

Mount Sinai Receives National Designation

The Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai has been named a National Cancer Institute (NCI)-designated Cancer Center, an honor reserved for an elite group of U.S. institutions committed to the research and treatment of cancer.

In conjunction with the NCI designation, The Tisch Cancer Institute received a five-year, \$11.2 million grant to support research and the recruitment of top physicians and scientists. More than 50 of the nation's leading cancer researchers have joined The Tisch Cancer Institute since it was established in 2008.

Sixty-nine cancer institutions in 35 states and the District of Columbia carry the NCI designation. To qualify, Mount Sinai met stringent requirements and demonstrated its strength in laboratory and clinical research, and population science.

In granting the designation, the NCI cited The Tisch Cancer Institute's focus on at-risk populations in East and Central Harlem that have a high incidence of aggressive prostate and breast cancers; its comprehensive liver cancer program; strong immunotherapy program; long-term expertise in environmental health; its World Trade Center First Responders Program; and Mount Sinai's commitment to reducing health disparities among underserved cancer patients.

Mount Sinai's cancer research teams have earned grants



Leaders at The Tisch Cancer Institute include, from left: Randall Holcombe, MD, Deputy Director; Steven J. Burakoff, MD, Director; and William Oh, MD, Associate Director, Clinical and Translational Research.

totaling \$79 million. Renowned physicians and scientists in cancer immunology, cancer cell signaling, cancer genomics and bioinformatics, cancer epidemiology, and cancer pathology are making new discoveries. Their collaborations across the Mount Sinai Health System have led to promising clinical trials.

New Discoveries in Cancer Immunotherapy



Jeremy Price, PhD, a lead author on the study in *Nature Immunology*.

Researchers at The Tisch Cancer Institute have uncovered an intriguing mechanism that may help explain why radiation therapy eradicates cancerous tumors in some patients but not in others.

Their study, reported in the September 7, 2015, issue of *Nature Immunology*, examined how special skin immune cells, known as Langerhans cells, perform in mice models of melanoma.

They found that when skin that harbors tumors is damaged by ionizing radiation, Langerhans cells begin to repair their affected DNA, making them resistant to radiotherapy. Langerhans cells also travel to nearby lymph nodes where they communicate with other immune cells and activate a population of regulatory T cells.

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Expert in Multiple Myeloma Joins Mount Sinai

Bart Barlogie, MD, PhD, a world-renowned physician who introduced the first curative therapy for multiple myeloma, a multidrug regimen known as Total Therapy, recently joined The Tisch Cancer Institute as Director of Research in the Multiple Myeloma Program.

Dr. Barlogie will work with the program's leader, Sundar Jagannath, MD, Professor of Medicine (Hematology and Medical Oncology), to develop new therapies to treat the disease, which is characterized by cancerous plasma cells that form in the bone marrow and crowd out normal, blood-forming cells. Their collaboration helps make Mount Sinai the nation's premier myeloma program. About 26,850 new cases of the disease occur in the United States each year, according to the American Cancer Society.

"I'm dedicating my efforts toward the improvement of patients with high-risk myeloma in whom we have made only negligible progress, as opposed to the 85 percent of patients presenting with genomically defined low-risk disease where we have a cure expectation of about 50 percent," says Dr. Barlogie, who served for 26 years as Director of the Myeloma Institute at the University of Arkansas for Medical Sciences, an institute he founded.

By collaborating with Dr. Jagannath, he says, "We have a unique opportunity to move the field forward with our understanding of the underlying mechanisms that cause cells to become malignant."

The physicians will work with colleagues in the Department of Genetics and Genomic Sciences and Department of Immunology to identify suitable drugs that target gene mutations found in bone marrow samples taken from patients. Mount Sinai offers a unique opportunity to advance the team's knowledge due to the depth and breadth of its basic science research, says Dr. Barlogie.

Dr. Barlogie's scientific career has focused on biological and therapeutic research, including chemotherapy, immunotherapy, and hematopoietic stem cell transplantation. He developed the first effective salvage regimen (VAD) for melphalan-prednisone refractory myeloma, introduced autologous transplantation for myeloma, and identified thalidomide as a first-in-class novel agent for the treatment



Bart Barlogie, MD, PhD

of myeloma. Together with John Shaughnessy, PhD, who also recently joined the Mount Sinai Health System, Dr. Barlogie developed gene expression profiling to identify molecular subclasses of myeloma and established a highly predictive risk model.

A Fellow of the American College of Physicians, Dr. Barlogie has served on the Board of Directors of the International Myeloma

Foundation. He has received numerous honors, including the prestigious Jan Waldenstrom Award, the Celgene Career Achievement Award in Hematology Research, and the Robert A. Kyle Lifetime Achievement Award from the International Myeloma Foundation. He was also honored in 2006 with the National Physician of the Year Award by Castle Connolly Medical Ltd.

His published work includes more than 600 peer-reviewed journal articles, including five in *The New England Journal of Medicine*, and 75 book chapters. Dr. Barlogie has served on the editorial boards of *Blood*, *Clinical Cancer Research*, and *Clinical Lymphoma, Myeloma & Leukemia*.

Optimizing Transplant Outcomes for Myelofibrosis

A reduced-intensity conditioning hematopoietic stem cell transplant (HSCT) that was successfully performed on Fran Stahl at The Tisch Cancer Institute in January 2014, ultimately gave Ms. Stahl back her life.

Today, Ms. Stahl, 67, has returned full-time to the job she loves, offering advice on housing to the disadvantaged. No longer out of breath, she enjoys taking walks with her husband, Michael, and her cocker spaniel, Nate. She receives regular follow-up treatments for myelofibrosis at The Mount Sinai Hospital, including immunosuppressive therapy for a mild case of graft vs. host disease.

The life-threatening events and a long recovery that followed her stem cell transplant—when Ms. Stahl was admitted to Mount Sinai's Intensive Care Unit with progressive



Fran Stahl underwent a successful stem cell transplant at Mount Sinai.

pneumonia—now belong to the past. At that time, Ms. Stahl fell into an eight-day coma, experienced multiorgan dysfunction, was placed on a respirator, and transferred to hospice care. Miraculously, after two days, she began to breathe on her own.

"It's really a testament to Mount Sinai's strength, that we achieved this level of comprehensive care and expertise for a very complicated patient," says John Mascarenhas, MD, Associate Professor of Medicine (Hematology and Medical Oncology), who was involved in her care. Over the past seven years, physicians at The Tisch Cancer Institute at the Mount Sinai Health System have performed these transplants in more than 50

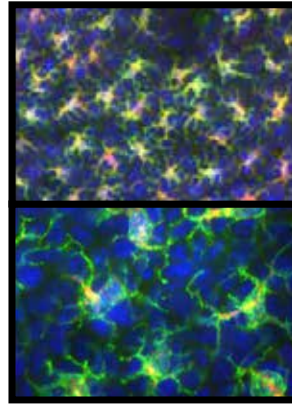
patients with advanced myelofibrosis, a rare disease, which affects an estimated one to two people per 100,000 annually.

➤ **New Discoveries in Cancer Immunotherapy** *continued from page 1*

“Now that we better understand the mechanisms of how Langerhans cells impact the immune system, we can work clinically to deplete this cell population,” says lead author Jeremy Price, PhD, who is in his final year of medical school at the Icahn School of Medicine at Mount Sinai. “We’re helping to inform a very active field of research that’s developing around how to make treatments involving radiation and immunotherapy even more effective.”



Miriam Merad, MD, PhD, is leading research into Langerhans cells.



Langerhans cells in green, as they appear in the skin of mice.

Indeed, the identification of immune checkpoint inhibitors that enable the body to unleash a powerful anticancer response without being restrained by the cancerous tumors is the most significant advance in cancer treatment in almost 40 years.

Miriam Merad, MD, PhD, Director of the Human Immune Monitoring Core at The Tisch Cancer Institute, and the study’s senior author, says the discovery of immune checkpoint inhibitors has given new impetus to her team’s work with Langerhans cells, which she initiated in 2002 as a postdoctoral student at Stanford University. Dr. Merad says that Mount Sinai’s study

on melanoma can apply to other organs and types of cancer throughout the body where cousins of Langerhans cells, known as dendritic cells, are also activated by radiotherapy.

Advances in cancer immunotherapy also are being led by Nina Bhardwaj, MD, PhD, Director of Immunotherapy, and Professor of Medicine (Hematology and Medical Oncology), at The Tisch Cancer Institute. Recently, a team led by Dr. Bhardwaj and Assistant Professor Benjamin Greenbaum, PhD, discovered a group of noncoding RNA molecules in cancer cells that sets off an immune response because they appear to have features similar to those of pathogens.

These RNA molecules—found in the part of the genome known as satellite DNA—do not produce proteins but can have important regulatory roles.

In clinical studies, Dr. Bhardwaj and her team are exploring multiple approaches to immunotherapy, from intratumoral injections to the development of personalized vaccines used in combination with traditional treatments such as surgery, radiation, and chemotherapy.

The Tisch Cancer Institute, working in collaboration with researchers led by Eric E. Schadt, PhD, Director of the Icahn Institute for Genomics and Multiscale Biology, Chair of the Department of Genetics and Genomic Sciences, and the Jean C. and James W. Crystal Professor of Genomics, is one of a handful of U.S. medical institutions currently pursuing personalized vaccines.

“Combining different immunotherapy strategies is an exciting new area of clinical research,” says Dr. Bhardwaj.

In a unique proof-of-concept study that will begin trials this year, Dr. Bhardwaj’s team will explore the feasibility of developing personalized vaccines for patients with multiple solid tumors.

The Myeloproliferative Disorders Program (MPD) in the Mount Sinai Health System is headed by Ronald Hoffman, MD, the Albert A. and Vera G. List Professor of Medicine (Hematology), and includes Dr. Mascarenhas; Alla Keyzner, MD, Assistant Professor of Medicine (Hematology and Medical Oncology); and Marina Kremyanskaya, MD, Assistant Professor of Medicine (Hematology and Medical Oncology).

Dr. Mascarenhas and Ronald Hoffman, MD, have focused their translational work on eliminating malignant stem cells through novel therapies and innovative transplant approaches. Dr. Hoffman leads the international Myeloproliferative Disorders Research Consortium (MPD-RC), which is funded by the National Cancer Institute and includes more than 40 member institutions from around the world.

“We have shown the curative potential of reduced-intensity conditioning (HSCT) in optimizing transplant outcomes in patients with this disease,” says Dr. Mascarenhas. “Fran is an example of our consortium’s contribution of the role of bone marrow transplant in myelofibrosis and highlights the multidisciplinary

expertise of Mount Sinai in caring for these special patients.”

“My experience at Mount Sinai was just incredible,” Ms. Stahl says. “They work as a team and there’s good communication between specialists. The whole staff is knowledgeable. The doctors and nurses have been so good, so confident, nice, and caring. It’s a really pretty special place.”

“It’s really a testament to Mount Sinai’s strength, that we achieved this level of comprehensive care and expertise for a very complicated patient.”

—John Mascarenhas, MD

Message from the Director of The Tisch Cancer Institute

The Tisch Cancer Institute's designation in 2015 as a National Cancer Institute (NCI) Cancer Center is tangible proof of the meaningful work we are accomplishing in research and clinical care.

In the highly competitive New York City marketplace, The Tisch Cancer Institute excels in areas such as immunotherapy and cancer genomics, and in the use of Big Data to diagnose and treat cancer. Our expertise in environmental health encompasses Mount Sinai's World Trade Center First Responders Program, which has diagnosed and treated more than 20,000 first responders and survivors for health issues stemming from the events of 9/11. Ongoing research continues to reveal the long-term effects of some of the carcinogens that were released into the air after the collapse of the World Trade Center. We understand that it could take years before certain diseases begin to manifest in patients.

Mount Sinai's unique catchment area includes some of the nation's wealthiest and poorest populations. Local, state, and federal lawmakers have commended our work in providing health care



Steven J. Burakoff, MD

outreach to the underserved with breast, colorectal, lung, prostate, and liver cancers, and in offering cancer therapies through clinical trials. Within the past few years we have recruited leaders in these areas, as well as in melanoma and bone marrow transplant.

With cancer grants totaling more than \$79 million, The Tisch Cancer Institute is committed to transforming the way we practice medicine to improve the health of our patients.

Innovation occurs each day in the labs and meeting rooms of the Leon and Norma Hess Center for Science and Medicine, a building that opened at the end of 2012 and devotes nearly half of its 500,000 square feet of space to cancer research and clinical care. Within the Hess Center, experts in medicine, oncology, genetics, pediatrics, neurology, and immunology collaborate in an atmosphere that fosters discovery.

Delivering High-Quality Health Care to All

The Tisch Cancer Institute's unique community outreach programs that deliver high-quality health care to all patients who live within its catchment area—regardless of income—played a key role in its recent designation as a National Cancer Institute (NCI) Cancer Center.

Encompassing one of the most disparate socioeconomic areas in the country, The Tisch Cancer Institute covers the Carnegie Hill section of Manhattan's Upper East Side and East and Central Harlem, a population of more than 500,000.

"Our NCI Cancer Center designation recognizes the work we have done in engaging our local communities and opens tremendous funding opportunities for the future," says Nina Bickell, MD, Co-Director for Health Equity and Community Engaged Research at the Icahn School of Medicine at Mount Sinai.

Dr. Bickell works closely with Lina Jandorf, Director of The Tisch Cancer Institute Community Outreach Programs to increase awareness and participation in screenings, diagnoses, and treatments for breast, cervical, and colorectal cancers within local African American and Hispanic communities. Ms. Jandorf says the Institute

connects with patients locally, through culturally and linguistically appropriate channels, such as faith-and-community-based organizations.

In one successful program, Mount Sinai researchers helped boost colonoscopy screening rates among African Americans to more than 70 percent by instructing health educators and patient peers in the community to phone patients to remind them of upcoming appointments. Patients of all races had shown a 40 percent screening rate prior to the program.

Dr. Bickell supervised another successful study that eliminated racial disparities in the treatment of early-stage breast cancer by



Nina Bickell, MD, and Lina Jandorf

maintaining better follow-up communication between the patients' surgeons and oncologists. This intervention was created after the Mount Sinai researchers learned that African-American and Hispanic women with early-stage breast cancer were more likely than Caucasian women to experience fragmented care. They were less likely to see medical oncologists to receive effective adjuvant treatment, at the rates of 1 to 3 (African American), 1 to 4 (Hispanic), and 1 to 6 (Caucasian).

"We made sure the women showed up to the oncologist, and if they didn't we sent the information to the surgeon," says Dr. Bickell.

"Becoming an NCI-designated cancer center enhances opportunities for discovery," adds Dr. Bickell. "It will help us translate those findings into therapies that will help us make a difference in the communities we serve."

Future plans call for Tisch researchers to partner with basic scientists at Mount Sinai to tackle the important question of why cancer manifests differently in different races. They will examine, for example, why black women, who tend to have higher rates of obesity and insulin resistance than white women, are more likely to be diagnosed with aggressive forms of cancer.