefulness of dietary fiber in cancer prevention has been controversial; some studies have suggested a high-fiber diet can be preventive and others, such as the Harvard Nurses' Health Study, found no statistically significant connection. But until now, no one had considered that fiber feeds more than human appetites; it also feeds beneficial *Clostridia* microbes in the gut. And that could explain the long-elusive fiber-cancer prevention connection.

Unlike the dangerous form that produces botulinum toxin, beneficial *Clostridia* species use fiber for fuel and, in the process, produce potentially anticarcinogenic short-chain fatty acids. Dr. Ahn hypothesizes that a diet high in fruits and vegetables provides an environment conducive to these beneficial bacteria, which may in turn reduce cancer risk. In a small pilot study with 82 participants, her research team established an association between greater fiber intake and a greater abundance of beneficial *Clostridia* and *Actinobacteria* species. The team also found a significant relationship between body mass index and overall gut microbiome composition in women but not in men. Overweight women tended to have less diversity and fewer beneficial

microbes in their gut, suggesting a link between obesity, diet, and potential cancer risk. These findings, published in *PLoS One* in 2015 provide clues that dietary fiber might reduce cancer risk by feeding "good" bacteria.

The study complements Dr. Ahn's December 2013 report, published in the *Journal of the National Cancer Institute*, which showed that patients with colon cancer have fewer beneficial bacteria and more harmful bacteria than people without the disease.

Now, Dr. Ahn has launched a prospective, five-year cohort study of 400 healthy adult volunteers from the NYC area with pilot funding from NYU Langone and the Perlmutter Cancer Center. The researchers will evaluate participants' diet and track the presence of microbial communities in the gut over time to evaluate disease risk. Ultimately, they hope to collect data from 10,000 to 20,000 individuals and learn whether the microbial composition in the gut differs in people who subsequently develop colorectal cancer.

Weakness Exposed in Common Cancer Gene

NYU Langone researchers have found a biological weakness in the workings of the most commonly mutated gene involved in human cancers, known as mutant K-Ras, which they say can be exploited by drug chemotherapies to thwart tumor growth. In that study, the researchers discovered how a frequently used chemotherapy drug could be much more effective in killing K-Ras cells when the cells' ability to check their DNA for damage was blocked, by cutting off the activity of two related genes, H-Ras and N-Ras. The results were reported online in *Cancer Cell* on February 10, 2014, by researchers in the laboratory of senior study 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; and lead study investigator Elda Grabocka, PhD.

▼ *Clostridium* bacteria

Dietary fiber
may reduce cancer risk by feeding "good" bacteria

bacteria in the human body outnumber human cells by
10 to 1

More than 1,000 species
of bacteria can be found on or in humans, but about 150 species are dominant

Just like a fingerprint
each person's microbiome is unique

Better Screening, Diagnosis, and Treatment for Men with Prostate Cancer

NYU Langone urologists are partnering across medical specialties to make detection of clinically significant prostate cancer a priority, while helping to preserve patients' quality of life.

Since the advent of prostate-specific antigen (PSA) screening in the late 1980s, the rate of death from prostate cancer has decreased by 40 percent. However, this savings in lives has come at the expense of millions of men who may have undergone unnecessary biopsies and treatment, primarily because of the limitations of PSA screening and random biopsy of the prostate.

"For the past five years at NYU Langone, we have been asking the question: 'How can we do even better than a 40 percent decrease in mortality while reducing the morbidity associated with unnecessary biopsies and treatment?'" says Herbert Lepor, MD, professor of urology, and biochemistry and molecular pharmacology, and the Martin Spatz Chair of the Department of Urology.

LEADING THE CHARGE FOR ACTIVE SURVEILLANCE

Over their lifetimes, one in seven men (14 percent) will develop prostate cancer, but only 3 percent will die from the disease. Given this long-term survival rate, when men are diagnosed with low-grade prostate cancer, active surveillance is a safe and increasingly viable approach, says Stacy Loeb, MD, assistant professor of urology and population health.

"The era of active surveillance has arrived, and it should no longer be considered experimental," Dr. Loeb said while leading a session in May 2015 on active surveillance at the American Urological Association annual meeting.

Working with the public health service and cancer registries in Sweden, where active surveillance has become the default option for men diagnosed with low-grade prostate cancer, Dr. Loeb is tracking the outcomes for patients under surveillance.

"The challenge is that we have no consensus on the best way to follow patients on active surveillance yet," Dr. Loeb says. A 2011 NIH consensus statement made the identification of the optimal protocol for conservative management of prostate cancer a priority.

Dr. Loeb and her colleagues are entering year three of a five-year NIH grant aimed at improving active surveillance protocols. The researchers are developing a mathematical model to determine the need for and timing of invasive repeat prostate biopsies and to evaluate how new developments, such as the use of magnetic resonance imaging (MRI) in surveillance, affect outcomes.

MRI IN COMBINATION WITH ACTIVE SURVEILLANCE

NYU Langone urologists pioneered three-dimensional co-registration of MRI and real-time transrectal ultrasound (TRUS) to detect only actionable prostate cancer. In support of the routine use of the technique, in 2015 Samir S. Taneja, MD, the James M. Neissa and Janet Riha Neissa Professor of Urologic Oncology, professor of urology and radiology, and director of Urologic Oncology, and his colleagues published the first research data showing that very few men with low suspicion scores on MRI have aggressive prostate cancer and these men may be spared treatment and future biopsies. The finding, published online in June 2015 in *European Urology*, is based on a retrospective study of 600 men who received prebiopsy MRI and underwent both systematic biopsy and MRI-guided biopsy. The study showed that MRI-targeted biopsy detects more high-grade cancers than systematic biopsy, so the technique can be used to more accurately stratify risk.

"There is heavy criticism of the use of MRI to decide who does or doesn't need a biopsy because of fear that we might miss high-grade cancers in men with low suspicion or normal MRIs," says Dr. Taneja. "But our data show that that risk is very, very low."

▲ Stacy Loeb, MD

▼ William C. Huang, MD, Samir S. Taneja, MD, and Herbert Lepor, MD

TARGETED MRI-GUIDED BIOPSY HITS THE MARK

For suspicious lesions requiring biopsy, radiologists and urologists use advanced MRI techniques, including dynamic contrast enhancement and diffusion-weighted imaging, to identify the site of significant cancers. The fusion biopsy technique, performed on more than 1,500 men at the Smilow Comprehensive Prostate Cancer Center, has been shown to be more effective in accurately assessing cancers than conventional biopsy.

To compare targeted biopsy with standard 12-core systematic biopsy, Department of Urology researchers followed the clinical outcomes of 452 consecutive men who received their first biopsy at NYU Langone between 2012 and 2015. The results, reported in December 2015 in the *Journal of Urology*, showed that the targeted approach identified more potentially harmful high-grade cancers and fewer low-grade cancers unlikely to cause harm. Cancers identified by systematic biopsy but not by targeted biopsy were nearly all (82 percent) classified as low-grade or clinically insignificant by the Epstein criteria and the UCSF-CAPRA assessment scores.

MOVING MRI IMAGING FROM DIAGNOSIS TO TREATMENT

NYU Langone's pioneering use of MRI-ultrasound (MRI-US) co-registration imaging to identify high-suspicion prostate lesions for targeted biopsy is now moving toward targeted treatment.

"We think that there are a lot of supportive data that most metastasis occurs from one dominant lesion within the prostate, and if you can identify that dominant lesion, then treating that lesion would probably remove the lethal potential of the disease," says Dr. Taneja. "That is a hypothesis that needs to be proven," he adds.

In a critical step in that direction, NYU Langone experts reported in *European Urology* in December 2015 that 96 percent of men undergoing targeted biopsy of the laser ablation zone within six months of treatment showed no cancer in the treatment zone. The clinical trial result represents one of the earliest published reports investigating focal laser ablation of prostate cancer. None of the 25 consecutive men who underwent focal laser ablation developed urinary incontinence or a change in sexual function, and the median time to return to work, normal physical activity, and sexual activity was 1.0, 3.5, and 7.5 days, respectively. This study provides compelling evidence that short-term oncological control can be achieved with virtually no adverse consequences. Dr. Lepor cautions, however, that long-term control has not yet been established.

Similarly, a surgical team led by Dr. Taneja recently completed the first-ever phase II clinical trial of MRI-US fusion biopsy–guided focal bipolar radiofrequency ablation in 21 men with localized prostate cancer (FUSAblate Trial). Six-month follow-up data are still being assessed; however, Dr. Taneja says that immediate results indicate no negative urinary or sexual side effects.

Targeted ablative treatment for prostate cancer can be performed with many energy sources, including laser, cryoablation, radiofrequency, and high-intensity focused ultrasound (HIFU). Unlike with radiofrequency and cryoablation, focal ablation using HIFU can be performed using MRI-US co-registration. William C. Huang, MD, associate professor of urology, recently led a multicenter FDA trial evaluating HIFU for recurrent disease following radiation therapy. Based on positive trial results, in October 2014 Dr. Lepor led a team of urology experts who made the case to the FDA for using HIFU to treat disease that recurs following radiation therapy. In October 2015, the FDA cleared HIFU for clinical use for prostate ablation. NYU Langone is one of just a few institutions with the Sonablate® HIFU surgical ablation system, and it is already among the first academic centers in the United States to perform a HIFU procedure.

"We must be mindful that the goal is to control the disease long-term," says Dr. Lepor. With our focal therapy studies, we are applying the same level of scientific rigor that we have applied to our large database of prostate surgery outcomes.

Targeted Therapies Offer Hope for NF2 Patients

Until recently, surgery was the only recourse for patients diagnosed with neurofibromatosis type 2 (NF2), a rare genetic disorder associated with multiple benign tumors of the nervous system.

However, new insights into the biological underpinnings of the disease have spurred development of molecularly targeted therapies that offer the first glimmers of hope for a cure. NYU Langone physicians are leaders in developing drug treatments for NF2 patients with bilateral vestibular schwannomas, which cause gradual hearing loss. The Comprehensive Neurofibromatosis Center is 1 of 13 U.S. clinical trial sites in the Neurofibromatosis Clinical Trials Consortium, which is dedicated to testing emerging NF2 therapies.

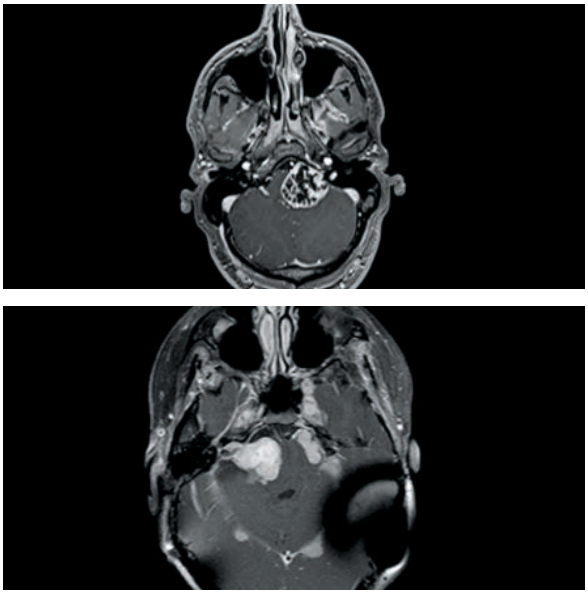
INSIGHTS TRIGGER NEW CLINICAL TRIALS

Matthias A. Karajannis, MD, associate professor of pediatrics and otolaryngology and director of the NF Clinical Research Program, reported on the progress of developing novel therapies tailored to NF patients in a review published in *Current Opinion in Pediatrics* in February 2015. He notes that recent insights into the biology of tumors with mutations in the NF2 gene have triggered a number of clinical trials using molecularly targeted agents already approved by the FDA for other tumors.

Dr. Karajannis was the first to lead and complete a prospective clinical drug trial specifically for NF2 patients. In the trial, lapatinib, an epidermal growth factor receptor inhibitor that is already approved for breast cancer, was well tolerated and led to tumor shrinkage and prolonged disease stabilization in some patients. Although hearing improvement was also observed in some patients, the hearing responses were generally minor and not sustained over the long term.

Bevacizumab, an anti-vascular endothelial growth factor monoclonal antibody, which is approved to treat several types of cancer, is also under investigation for NF2, says Dr. Karajannis. According to anecdotal clinical experience in patients treated on a compassionate care basis, the drug, which is the focus of several ongoing clinical trials sponsored by the NF Clinical Trials Consortium and others, may have the potential to dramatically improve hearing and shrink tumors.

Dr. Karajannis is leading a "phase 0" trial, funded by the National Cancer Institute, in which volunteers take a short course of everolimus prior to scheduled surgery. It is hoped that the data from this study will provide valuable information about the drug's penetration and effects within the tumor tissue. Dr. Karajannis is also conducting a clinical trial of axitinib—the first human study to test a multikinase inhibitor for treatment of NF2-related tumors. "Axitinib is a drug that attacks several points along the tumor proliferation pathway in NF2," says J. Thomas Roland Jr., MD, the Mendik Foundation Professor of Otolaryngology, professor of neurosurgery, and chair of the Department of Otolaryngology—Head and Neck Surgery, and co-director of the Cochlear Implant Center at NYU Langone.



▲ Radiological images of neurofibromatosis

NF2 PRESENTS UNIQUE CHALLENGES

One of the major challenges in treating NF2 is battling multiple tumors that progress at different rates, says Dr. Roland. In addition, NF2 mutations affect multiple cellular signaling pathways, many of which are poorly understood and have not yet been successfully targeted pharmacologically. "A patient might have 20 tumors but only 3 that respond to drug treatment," Dr. Roland says. "We've seen amazing cases of tumors shrinking to half their original size and hearing completely restored, but we also see patients who have no response at all to drug treatment."

PERSONALIZED THERAPIES ON THE HORIZON

The eventual goal is to develop personalized therapies based on the unique biology of patients' tumors, says Dr. Karajannis. "Although a number of molecular targets have been validated preclinically in NF2 tumors and some agents have already shown promise in the clinical realm, effective medical therapies for NF2 that achieve sustained tumor regression remain elusive," he says. "Progress will require a better understanding of the biology of NF2 tumors, development of more potent and specific drugs, and identification of biomarkers that help us understand which patients will most likely benefit from a given therapy."

▲ John G. Golfinos, MD, and J. Thomas Roland Jr., MD

1 of 13
recruitment sites

in the Neurofibromatosis Clinical Trials Consortium

PSYCHOSOCIAL ISSUES MAY BE UNDERTREATED IN NF2

Although NF2 is a benign disease, patients often report significantly higher levels of stress and anxiety than patients with cancer, according to a study led by NYU Langone researchers. Their findings suggest that psychosocial support should be a key part of effective NF2 clinical management.

Using a 63-item questionnaire, the researchers assessed quality of life (QOL) in 11 domains and found that the areas most predictive of overall QOL were psychosocial factors, including depression and anxiety, future uncertainty, and pain. Many patients who completed the questionnaire added comments describing their significant depression and guilt about passing on the genetic disease to their children. The results were published in October 2015 in *Otolaryngology—Head and Neck Surgery*.

Although the questionnaire used in the study just described required a significant time commitment, simpler tools can also be effective in assessing QOL, the authors noted. The NF2 Impact of QOL, or NFTI-QOL, for example, has eight items and takes less than three minutes to complete.

Pain and anxiety appear to be undertreated in this population, says Dr. Roland, the study's senior investigator. "Multidisciplinary NF2 teams should consider greater use of mental health providers and pain management specialists, as treating these symptoms can greatly improve overall QOL," he says.

NYU Langone's team spans a wide range of specialties including pediatric oncology, neurology, neurosurgery, otolaryngology, genetics, plastic surgery, orthopaedic surgery, pain management, nursing, and a variety of mental health and rehabilitation services.

Implementation Science Removing Barriers to Smoking Cessation Programs

So much effort has already gone into finding effective treatments for smoking cessation that one might reasonably ask why the topic needs more attention. But the fact that we now know what works is exactly the point, says Donna R. Shelley, MD, MPH.

Cessation pharmacotherapy combined with counseling has been shown to produce significant and sustained reductions in tobacco use and should be delivered to all smokers who are seeking to quit. Unfortunately, delivering proven treatments can be challenging. There are issues surrounding inconsistent insurance reimbursement as well as the need to create a workflow that clearly defines who delivers the care and when.

HELPING PATIENTS GET FROM "I WANT TO QUIT" TO "I QUIT!"

Dr. Shelley, professor of medicine and population health, is helping move these proven treatments into routine clinical use by applying principles of implementation science to improve quality of care. Providers and staff do not always have the expertise to make the system changes that can help to improve quality. Therefore, Dr. Shelley is testing the use of practice facilitation, in which trained quality improvement specialists help providers optimize workflow and use of their electronic health record to integrate best practices for tobacco use treatment into physicians' regular workflow in the primary care setting.

A NATIONAL MODEL FOR QUALITY CARE

Dr. Shelley's pioneering work in this emerging field has attracted national attention. Last June, her team was one of only seven nationwide chosen to participate in a $15 million, three-year study, funded by the Agency for Healthcare Research and Quality, to help primary care practices improve cardiovascular health by increasing adoption of evidence-based treatment, also known as the ABCs of Heart Health. These ABCs include low-dose aspirin use when indicated, blood pressure control, cholesterol management, and smoking cessation. The project, which includes a partnership between NYU School of Medicine, the NYC Department of Health and Mental Hygiene's Primary Care Improvement Program, and the Community Health Care Association of New York State. The team will leverage NYU Langone's Clinical and Translational Science Institute's on-site data management service, called DataCore, to track patient outcomes across 300 primary care practices.

The project is expected to provide critical new knowledge to facilitate the widespread dissemination and implementation of cardiovascular disease prevention guidelines across the United States. This approach may serve as a national model for implementing other practice guidelines, including those that affect cancer treatment.

INTEGRATING SMOKING CESSATION WITH CANCER CARE

Dr. Shelley sees Medicare's decision to pay for lung cancer screening both as a way to increase smokers' access to this important test and, when patients come in for the test, as an opportunity to offer smoking cessation treatment. She and colleagues at NYU Langone and Memorial Sloan Kettering Cancer Center have submitted a grant application to study such a program.

Smoking cessation is often not integrated into the routine practice of oncologists or the primary care physicians who follow up with cancer patients after treatment, Dr. Shelley says.

There is compelling evidence, highlighted in the 2014 Surgeon General's report on the health consequences of smoking, that current smokers face an increased risk for second primary cancers and may raise their the risk of recurrence, as well as have a poorer response to treatment and increased treatment-related toxicity.

"The most important thing a healthcare provider can do for a smoker's health is help them quit," says Dr. Shelley. "So, this is something providers should be doing on a routine basis. The question is how to make it routine."

Part of Dr. Shelley's research is to figure out how to optimize the use of electronic health records and leverage the data to make the delivery of quality care more efficient.

"Electronic health records have changed the whole landscape of this work," Dr. Shelley notes. "We're looking at workflow using dashboards and registries created with data from the electronic health records. We want to make providers' jobs easier, not harder, and we can do that by helping them do what they really want to do, which is provide excellent care."

Tobacco Cessation Program Highlights

DATACORE TAMES BIG DATA

Biomedical research is increasingly dominated by data. The explosion in *omics*—genomics, proteomics, metabolomics—combined with an avalanche of demographic data from electronic health records and social media has brought an unprecedented level of complexity to data management.

Helping to address the complexity is DataCore, a recent Research IT initiative created in partnership with the Clinical and Translational Science Institute and the Office of Science and Research. It offers researchers a suite of IT tools and services to collect, store, track, and analyze vast collections of data, services that have not been as readily available on campus. Since its launch last year, DataCore has helped more than two dozen investigators develop grant applications for clinical trials.

For Dr. Shelley, the resource has been transformative—a true turning point in her research. The service is helping her team manage the electronic health records of more than 100,000 patients from 250 small to medium-size primary care practices in the Agency for Healthcare Research and Quality study.

"DataCore offers technical support for the entire spectrum of clinical research taking place at NYU Langone, from very small single-center observational studies to large multicenter clinical trials where people all over the world are entering data," explains Judith S. Hochman, MD, the Harold Snyder Family Professor of Cardiology and senior associate dean for clinical sciences.

REMOVING BARRIERS TO SMOKING CESSATION IN VIETNAM

At current rates of smoking, tobacco use will kill one in four men in Vietnam by 2024. Despite this harsh figure, smoking cessation services are largely unavailable in Vietnam. Dr. Shelley and colleagues in Hanoi, Vietnam, are studying ways to break through implementation inertia, by expanding the role of community health workers to include delivering evidence-based tobacco use treatment. Preliminary findings indicate that implementing a system that allows primary care providers to refer smokers to community health workers is a promising model for ensuring that smokers get the help they need and for reducing the burden of tobacco use in Vietnam.

ENLISTING DENTISTS TO DELIVER TOBACCO COUNSELING

Dr. Shelley and her research team are taking practice facilitation into an unexpected setting: dental clinics. Dentists are well positioned to provide counseling about tobacco cessation treatment because they reach people who might not visit a physician's office regularly. By implementing a clinical decision support system, Dr. Shelley's group is helping dentists to provide regular guidance on effective tobacco cessation treatment during patient encounters. The system helps dentists recommend and prescribe approved medications and facilitate patient referrals.

6,587,000

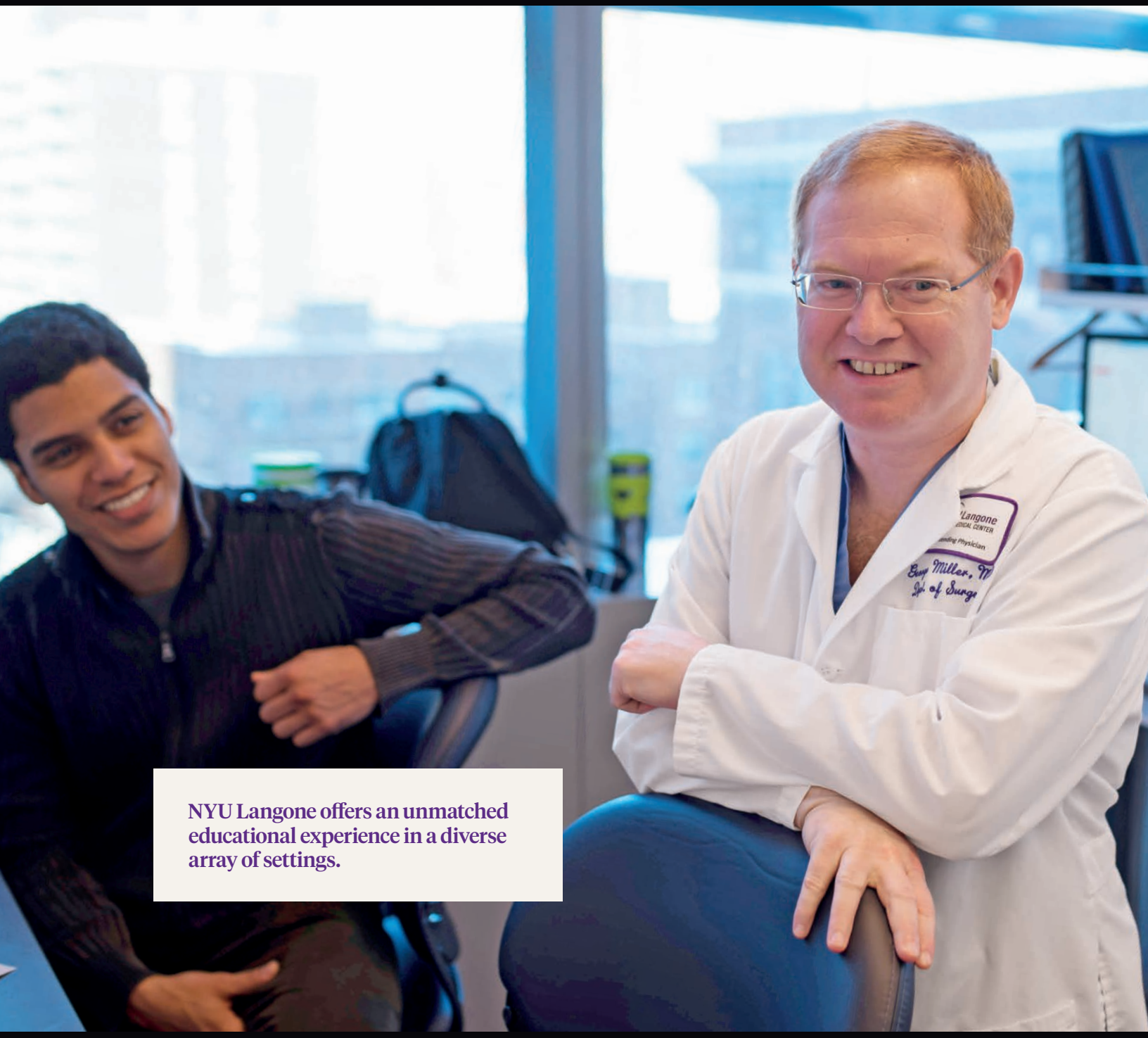
premature deaths from smoking-related cancers in the U.S.

1964–2014

"The most important thing you can do for a smoker's health is help them quit."

— DONNA R. SHELLEY, MD, MPH

A NEW GENERATION OF PHYSICIAN-SCIENTISTS



NYU Langone offers an unmatched educational experience in a diverse array of settings.

▲ Alejandro Torres-Hernandez, MD, and George Miller, MD

New T32 Grant to Train Physician-Scientists in GI Cancer Research

George Miller, MD, associate professor of surgery and cell biology, is the principal investigator on a new T32 grant from the National Cancer Institute. This grant will provide funding to train four residents or fellows per year in gastrointestinal oncology. Trainees will be selected from NYU Langone Surgery residents, Radiation Oncology residents, Medical Oncology fellows, and Gastroenterology fellows. They will spend two years in laboratory- or population-based cancer research. The grant has a five-year term and is renewable. Dr. Miller is also director of the S. Arthur Localio Laboratory, where he conducts groundbreaking research on tumor immunity and the microbiome.

Inaugural Fellows of the Schwartz Gastrointestinal Cancer Research Program Enter Second Year

Launched in 2014, the Bernard and Irene Schwartz Gastrointestinal Cancer Postdoctoral Fellowship Program is among the first in the country dedicated to training physician-scientists in gastrointestinal cancer research. The fellowship has since supported its first class of investigators, who will receive funding through 2016: Donnele Daley, MD, in the Department of Surgery; Daniel Lin, MD, in the Division of Hematology and Medical Oncology; Philmo Oh, MD, PhD, in the Department of Radiation Oncology; and Despina Siolas, MD, PhD, in the Division of Hematology and Medical Oncology. Trainees are selected from NYU Langone Surgery residents, Radiation Oncology residents, Hematology/Oncology fellows, and Gastroenterology fellows. The Schwartz Fellowship leverages NYU Langone's world-class cancer research laboratories and distinguished population science programs to educate future physicians-scientists who will seek to produce innovative therapies for patients with GI cancers.

Hematology-Oncology Fellows Have Record Year of Achievements

2015 marked a record year for NYU Langone's Hematology/Oncology fellows, supported by a recently renewed T32 grant. The fellows published 10 articles in peer-reviewed journals, including the *American Journal of Medicine, British Journal of Haematology,* and *Translational Cancer Research*. The fellows also delivered presentations at the San Antonio Breast Cancer Symposium, the American Society of Clinical Oncology Annual Conference, and the American Society of Clinical Oncology Gastrointestinal Cancers Symposium, among others. The year was also punctuated by individual achievements, including:

- **Francesca Montanari, MD,** was selected as a finalist for the American Society of Hematology Research Fellow Training Award.
- **Vijay Narendran, MD,** traveled with a team of oncologists to train a group of new medical oncologists in Tegucigalpa, Honduras, about gastrointestinal cancers.

Cancer-Related Fellowships and Training Opportunities

Bernard and Irene Schwartz Gastrointestinal Cancer Postdoctoral Fellowship Program

Micrographic Surgery and Dermatologic Oncology

Interdisciplinary Melanoma Cooperative Group Translational Research

Gynecologic Oncology

Hematology/Medical Oncology

Head and Neck Surgery (in development)

Medical Scientist Training Program

Molecular Oncology

Pediatric Neuro-Oncology

Pediatric Hematology/Oncology

Stem Cell and Cancer Biology

Urologic Oncology

Select Publications

Adams S, Gray RJ, Demaria S, Goldstein L, Perez EA, Shulman LN, Martino S, Wang M, Jones VE, Saphner TJ, Wolff AC, Wood WC, Davidson NE, Sledge GW, Sparano JA, Badve SS. Prognostic value of tumor-infiltrating lymphocytes in triple-negative breast cancers from two phase III randomized adjuvant breast cancer trials: ECOG 2197 and ECOG 1199. *J Clin Oncol*. 2014;32(27):2959-2966.

Ananthakrishnan AN, Du M, Berndt SI, Brenner H, Caan BJ, Casey G, Chang-Claude J, Duggan D, Fuchs CS, Gallinger S, Giovannucci EL, Harrison TA, Hayes RB, Hoffmeister M, Hopper JL, Hou L, Hsu L, Jenkins MA, Kraft P, Ma J, Nan Hi, Newcomb PA, Ogino S, Potter JD, Seminara D, Slattery ML, Thornquist M, White E, Wu K, Peters U, Chan AT. Red meat intake, NAT2, and risk of colorectal cancer: a pooled analysis of 11 studies. *Cancer Epidemiol Biomarkers Prev*. 2015;24(1):198-205.

Basu-Roy U, Bayin NS, Rattanakorn K, Han E, Placantonakis DG, Mansukhani A, Basilico C. Sox2 antagonizes the Hippo pathway to maintain stemness in cancer cells. *Nat Commun*. 2015;6:6411.

Bowman CJ, Ayer DE, Dynlacht BD. Foxk proteins repress the initiation of starvation-induced atrophy and autophagy programs. *Nat Cell Biol*. 2014;16(12):1202-1214.

Bratt O, Folkvaljon Y, Hjälm Eriksson M, Akre O, Carlsson S, Drevin L, Franck Lissbrant I, Makarov D, Loeb S, Stattin P. Undertreatment of men in their seventies with high-risk nonmetastatic prostate cancer. *Eur Urol*. 2015;68(1):53-58.

Bryk DJ, Llukani E, Huang WC, Lepor H. Natural history of pathologically benign cancer suspicious regions on multiparametric magnetic resonance imaging following targeted biopsy. *J Urol*. 2015;194(5):1234-1240.

Cerhan JR, Berndt SI, Vijai J, Ghesquieres H, McKay J, Wang SS, Wang Z, Yeager M, Conde L, de Bakker PI, Nieters A, Cox D, Burdett L, Monnereau A, Flowers CR, De Roos AJ, Brooks-Wilson AR, Lan Q, Severi G, Melbye M, Gu J, Jackson RD, Kane E, Teras LR, Purdue MP, Vajdic CM, Spinelli JJ, Giles GG, Albanes D, Kelly RS, Zucca M, Bertrand KA, Zeleniuch-Jacquotte A, Lawrence C, Hutchinson A, Zhi D, Habermann TM, Link BK, Novak AJ, Dogan A, Asmann YW, Liebow M, Thompson CA, Ansell SM, Witzig TE, Weiner GJ, Veron AS, Zelenika D, Tilly H, Haioun C, Molina TJ, Hjalgrim H, Glimelius B, Adami HO, Bracci PM, Riby J, Smith MT, Holly EA, Cozen W, Hartge P, Morton LM, Severson RK, Tinker LF, North KE, Becker N, Benavente Y, Boffetta P, Brennan P, Foretova L, Maynadie M, Staines A, Lightfoot T, Crouch S, Smith A, Roman E, Diver WR, Offit K, Zelenetz A, Klein RJ, Villano DJ, Zheng T, Zhang Y, Holford TR, Kricker A, Turner J, Southey MC, Clavel J, Virtamo J, Weinstein S, Riboli E, Vineis P, Kaaks R, Trichopoulos D, Vermeulen RC, Boeing H, Tjonneland A, Angelucci E, Di Lollo S, Rais M, Birmann BM, Laden F, Giovannucci E, Kraft P, Huang J, Ma B, Ye Y, Chiu BC, Sampson J, Liang L, Park JH, Chung CC, Weisenburger DD, Chatterjee N, Fraumeni JF Jr, Slager SL, Wu X, de Sanjose S, Smedby KE, Salles G, Skibola CF, Rothman N, Chanock SJ. Genome-wide association study identifies multiple susceptibility loci for diffuse large B cell lymphoma. *Nat Genet*. 2014;46(11):1233-1238.

Chatterjee S, Zagelbaum J, Savitsky P, Sturzenegger A, Huttner D, Janscak P, Hickson ID, Gileadi O, Rothenberg E. Mechanistic insight into the interaction of BLM helicase with intra-strand G-quadruplex structures. *Nat Commun*. 2014;5:5556.

Chen YH, Jones MJ, Yin Y, Crist SB, Colnaghi L, Sims RJ 3rd, Rothenberg E, Jallepalli PV, Huang TT. ATR-mediated phosphorylation of FANCI regulates dormant origin firing in response to replication stress. *Mol* Cell. 2015;58(2):323-338.

Cimmino L, Dawlaty MM, Ndiaye-Lobry D, Yap YS, Bakogianni S, Yu Y, Bhattacharyya S, Shaknovich R, Geng H, Lobry C, Mullenders J, King B, Trimarchi T, Aranda-Orgilles B, Liu C, Shen S, Verma AK, Jaenisch R, Aifantis I. TET1 is a tumor suppressor of hematopoietic malignancy. *Nat Immunol*. 2015;16(6):653-662.

Cosetti MK, Golfinos JG, Roland JT Jr. Quality of life (QoL) assessment in patients with neurofibromatosis type 2 (NF2). *Otolaryngol Head Neck Surg*. 2015;153(4):599-605.

Dandekar S, Romanos-Sirakis E, Pais F, Bhatla T, Jones C, Bourgeois W, Hunger SP, Raetz EA, Hermiston ML, Dasgupta R, Morrison DJ, Carroll WL. Wnt inhibition leads to improved chemosensitivity in paediatric acute lymphoblastic leukaemia. Brit J *Haematol*. 2014;167(1):87-99.

Di Micco R, Fontanals-Cirera B, Low V, Ntziachristos P, Yuen SK, Lovell CD, Dolgalev I, Yonekubo Y, Zhang G, Rusinova E, Gerona-Navarro G, Canamero M, Ohlmeyer M, Aifantis I, Zhou MM, Tsirigos A, Hernando E. Control of embryonic stem cell identity by BRD4-dependent transcriptional elongation of super-enhancer-associated pluripotency genes. *Cell Rep*. 2014;9(1):234-247.

Dominianni C, Sinha R, Goedert JJ, Pei Z, Yang L, Hayes RB, Ahn J. Sex, body mass index, and dietary fiber intake influence the human gut microbiome. *PLoS One*. 2015;10(4):e0124599.

Doshi AM, Campbell N, Hajdu CH, Rosenkrantz AB. Differentiation of malignant omental caking from benign omental thickening using MRI. *Abdom Imaging*. 2015;40(5):1157-1163.

Grabocka E, Commisso C, Bar-Sagi D. Molecular pathways: targeting the dependence of mutant RAS cancers on the DNA damage response. *Clin Cancer Res*. 2015;21(6):1243-1247.

Grabocka E, Pylayeva-Gupta Y, Jones MJ, Lubkov V, Yemanaberhan E, Taylor L, Jeng HH, Bar-Sagi D. Wild-type H- and N-Ras promote mutant K-Ras-driven tumorigenesis by modulating the DNA damage response. *Cancer Cell*. 2014;25:243-256.

Grin B, Loeb S, Roehl K, Cooper PR, Catalona WJ, Helfand BT. A rare 8q24 single nucleotide polymorphism (SNP) predisposes North American men to prostate cancer and possibly more aggressive disease. *BJU Int*. 2015;115(1):101-105.

Gumaste PV, Fleming NH, Silva I, Shapiro RL, Berman RS, Zhong J, Osman I, Stein JA. Analysis of recurrence patterns in acral versus nonacral melanoma: should histologic subtype influence treatment guidelines? *J Natl Compr Canc Netw*. 2014;12(12):1706-1712.

Guo G, Chmielecki J, Goparaju C, Heguy A, Dolgalev I, Carbone M, Seepo S, Meyerson M, Pass HI. Whole-exome sequencing reveals frequent genetic alterations in BAP1, NF2, CDKN2A, and CUL1 in malignant pleural mesothelioma. *Cancer Res*. 2015;75(2):264-269.

Hanniford D, Segura MF, Zhong J, Philips E, Jirau-Serrano X, Darvishian F, Berman RS, Shapiro RL, Pavlick AC, Brown B, Osman I, Hernando E. Identification of metastasis-suppressive microRNAs in primary melanoma. *J Natl Cancer Inst*. 2015;107(3):dju494.

Hanniford D, Zhong J, Koetz L, Gaziel-Sovran A, Lackaye DJ, Shang S, Pavlick A, Shapiro R, Berman R, Darvishian F, Shao Y, Osman I, Hernando E. A miRNA-based signature detected in primary melanoma tissue predicts development of brain metastasis. *Clin Cancer Res*. 2015;21(21):4903-4912.

He F, Melamed J, Tang M, Huang C, Wu X. Oncogenic HRAS activates epithelial-to-mesenchymal transition and confers stemness to p53-deficient urothelial cells to drive muscle invasion of basal subtype carcinomas. Cancer *Res*. 2015;75(10):2017-2028.

Hochster HS, Uboha N, Messersmith W, Gold PJ, ONeil BH, Cohen D, Denlinger C, Cohen S, Leichman CG, Leichman L, Lenz HJ. Phase II study of selumetinib (AZD6244, ARRY-142886) plus irinotecan as second-line therapy in patients with K-RAS mutated colorectal cancer. *Cancer Chemother Pharmacol*. 2015;75(1):17-23.

Hsu L, Jeon J, Brenner H, Gruber SB, Schoen RE, Berndt SI, Chan AT, Chang-Claude J, Du M, Gong J, Harrison TA, Hayes RB, Hoffmeister M, Hutter CM, Lin Y, Nishihara R, Ogino S, Prentice RL, Schumacher FR, Seminara D, Slattery ML, Thomas DC, Thornquist M, Newcomb PA, Potter JD, Zheng Y, White E, Peters U. Colorectal transdisciplinary (CORECT) study; genetics and epidemiology of colorectal cancer consortium (GECCO). *Gastroenterology*.;148(7):1330-1339.e14.

Huang Z, Tan L, Wang H, Liu Y, Blais S, Deng J, Neubert TA, Gray NS, Li X, Mohammadi M. DFG-out mode of inhibition by an irreversible type-1 inhibitor capable of overcoming gate-keeper mutations in FGF receptors. *ACS Chem Biol*. 2015;10(1):299-309.

Jones CL, Gearheart CM, Fosmire S, Delgado-Martin C, Evensen NA, Bride K, Waanders AJ, Pais F, Wang J, Bhatla T, Bitterman DS, de Rijk SR, Bourgeois W, Dandekar S, Park E, Burleson TM, Madhusoodhan PP, Teachey DT, Raetz EA, Hermiston ML, Müschen M, Loh ML, Hunger SP, Zhang J, Garabedian MJ, Porter CC, Carroll WL. MAPK signaling cascades mediate distinct glucocorticoid resistance mechanisms in pediatric leukemia. *Blood*. 2015;126(19):2202-2212.

Kamphorst JJ, Nofal M, Commisso C, Hackett SR, Lu W, Grabocka E, Vander Heiden MG, Miller G, Drebin JA, Bar-Sagi D, Thompson CB, Rabinowitz JD. Human pancreatic cancer tumors are nutrient poor and tumor cells actively scavenge extracellular protein. *Cancer Res*. 2015;75(3):544-553.

Karajannis MA, Ferner RE. Neurofibromatosis-related tumors: emerging biology and therapies. *Curr Opin Pediatr*. 2015;27(1):26-33.

Kourtis N, Moubarak RS, Aranda-Orgilles B, Lui K, Aydin IT, Trimarchi T, Darvishian F, Salvaggio C, Zhong J, Bhatt K, Chen EI, Celebi JT, Lazaris C, Tsirigos A, Osman I, Hernando E, Aifantis I. FBXW7 modulates cellular stress response and metastatic potential through HSF1 post-translational modification. *Nat Cell Biol*. 2015;17(3):322-332.

Lee HW, Wang HT, Wang MW. Chin C, Huang, W, Lepor H, Wu XR, Rom WN, Chen LC, Tang MS. Cigarette side-stream smoke lung and bladder carcinogenesis: inducing mutagenic acrolein-DNA adducts, inhibiting DNA repair and enhancing anchorage-independent-growth cell transformation. *Oncotarget*. 2015;6(32):33226-33236.

Lepor H. Is targeted therapy of prostate cancer ready for prime time? *Eur Urol*. 2015;69(2):221-222.

Lepor H, Llukani E, Sperling D, Fütterer JJ. Complications, recovery, and early functional outcomes and oncologic control following in-bore focal laser ablation of prostate cancer. *Eur Urol*. 2015;68(6):924-926.

Mateos-Gomez PA, Gong F, Nair N, Miller KM, Lazzerini-Denchi E, Sfeir A. Mammalian polymerase θ promotes alternative NHEJ and suppresses recombination. *Nature*. 2015;518(7538):254-257.

McCullough LE, Eng SM, Bradshaw PT, Cleveland RJ, Steck SE, Terry MB, Shen J, Crew KD, Rossner P Jr, Ahn J, Ambrosone CB, Teitelbaum SL, Neugut A, Santella RM, Gammon MD. Genetic polymorphisms in DNA repair and oxidative stress pathways may modify the association between body size and postmenopausal breast cancer. *Ann Epidemiol*. 2015;25(4):263-269.

Mendhiratta N, Lee T, Prabhu V, Llukani E, Lepor H. 10-year mortality after radical prostatectomy for localized prostate cancer in the prostate-specific antigen screening era. *Urology*. 2015;86(4):783-789.

Mendhiratta N, Meng X, Rosenkrantz AB, Wysock JS, Fenstermaker M, Huang R, Deng FM, Melamed J, Zhou M, Huang WC, Lepor H, Taneja SS. Pre-biopsy MRI and MRI-ultrasound fusion-targeted prostate biopsy in men with previous negative biopsies: impact on repeat biopsy strategies. *Urology*. 2015;86(6):1192-1199.

Meng X, Rosenkrantz AB, Mendhiratta N, Fenstermaker M, Huang R, Wysock JS, Bjurlin MA, Marshall S, Deng FM, Zhou M, Melamed J, Huang WC, Lepor H, Taneja SS. Relationship between prebiopsy multiparametric magnetic resonance imaging (MRI), biopsy indication, and MRI-ultrasound fusion-targeted prostate biopsy outcomes. *Eur Urol*. 2015 Jun 22. [Epub ahead of print]

Mohamed HT, El-Shinawi M, Nouh MA, Bashtar AR, Elsayed ET, Schneider RJ, Mohamed MM. Inflammatory breast cancer: high incidence of detection of mixed human cytomegalovirus genotypes associated with disease pathogenesis. *Front Oncol*. 2014;4:246.

Mullenders J, Aranda-Orgilles B, Lhoumaud P, Keller M, Pae J, Wang K, Kayembe C, Rocha PP, Raviram R, Gong Y, Premsrirut PK, Tsirigos A, Bonneau R, Skok JA, Cimmino L, Hoehn D, Aifantis I. Cohesin loss alters adult hematopoietic stem cell homeostasis, leading to myeloproliferative neoplasms. *J Exp Med*. 2015;212(11):1833-1850.

Murphy N, Cross AJ, Huang WY, Rajabzadeh-Heshejin V, Stanczyk F, Hayes R, Gunter MJ. A prospective evaluation of C-peptide levels and colorectal adenoma incidence. *Cancer Epidemiol*. 2015;39(2):160-165.

Narendra V, Rocha PP, An D, Raviram R, Skok JA, Mazzoni EO, Reinberg D. CTCF establishes discrete functional chromatin domains at the Hox clusters during differentiation. *Science*. 2015;347(6225):1017-1021.

Nobel YR, Cox LM, Kirigin FF, Bokulich NA, Yamanishi S, Teitler I, Chung J, Sohn J, Barber CM, Goldfarb DS, Raju K, Abubucker S, Zhou Y, Ruiz VE, Li H, Mitreva M, Alekseyenko AV, Weinstock GM, Sodergren E, Blaser MJ. Metabolic and metagenomic outcomes from early-life pulsed antibiotic treatment. *Nat Commun*. 2015;6:7486.

Ntziachristos P, Tsirigos A, Welstead GG, Trimarchi T, Bakogianni S, Xu L, Loizou E, Holmfeldt L, Strikoudis A, King B, Mullenders J, Becksfort J, Nedjic J, Paietta E, Tallman MS, Rowe JM, Tonon G, Satoh T, Kruidenier L, Prinjha R, Akira S, Van Vlierberghe P, Ferrando AA, Jaenisch R, Mullighan CG, Aifantis I. Contrasting roles of histone 3 lysine 27 demethylases in acute lymphoblastic leukaemia. *Nature*. 2014;514(7523):513-517.

Pagan JK, Marzio A, Jones MJ, Saraf A, Jallepalli PV, Florens L, Washburn MP, Pagano M. Degradation of Cep68 and PCNT cleavage mediate Cep215 removal from the PCM to allow centriole separation, disengagement and licensing. *Nat Cell Bio*. 2015;17(1):31-43.

Perez-Andreu V, Roberts KG, Xu H, Smith C, Zhang H, Yang W, Harvey RC, Payne-Turner D, Devidas M, Cheng IM, Carroll WL, Heerema NA, Carroll AJ, Raetz EA, Gastier-Foster JM, Marcucci G1, Bloomfield CD, Mrózek K, Kohlschmidt J, Stock W, Kornblau SM, Konopleva M, Paietta E, Rowe JM, Luger SM, Tallman MS, Dean M, Burchard EG, Torgerson DG, Yue F, Wang Y, Pui CH, Jeha S, Relling MV, Evans WE, Gerhard DS, Loh ML, Willman CL, Hunger SP, Mullighan CG, Yang JJ. A genome-wide association study of susceptibility to acute lymphoblastic leukemia in adolescents and young adults. *Blood*. 2015;125(4):680-686.

Pitt LA, Tikhonova AN, Hu H, Trimarchi T, King B, Gong Y, Sanchez-Martin M, Tsirigos A, Littman DR, Ferrando AA, Morrison SJ, Fooksman DR, Aifantis I, Schwab SR. CXCL12-producing vascular endothelial niches control acute T cell leukemia maintenance. *Cancer Cell*. 2015;27(6):755-768.

Pusztai L, Moulder S, Altan M, Kwiatkowski D, Valero V, Ueno NT, Esteva FJ, Avritscher R, Qi Y, Strauss L, Hortobagyi GN, Hatzis C, Symmans WF. Gene signature-guided dasatinib therapy in metastatic breast cancer. *Clin Cancer Res*. 2014;20(20):5265-5271.

Rendleman J, Vogelsang M, Bapodra A, Adaniel C, Silva I, Moogk D, Martinez CN, Fleming N, Shields J, Shapiro R, Berman R, Pavlick A, Polsky D, Shao Y, Osman I, Krogsgaard M, Kirchhoff T. Genetic associations of the interleukin locus at 1q32.1 with clinical outcomes of cutaneous melanoma. *J Med Genet*. 2015;52(4):231-239.

Roberts KG, Li Y, Payne-Turner D, Harvey RC, Yang YL, Pei D, McCastlain K, Ding L, Lu C, Song G, Ma J, Becksfort J, Rusch M, Chen SC, Easton J, Cheng J, Boggs K, Santiago-Morales N, Iacobucci I, Fulton RS, Wen J, Valentine M, Cheng C, Paugh SW, Devidas M, Chen IM, Reshmi S, Smith A, Hedlund E, Gupta P, Nagahawatte P, Wu G, Chen X, Yergeau D, Vadodaria B, Mulder H, Winick NJ, Larsen EC, Carroll WL, Heerema NA, Carroll AJ, Grayson G, Tasian SK, Moore AS, Keller F, Frei-Jones M, Whitlock JA, Raetz EA, White DL, Hughes TP, Guidry Auvil JM, Smith MA, Marcucci G, Bloomfield CD, Mrózek K, Kohlschmidt J, Stock W, Kornblau SM, Konopleva M, Paietta E, Pui CH, Jeha S, Relling MV, Evans WE, Gerhard DS, Gastier-Foster JM, Mardis E, Wilson RK, Loh ML, Downing JR, Hunger SP, Willman CL, Zhang J, Mullighan CG. Targetable kinase-activating lesions in Ph-like acute lymphoblastic leukemia. *N Engl J Med*. 2014;371(11):1005-1015.

Rosenkrantz AB, Balar AV, Huang WC, Jackson K, Friedman KP. Comparison of coregistration accuracy of pelvic structures between sequential and simultaneous imaging during hybrid PET/MRI in patients with bladder cancer. *Clin Nucl Med*. 2015;40(8):637-641.

Rosenkrantz AB, Ream JM, Nolan P, Rusinek H, Deng FM, Taneja SS. Prostate cancer: utility of whole-lesion apparent diffusion coefficient metrics for prediction of biochemical recurrence after radical prostatectomy. *AJR Am J Roentgenol*. 2015;205(6):1208-1214.

Singh B, Smith JA, Axelrod DM, Ameri P, Levitt H, Danoff A, Lesser M, de Angelis C, Illa-Bochaca I, Lubitz S, Huberman D, Darvishian F, Kleinberg DL. Insulin-like growth factor-I inhibition with pasireotide decreases cell proliferation and increases apoptosis in pre-malignant lesions of the breast: a phase 1 proof of principle trial. *Breast Cancer Res*. 2014;16(6):463.

Tan L, Wang J, Tanizaki J, Huang Z, Aref AR, Rusan M, Zhu SJ, Zhang Y, Ercan D, Liao RG, Capelletti M, Zhou W, Hur W, Kim N, Sim T, Gaudet S, Barbie DA, Yeh JR, Yun CH, Hammerman PS, Mohammadi M, Jänne PA, Gray NS. Development of covalent inhibitors that can overcome resistance to first-generation FGFR kinase inhibitors. *Proc Natl Acad Sci U S A*. 2014;111(45):E4869-E4877.

Tsai FD, Lopes MS, Zhou M, Court H, Ponce O, Fiordalisi JJ, Gierut JJ, Cox AD, Haigis KM, Philips MR. K-Ras4A splice variant is widely expressed in cancer and uses a hybrid membrane-targeting motif. *Proc Natl Acad Sci U S A*. 2015;112(3):779-784.

Van Batavia J, Yamany T, Molotkov A, Dan H, Mansukhani M, Batourina E, Schneider K, Oyon D, Dunlop M, Wu XR, Cordon-Cardo C, Mendelsohn C. Bladder cancers arise from distinct urothelial sub-populations. Nat Cell *Biol*. 2014;16(10):982-991.

Zhang D, Wang Y, Liang Y, Zhang M, Wei J, Zheng X, Li F, Meng Y, Zhu NW, Li J, Wu XR, Huang C. Loss of p27 upregulates MnSOD in a STAT3-dependent manner, disrupts intracellular redox activity and enhances cell migration. *J Cell Sci*. 2014;127(Pt 13):2920-2933.

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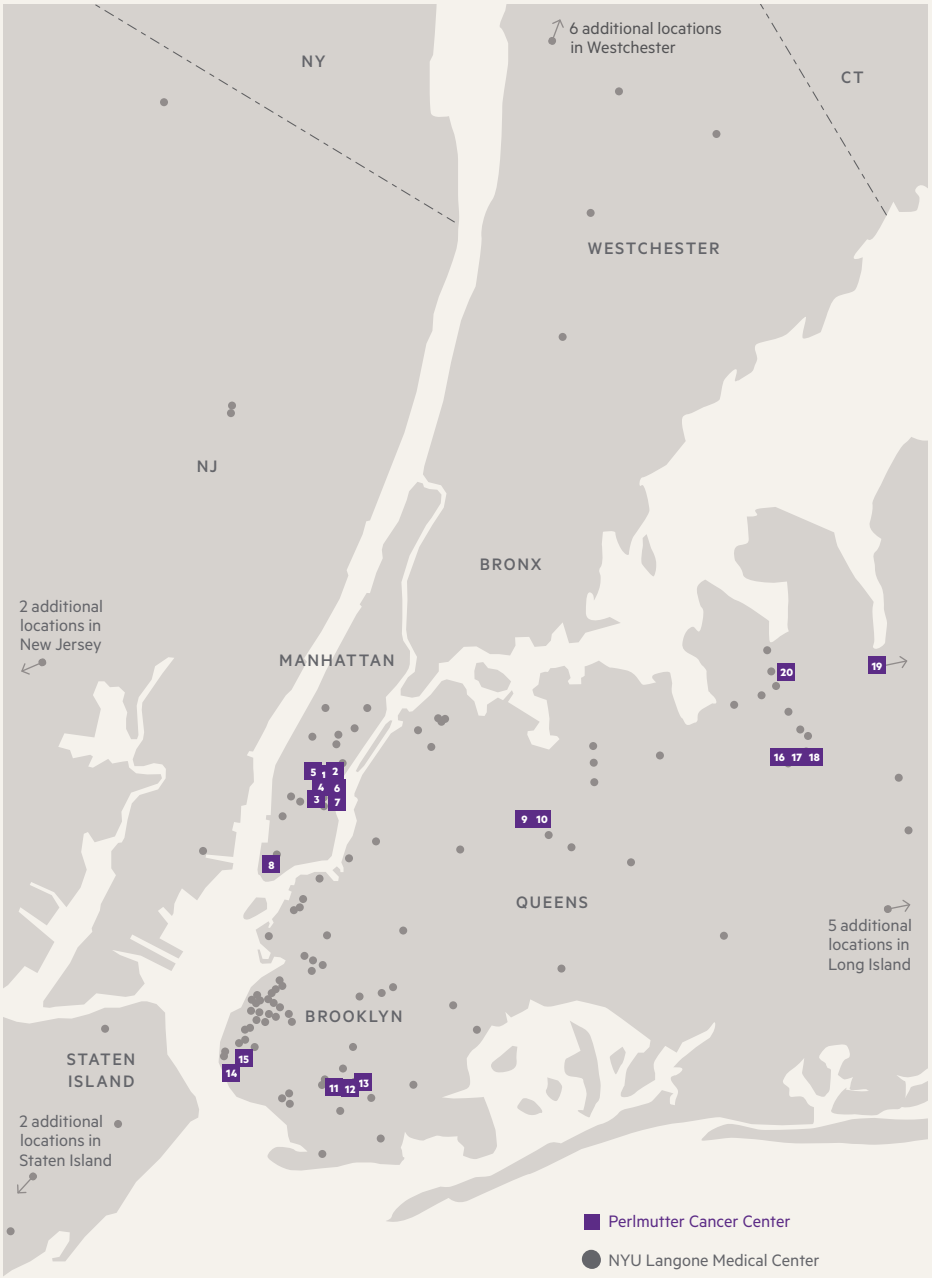

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38,554
Patient Discharges

1,216,428
Hospital-Based Outpatient Visits

5,766
Births

2,900,000
Faculty Group Practice
Office Visits

1,469
Full-Time Faculty

1,392
Part-Time Faculty

2,627
Voluntary Faculty

128
Endowed Professorships

2,740
Physicians

3,465
Registered and Advanced
Practice Nurses

730
Allied Health Professionals

611
MD Candidates

79
MD/PhD Candidates

272
PhD Candidates

400
Postdoctoral Fellows

1,063
Residents and Fellows

3,800
Publications

550,000
Square Feet of Research Space

$178,000,000
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$295,000,000
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