

ADVANCES IN ONCOLOGY

Prestigious SPORE Grant to Advance Prostate Cancer Care

Weill Cornell Medicine has been awarded a five-year, \$11.3 million Specialized Programs of Research Excellence (SPORE) grant from the National Cancer Institute to improve the detection and treatment of aggressive prostate cancer (PCa). Established in 1992, SPORE grants serve as the cornerstone of the NCI's efforts to promote collaborative, interdisciplinary translational cancer research.

This SPORE grant – the first ever awarded to Weill Cornell Medicine – will expand an already vibrant basic and translational research program in

prostate cancer at Weill Cornell Medicine's Sandra and Edward Meyer Cancer Center and Caryl and Israel Englander Institute for Precision Medicine. In addition, the grant provides yearly funding to support new high-risk and high-reward studies led by Weill Cornell Medicine researchers, as well as a career enhancement program for junior investigators who seek to enter into the field of prostate cancer research.

Himisha Beltran, MD, Director of Clinical Activities at the Englander Institute for Precision Medicine, serves as a co-leader of this important research endeavor.

"The SPORE grant will facilitate collaboration and accelerate the translation of scientific discoveries into the clinic," says Dr. Beltran, who is also an oncologist at NewYork-Presbyterian/Weill Cornell Medical Center.

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The five-year, \$11.3 million SPORE grant will further advance investigations that span basic, clinical, and translational research in prostate cancer.

Renowned Surgeon Leads Columbia Breast Surgery Program



Dr. Roshni Rao

NCI-designated Herbert Irving Comprehensive Cancer Center at Columbia. Dr. Rao previously served as Director of the George N. Peters Center for Breast Surgery at the University of Texas Southwestern Medical Center in Dallas, Texas. She completed her Breast Surgery Fellowship training at the University of Texas MD Anderson Cancer Center.

A skilled surgeon and renowned researcher in locally advanced and metastatic breast cancer, Dr. Rao provides expertise in early stage breast cancer, innovative localization techniques, and tumescent mastectomy. In addition, she has a particular interest in ethnic disparities in breast cancer and patient engagement with healthcare technology.

A Novel Approach to Nipple-Sparing Mastectomy

Dr. Rao recently pioneered a novel approach to nipple-sparing mastectomy for select patients who were not previously appropriate candidates for this surgery. In a refinement of the standard nipple-sparing mastectomy, Dr. Rao is employing a minimally invasive endoscopic video-assisted approach to the procedure.

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In October 2017, Roshni Rao, MD, joined NewYork-Presbyterian/Columbia University Medical Center, as Chief of Breast Surgery in the Comprehensive Breast Center. In her new role, Dr. Rao collaborates closely with the Breast Center's team of specialists across every discipline, including radiology, medical oncology, radiation oncology, and plastic surgery. The Comprehensive Breast Center is part of the

Prestigious SPORE Grant to Advance Prostate Cancer Research *(continued from page 1)*



Dr. Himisha Beltran

“The grant provides the opportunity to build on a program that we’ve been very proud of for many years, and to continue to develop an infrastructure that promotes investigations that span basic science, clinical, and translational research,” says Dr. Beltran.

The Weill Cornell Medicine SPORE grant has four major objectives:

- Develop accurate biomarkers to assess the risk of PCa disease progression
- Develop new therapeutic approaches for clinically localized and castrate-resistant prostate cancer that are hypothesis-driven, based

on newly acquired knowledge of PCa biology and genomics, and represent a paradigm shift in treatment

- Leverage existing and expand new infrastructure for the successful translation of pre-clinical studies into the clinic
- Train the next generation of PCa investigators

A basic scientist and translational clinical investigator will lead each of the following projects:

- Non-Invasive Clinical Assay for Early Detection of Treatment Resistance in Patients with Metastatic Prostate Cancer
- Targeting N-Myc and EZH2-Driven Castrate-Resistant Prostate Cancer
- Toward Understanding Prostate Cancer Heterogeneity
- Targeting Genomic Instability in Distinct Subclasses of Prostate Cancer

“This is an amazing accomplishment and a major milestone for Weill Cornell Medicine,” says **Lewis C. Cantley, PhD**, Meyer Director of the Sandra and Edward Meyer Cancer Center. “It will provide dedicated support for prostate cancer research that can be leveraged to help develop other types of program projects and grants. We believe this will yield some of the best research at our institution, inspiring our top investigators to consider how their science might be applied to address the challenges of understanding prostate cancer.”

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NewYork-Presbyterian Establishes the William Rhodes and Louise Tilzer-Rhodes Center for Glioblastoma

NewYork-Presbyterian has established the William Rhodes and Louise Tilzer-Rhodes Center for Glioblastoma led by renowned experts in neuro-oncology from Columbia University Medical Center and Weill Cornell Medicine. The Center is focused on pursuing groundbreaking research and providing advanced treatments for glioblastoma and other deadly brain cancers. Made possible by a major gift from Mr. Rhodes, a Life Trustee of NewYork-Presbyterian since 1992, the program was created to honor Louise Tilzer-Rhodes, who passed away from glioblastoma in 2016.

“Thanks to the generosity of Mr. Rhodes, we have an opportunity to make tremendous strides in our understanding and treatment of glioblastomas,” says Steven J. Corwin, MD, President and CEO of NewYork-Presbyterian. “NewYork-Presbyterian is committed to becoming the world’s leader in the fight against this deadly disease.”

“Glioblastoma has had a profound impact on my family and countless others,” says Mr. Rhodes. “It’s so important that we bring together and empower the brightest minds to bring new therapies – and one day, a cure – to patients.”

The William Rhodes and Louise Tilzer-Rhodes Center for Glioblastoma at NewYork-Presbyterian aims to advance care for glioblastoma and other brain cancers via a three-pronged approach: providing multidisciplinary, research-driven patient care, with a focus on genomic and precision medicine; emphasizing translational research

to rapidly bring promising new therapies from the bench to the bedside; and educating the next generation of clinicians and scientists with new fellowships created to expose young physicians to the most cutting-edge work being done in the field.

William Rhodes and Louise Tilzer-Rhodes Center for Glioblastoma – Leadership

Jeffrey N. Bruce, MD

Co-Director, Brain Tumor Center
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Chief, Division of Neuro-Oncology
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Howard A. Fine, MD

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Renowned Surgeon Leads Columbia Breast Surgery Program *(continued from page 1)*

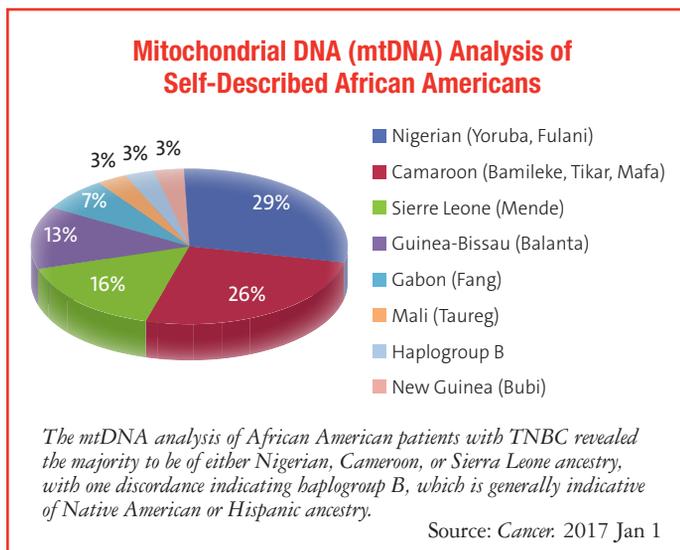
“When performing a mastectomy, we have to know the anatomic borders going up to the clavicle, and then to the latissimus muscle, and then to the lateral border of the sternum,” says Dr. Rao. “Covering that amount of area through such a small incision is technically more challenging. Using cameras that have traditionally been used for laparoscopic surgery allow us to better visualize the planes between the breast and the muscle and between the breast and the skin”. The visualization with the video-endoscopic approach allows us to push the envelope, if you will, and still be able to do the operation that’s oncologically correct. We are able to remove 99 percent of the tissue to preserve the cosmesis and still be able to see what we need to see. It is obviously much safer for the patient and offers a less noticeable scar with excellent cosmetic outcomes.”

Understanding Unusual Disparities in the Development of TNBC

Triple-negative breast cancer (TNBC) is aggressive and therapeutically challenging, and is more likely to be seen in African American and Hispanic populations, as well as in women who are BRCA1 gene carriers. Dr. Rao wants to know why. To that end, she has been exploring genetic ancestry testing through mitochondrial DNA (mtDNA), which is distinct from nuclear DNA as it is maternally inherited and allows for origin determination. Dr. Rao conducted one of the first studies of self-described African American, White, and Hispanic patients with TNBC to identify mtDNA patterns, the findings of which were published in the January 2017 issue of *Cancer*.

“The results were very interesting,” says Dr. Rao. “We found a 27 percent rate in the Hispanic group of what I call discordance, where patients thought they were of one ethnicity, but their mitochondrial DNA actually demonstrated something different, and 13 percent discordance in the entire group. Many of the Hispanic patients had African American ancestry that they weren’t aware of and, in fact, some of them had Ashkenazi Jewish ancestry.”

Dr. Rao concluded that the identification of mtDNA patterns with a predisposition toward TNBC may allow for risk stratification and that further studies that identify the impact of variation in mtDNA and its association with TNBC would assist in personalizing risk assessment, allowing for the potential development of ethnically tailored therapeutic interventions.



“Obviously, individuals have different side effects from different types of chemotherapies,” continues Dr. Rao, “but part of the focus of this research also seeks to predict who is going to do better with chemotherapy versus a different agent. Research supports the fact that if you use a taxane-based agent, which is a very specific, very commonly used type of chemotherapy in breast cancer, it is more likely that African American patients will get neuropathy. So, if you have someone who has African American ancestry that they may not know about, then perhaps we need to change the agents that we’re using to minimize their long-term side effects.”

A Role for Exercise in Treatment

In another investigation, Dr. Rao is exploring the role of exercise during chemotherapy. Patients undergoing neoadjuvant chemotherapy are traditionally directed to rest during treatment. Dr. Rao has hypothesized that since breast cancer is linked to obesity, perhaps losing weight and exercising might have a positive impact on tumor biology.

“People always ask me why rates of breast cancer are going up. One reason is the obesity epidemic,” says Dr. Rao. “When I was working in Texas, before joining NewYork-Presbyterian, I wanted to get in better shape, so I signed up for an hour-long ‘boot camp’ class three times a week,” says Dr. Rao. “After a month, I felt great, and I ended up collaborating with a personal trainer to set up a study to see if exercise could make a difference in overweight breast cancer patients who were undergoing chemotherapy.”

In a pilot study of 10 patients with stage 2-3 breast cancer, estrogen and progesterone receptor positive, with a BMI >25, five patients were randomized to standard neoadjuvant chemotherapy plus a supervised intensive exercise regimen and five received chemotherapy alone.

“In the exercise group, we had patients work with a trainer three times a week, then compared them with the second group, which received chemotherapy but didn’t exercise,” says Dr. Rao. “The patients who worked out not only lost weight, their tumors shrunk more quickly and were less aggressive. I want to take this research to the next level here at the Herbert Irving Comprehensive Cancer Center by seeing how exercise might help breast cancer patients get through chemotherapy more easily, with less nausea and fatigue.”

As a breast surgeon, Dr. Rao likens her role as the quarterback of the patient’s healthcare team. “Patients see me as the starting point of their treatment, as well as their advocate,” she says. “Cancer treatment can be harsh; chemotherapy can affect the health of a patient’s heart down the line, as well as her long-term survivorship. At the Herbert Irving Comprehensive Cancer Center, the focus is on total patient care, which is why I’m so honored and excited to be at Columbia. Women going through breast cancer are very motivated to get better, and I plan on continuing to build upon the tradition here of helping them survive and to thrive.”

Reference Article

Rao R, Rivers A, Rahimi A, Wooldridge R, Rao M, Leitch M, Euhus D, Haley BB. Genetic ancestry using mitochondrial DNA in patients with triple-negative breast cancer (GAMiT Study). *Cancer*. 2017 Jan 1; 123(1):107-13.

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Comprehensive Programs Address Brain and CNS Metastases

Central Nervous System Metastases Clinic

Andrew B. Lassman, MD, is Chief, Division of Neuro-Oncology and Co-Director of the Brain Tumor Center at NewYork-Presbyterian/Columbia. Guy M. McKhann II, MD, is Director of Awake Brain Mapping for Tumors and Epilepsy in Columbia's Department of Neurological Surgery. Catherine A. Shu, MD, is a medical oncologist who specializes in lung and thoracic cancers.

These physicians are key members in the Central Nervous System Metastases Clinic (CNSMets), recently established to coordinate and advance the treatment of brain, leptomeningeal, skull base, spinal cord, and spine metastases. Under the auspices of Columbia's Division of Neuro-Oncology, CNSMets grew out of the need to organize and focus the complex array of specialist expertise – neurosurgery, neurology, radiation oncology, medical oncology, palliative care, social work, neuro-radiology, neuropathology, molecular pathology, and complementary and alternative medicine among others – to address the many and varied challenges that can accompany brain metastases.

“Patients who have central nervous system – brain or leptomeningeal – metastases often need to see several different specialists on different days in different locations,” says Dr. Lassman. “Many of our patients are frequently dealing with physical disabilities and concurrent cognitive limitations making it difficult to navigate the numerous and varied appointments. Our program makes it logistically easier for patients to obtain care, including rapid access to appointments.”

The CNSMets Clinic utilizes a multidisciplinary and multi-tumor site approach that allows for high level discussion of unique cases and rapid planning of individualized, cutting-edge therapy for each patient.

“I think the key factor in this day and age is finding ways to optimize communication among physicians and with the patient,” says Dr. McKhann. “It is so important for patients with metastatic brain disease to have coordinated, multidisciplinary care where teams of experts are reviewing not just what's going on in the brain, but what is happening in the body as a whole. Then you can integrate their treatment in the best possible way.”

The CNSMets Clinic takes place every Wednesday afternoon. Patients are first seen by a neuro-oncologist. Cases are then discussed at a multidisciplinary tumor board specifically for brain and spine metastases led by neuro-oncologist Teri N. Kreisl, MD. Dr. Kreisl and representatives from relevant specialties develop a consensus of opinion for a comprehensive treatment plan. Depending on the plan of care, patients may then meet with consultative specialists that same afternoon.

Among the immediate benefits of the tumor board, Dr. Lassman cites the team's extensive knowledge of Columbia's many ongoing trials to identify the one that is most appropriate for an individual patient. “This approach, where we are co-located together, can yield



Dr. Andrew B. Lassman



Dr. Guy M. McKhann II



Dr. Catherine A. Shu

additional therapeutic options for the patient,” says Dr. Lassman. “Our goal is to apply new treatments that may lengthen life or improve quality of life. Sometimes that involves using standard technology in a new way. Through the tumor board, clinical trials and other research efforts that, without the tumor board mechanism, may not otherwise have been brought to light, are able to be shared and determined for their appropriateness for the patient.”

For Dr. McKhann and his surgical colleagues, the tumor board optimizes the process of coming to key surgical decisions. “The coordination of therapies with sensitivity in timing helps in the decision-making regarding employing open surgery, the Gamma Knife, often a combination of both, or no surgery at all,” notes Dr. McKhann. “For example, when timed with Gamma Knife procedures, the efficacy of some chemotherapy protocols is enhanced by increasing the permeability of the blood-brain barrier. Sometimes immunotherapy has proven more effective than chemotherapy and can be a factor in delaying or avoiding surgery. It's also how symptomatic the patient is. If they're particularly symptomatic, it will push them more towards surgery and away from the Gamma Knife. However, if it's a single seizure and the patient is otherwise asymptomatic, and we already know this is clearly metastatic disease, then the Gamma Knife is going to make sense.”

“The CNSMets Clinic is a very unique, patient-focused experience that involves all specialties who participate in our tumor board,” says Dr. Shu. “Oftentimes the patient is on site and one or several of us may speak to the patient following our meeting. It makes good sense from the patient's perspective having information right away from multiple sources. Instead of the patient going to four different clinics, we have four different specialties come directly to the patient. It is a very successful collaboration.”

“Even if I'm not treating the brain, it's important for me to know what's going on,” adds Dr. Shu. “For example, do I have to hold their chemotherapy? Are they going to be taken off any systemic steroids? The tumor board helps the medical oncologists stay in the loop about the patient's brain disease and treatment updates that affect our role.”

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Comprehensive Programs Address Brain and CNS Metastases *(continued from page 4)*

Brain Metastases Clinic

“Today, therapeutic advances are making it possible for patients with cancer to live longer and with better quality of life,” says **David M. Nanus, MD**, Chief of the Division of Hematology and Medical Oncology at NewYork-Presbyterian/Weill Cornell. “At the same time, however, higher survival rates have also been accompanied by a higher incidence of cancer spreading to the brain. Cancer cells are basically smart. Their goal is to grow, so they’ll find a new environment in which to grow. The brain acts like a sanctuary site for many treatments.”

“The Brain Metastases Clinic at the Weill Cornell Brain and Spine Center is a much-needed program for these patients,” adds Dr. Nanus. “They are provided with access to comprehensive care that promotes their physical and psychological well-being, while addressing the myriad clinical issues, including the toxic side effects of therapy, that accompany this diagnosis.”

The Brain Metastases Clinic provides comprehensive care to patients diagnosed with metastatic brain tumors and leptomeningeal disease. “A brain metastasis is a critical point in a patient’s cancer care,” says neurosurgeon **Rohan Ramakrishna, MD**, Director of the Brain Metastases Clinic. “I’ve seen the consequences of brain metastases on patients. It’s not the immediate aftermath; it’s what happens months and years following treatment and the problems they can encounter. The consequences of combinations of those therapies often are not managed in a proactive way. For example, patients can suffer chronic pain issues, depression, dementia, neurocognitive and rehabilitation issues, and spiritual concerns related to their own mortality.”

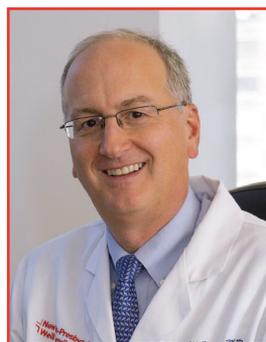
“Our multidisciplinary group includes not only neurosurgery, radiation oncology and medical oncology, but also psycho-oncology, a burgeoning field in this area, as well as palliative care,” continues Dr. Ramakrishna. “We have also incorporated an integrated health program that offers acupuncture, yoga, mindfulness, and meditation. We believe that integrative therapies that address the whole patient should be as important as any of the traditional therapies offered to control the patient’s brain cancer.”

Navigating a large healthcare system is particularly difficult for a patient with brain cancer. “Figuring out which doctor to go to and which appointments to schedule can be overwhelming,” says Dr. Ramakrishna. To that end, the program offers a program coordinator who answers 646-NYP-METS. “The goal is to spare the patient from having to call so many different physicians. The navigator will determine the patient’s availability and then put together a day of scheduled appointments. It’s concierge medicine that caters to the patient’s needs.”

Research is another component of the program. “Our goal is to study the impact of a comprehensive program like this on the well-being of our patients,” says Dr. Ramakrishna. “We do quality-of-life questionnaires with patients, each of whom is unique with different cancers and different systemic disease. We also plan to study how we can make radiation therapy less toxic on the brain. Neurocognitive decline happens after radiation, but it also happens in patients who have brain mets, period. Learning how to minimize the complications of neurocognitive decline, as a result of not only the disease, but also the therapy, is integral to our research strategy.”



Dr. Rajiv S. Magge



Dr. David M. Nanus



Dr. Rohan Ramakrishna

Neuro-oncologist **Rajiv S. Magge, MD**, believes that the depth of expertise at the Brain Metastases Clinic allows physicians to tackle it from several directions. “Unfortunately, the brain is a place where metastases can potentially be shielded from systemic treatment,” says Dr. Magge. “We’re trying to focus on better treatments that may target metastases in the brain. Newer systemic treatments may get past the blood-brain barrier. These include immunotherapy, which has shown efficacy in treating brain metastases from specific cancers, especially lung cancer and melanoma.”

“With the advent of 3-D cross-sectional imaging and a better understanding of the natural history of cancer, we can focus our treatments more on the tumor deposits themselves,” says **Jonathan P.S. Knisely, MD**, Medical Director of Stich Radiation Oncology at NewYork-Presbyterian/Weill Cornell, Director of Neuro-Oncology in the Department of Radiation Oncology, and Associate Director of the Brain Tumor Center. “This enables us to minimize the dose of radiation delivered to normal tissue, while greatly increasing the dose of radiation to the tumor deposits.”

“With an MRI scan we can see precisely where a spot or spots are within the brain,” continues Dr. Knisely. “This allows us to map out exactly where the tumor is and where any normal tissues are that you don’t want to have irradiated. We can then treat that very small volume with very high doses of radiation that will often achieve a 95 percent control rate at one year’s time.”

“Managing disease that spreads to the brain is an area of study that is needed more and more today,” says Dr. Nanus. “It used to be that if you wanted to get a new drug for metastatic cancer, nothing was available in clinical trials. Now we have a number of trials where there is a cohort specifically for patients with brain metastases.”

Drawing on his neuro-oncology and neurology background, Dr. Magge says, “I would like to be considered a resource – especially for the medical oncologist – to help manage and follow patients with brain metastases. We work with oncologists in coordinating management and helping decide which treatments – systemic therapy, surgery, and/or radiation – may be most effective.”

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