A genetic variation that is prevalent in people of African or Hispanic/Latino ancestry was significantly associated with heart failure in a study by researchers at the Icahn School of Medicine at Mount Sinai and the Perelman School of Medicine at the University of Pennsylvania. The study, published in December 2019 in *JAMA: The Journal of the American Medical Association*, found underdiagnosis of affected patients and made a strong argument for wider genetic screening of the potentially deadly mutation, researchers say.

The team reported a significant association between the variation, TTR V142I, and a serious heart disorder, hereditary transthyretin amyloid cardiomyopathy (hATTR-CM). The TTR V142I gene variant, previously known as TTR V122I, causes the liver to produce misformed molecules of the transthyretin protein. The protein forms clusters, called amyloids, that can deposit in tissues throughout the body, including the nerves, kidneys, and joints. When amyloids lodge in the heart, they cause hATTR-CM, in which the walls of the heart become thicker and stiffer—in the worst case leading to heart failure.

"Using clinical data linked to the genetic data at the BioMe™ Biobank of Mount Sinai, we found that up to 4 percent of African-Americans and 1 percent of Hispanic/Latino Americans carried this mutation," says a corresponding author of the study, Girish Nadkarni, MD, Assistant Professor of Medicine (Nephrology), and Co-Director of the BioMe Phenomics Center in The Charles Bronfman Institute for Personalized Medicine.

### Novel Cancer Immunotherapies Show Promise

Researchers at the Icahn School of Medicine at Mount Sinai are pioneering two novel approaches to cancer immunotherapy that are promising for patients with non-Hodgkin lymphoma and other solid tumors, which have been stubbornly resistant to therapies such as checkpoint blockade. One new approach is an *in situ* vaccination that worked so well in patients with advanced-stage lymphoma that it is now undergoing trials for breast cancer, as well as head and neck cancers. The other therapy captures the synergy of checkpoint blockade and stem cell transplantation in the form of a highly promising treatment known as immunotransplant. Joshua Brody, MD, Director of the Lymphoma Immunotherapy Program and Assistant Professor of Medicine (Hematology and Medical Oncology) at The Tisch Cancer Institute at Mount Sinai, is the lead investigator for both therapies.

The *In Situ* Vaccination

This vaccination approach involves injecting immune stimulants directly into a single tumor site, which "teaches" the immune system to recognize
It first appeared as a small rash a few weeks after Noor Nunez was born in 2018 in Kuwait, where she lives with her three older siblings, her Saudi mother, Rania Al-Mutairi, and American father, Joe Nunez. The red mark on her skin, however, was not a rash, but a bright red hemangioma, a benign tumor caused by an abnormal cluster of small blood vessels on or under the surface of the skin. As it grew, it looked as though baby Noor had a small tomato in the middle of her face—located right between her eyes.

Doctors in Kuwait, however, didn’t seem to know how to treat it. They told her parents that it was superficial, and they prescribed topical creams, assuring them it would go away. When it kept growing in size and thickness—and people had started pointing and staring at Noor—her father, a contractor based in Kuwait with the U.S. Army, became determined to find treatment, even if it meant leaving the country.

When Noor was about 5 months old, and as the hemangioma continued to grow, Mr. Nunez started to research treatment options online. “I knew we had to do something to correct this, or it would affect her for the rest of her life,” he says. “I started contacting centers specializing in vascular birthmarks all over the world, but few doctors responded.” However, when he sent an email to Gregory M. Levitin, MD, Director of the Vascular Birthmark and Malformations Program at New York Eye and Ear Infirmary of Mount Sinai, Dr. Levitin replied immediately. After reviewing the photos that Mr. Nunez had sent, Dr. Levitin knew he could help Noor. In late July 2019, around the time of Noor’s first birthday, the Nunez family traveled to New York Eye and Ear for surgery. Dr. Levitin, who is also Senior Faculty of Ear, Nose and Throat (Otolaryngology)—Head and Neck Surgery at the Icahn School of Medicine at Mount Sinai, is a nationally recognized expert in the diagnosis and management of hemangiomas and vascular birthmarks.

Hemangiomas typically begin to appear one to three weeks after birth and often fade with time. However in Noor’s case, the hemangioma was so large and deep that it blocked almost half of her eye’s visual field and distorted the bridge of her nose. It was so deep that 90 percent of it was below the surface of the skin. Due to its location and size, it was one of the most challenging hemangioma cases Dr. Levitin says he has ever encountered. “It was highly vascular, so there was concern about excessive bleeding, and it was in the middle of her face near her eyes, so we had to find the precise place to make an incision in order to debulk the tumor without leaving her disfigured,” recalls Dr. Levitin. “In the end, we placed the incision within the shadow line between her eyebrow and her eye—then, millimeter by millimeter, we carefully removed each feeding blood vessel in a three-hour surgery during which she lost no more than three teaspoons of blood.”

Due to the complexity of the case, the hemangioma could not be removed in its entirety without risking complications or skin grafts, but Dr. Levitin was still able to remove more than 80 percent of the tumor, leaving Noor’s eyes and eyebrows symmetrical, restoring her nose, and significantly improving her appearance. The family regularly shares updates with Dr. Levitin on the hemangioma as it continues to shrink and fade; however, Noor will likely return to New York Eye and Ear this year for two laser treatments to reduce the redness and improve the texture of the hemangioma. According to Dr. Levitin, “In two or three years—maybe less—she will appear almost normal.”

Dr. Levitin fully understands how the family was willing to do everything they could for Noor. “I became passionate about this specialty when one of my twin daughters was born with a disfiguring hemangioma,” he says. “As a head and neck surgeon, and as a parent, I knew I could give other patients the medical expertise and the attentive care they need during a difficult time. I feel like my patients are part of my extended family.”

Beyond the successful surgery, Mr. Nunez says his family was additionally impressed with the caring staff at New York Eye and Ear. “My wife was floored by the treatment Noor got,” says Mr. Nunez. “Watching how the nurses and staff treat patients and their families, it was beautiful to see,” he says.
The Mount Sinai Medical-Legal Partnership (MSMLP), a nonprofit organization that provides free legal assistance to the neediest patients, recently celebrated two pediatric initiatives and honored the late Mount Sinai Trustee Blaine V. “Fin” Fogg.

Cyrus Vance Jr., District Attorney of New York County, was keynote speaker of the event held in November at Mount Sinai’s Corporate Services Center. He applauded the success of an initiative at Mount Sinai St. Luke’s—funded by a $1.3 million grant from his office—that helps patients and their families navigate the special education system. Lawyers from MSMLP and The Legal Aid Society in New York City have aided about 200 students since the initiative began in 2018.

In addition, a new program based at The Mount Sinai Hospital was announced at the event. It is helping young patients and their families address legal issues with housing, immigration, and access to health care. MSMLP also serves patients across the Health System, including legal clinics at the Mount Sinai Adolescent Health Center and the Mount Sinai Center for Transgender Medicine and Surgery.

“We look at the needs of patients in a holistic manner,” said Barbara Berger Opotowsky, President of MSMLP, “and we believe that demolishing legal barriers can help materially improve the health of our patients and the community we serve.” Speakers at the event expressed gratitude to Mr. Fogg, a Mount Sinai Trustee for three decades and President of The Legal Aid Society until his death in July 2019. “I have no doubt that his commitment to service will continue to inspire us all for many years to come,” said Beth Essig, Executive Vice President and General Counsel, Mount Sinai Health System.

Gene Variant Is Strongly Linked to Heart Failure

(continued from page 1)

The association of the TTR V142I variant with the clinical diagnosis of heart failure was evaluated in 9,694 individuals of African and Hispanic/Latino ancestry, using health records linked to genetic data from the BioMe Biobank and the Penn Medicine Biobank. Among carriers of the TTR V142I variant, the rate of diagnosis with hATTR-CM was assessed. The findings indicated both high rates of underdiagnosis and prolonged time to the appropriate diagnosis, says senior author Ron Do, PhD, Assistant Professor of Genetics and Genomic Sciences, and Co-Director of the BioMe Phenomics Center. Only 11 percent of individuals with the genetic variant and heart failure had been diagnosed with hATTR-CM, with an average time to appropriate diagnosis of three years.

“Our hope is if we can find individuals with amyloid cardiomyopathy early through genetic screening, we can start them on therapy before a heart transplant becomes the only clinical solution,” says Sumeet S. Mitter, MD, Assistant Professor of Medicine (Cardiology), and a leader of the multidisciplinary Clinical Amyloid Program at the Icahn School of Medicine. “Early diagnosis is even more important, given recent advances in treatment for hATTR-CM.” Treatment was limited to supportive care until May 2019, when the U.S. Food and Drug Administration approved the breakthrough drug tafamidis, made by Pfizer. However, timely diagnosis is critical, since the therapy stops amyloids from depositing in tissues, but does not reverse the course of the disorder.

The experience of a Mount Sinai patient, Wilbert Gibson, is emblematic. Mr. Gibson, 63, began having worrisome symptoms in early 2019. “My weight shot up from about 170 to nearly 200 pounds,” he says. “My legs were swelling; I was having shortness of breath.” Mr. Gibson was diagnosed with cardiac amyloidosis and found to have the TTR V142I mutation. His heart failure was so advanced that he required a transplant. He received a new heart in June 2019 and says he feels restored and grateful. However, he echoes clinicians and researchers in calling for more awareness of the gene variant, its prevalence in some populations, and its association with heart failure. “People should know about this,” Mr. Gibson says.
and destroy cancer cells at that site and throughout the body. “We’re teaching dendritic cells—the generals of the immune system army—to specifically recognize tumor antigens, which then instruct the T cells, the immune system’s soldiers, to go forth and kill the cancer cells while sparing non-cancer cells,” says Dr. Brody.

As reported in the April 2019 issue of Nature Medicine, this therapy involves several steps that begin with injection of a small molecule that calls the dendritic cells to action, followed by low-dose radiation to kill the tumor cells. These dying cells, in turn, release antigens into the immune system that are recognized by the dendritic cells and presented to the T cells as part of the “coaching” process.

The results were encouraging among a cohort of 11 patients with non-Hodgkin lymphoma. In earlier tests with lab mice, the vaccine was able to cure about 40 percent of lymphoma tumors, Dr. Brody says. When combined with checkpoint blockade, the cure rate nearly doubled. Dr. Brody reports that when testing the therapy in patients, “We saw some who had profound regressions of their entire tumor burden. After treating one site, tumors throughout the body melted away.”

The next step in the development of the vaccine began last spring when Mount Sinai began recruiting patients for a clinical trial that combines the vaccine therapy with checkpoint blockade—a widely used treatment that effectively removes the brakes from T cells so they are free to attack cancer cells. This trial will target lymphomas, as well as breast cancer and head and neck cancers.

**Immunotransplant Therapy**

While PD-1 blockade has been effective for some lymphoma patients, its ability to help those with non-Hodgkin lymphoma has been more challenging. Even anti-PD-1/anti-CTLA4 dual checkpoint blockade has yielded limited efficacy, perhaps due to insufficient T cell activation.

Recently, Dr. Brody and his team found that combining immunotherapy and stem cell transplantation may be beneficial. In this first-of-its-kind approach, reported in Cancer Discovery, the researchers were able to increase the cancer-killing immune response tenfold when tested in the lab, making it effective against not just non-Hodgkin lymphoma but also melanoma and lung cancer.

“In the lab, immunotransplant either prolonged survival greatly compared to immunotherapy alone or actually cured a significant portion of mice with melanoma and lung cancer,” Dr. Brody says.

Immunotransplant works through the principle of homeostatic proliferation: when T cells are put into an empty organism or body, they become activated and begin to wildly multiply. In immunotransplant, T cells are withdrawn from the blood through apheresis, clearing the way for their reintroduction as infused immune cells. As they proliferate, these reinvigorated T cells build the immune system back up, become activated, and enable checkpoint blockade to achieve its full cancer-fighting potential.

The fact that checkpoint blockade has become the standard of care for treating melanoma, kidney cancer, lung cancer, and other diseases underscores the promise of immunotransplant. “We’ve shown we can increase the power of checkpoint blockade immunotherapy to prolong survival and induce cures in aggressive cancers, and that means not just lymphomas but solid tumor types,” says Dr. Brody.

### Bringing Art Experiences to Oncology Patients

During an appreciation luncheon held on Wednesday, November 13, Mount Sinai Health System leadership, along with faculty and staff, celebrated nine talented artists who work at Mount Sinai through The Creative Center at University Settlement’s Hospital Artist-in-Residence Program providing art experiences to oncology patients and their caregivers as they receive treatment. The event included vivid and inspiring stories about care and compassion, and the powerful impact art has on enhancing the patient and staff experience. The lunch, held in the Annenberg Center for Innovation and Discovery, was hosted by Sinai Spotlight, a Health System employee recognition and appreciation program sponsored by the Division of Talent Development & Learning, in partnership with the Mount Sinai Health System Office of Development.

The artists work in various locations throughout the Health System—both bedside and at outpatient units—helping patients, and even their visitors, to momentarily turn a traumatic, frightening, or overwhelming experience into one of joy, life, and positivity through art.

Artist Sascha Mallon, who has participated in the program for nine years, meets with inpatients at the bone marrow transplantation center and outpatients at The Mount Sinai Hospital. Ms. Mallon says she first determines their eagerness to participate, and then, their preferences. “They make macramé and jewelry. They sculpt and paint. I find out what is exciting for them,” says Ms. Mallon. “I don’t see the illness—the doctors and nurses do. I see the healthy part of the patient, the strong part, the happy part.”
First Place for Neurosurgery

The Department of Neurosurgery at the Icahn School of Medicine at Mount Sinai received the first place award for most accepted abstracts by residents at the 2019 Congress of Neurological Surgeons (CNS) Annual Meeting, which took place in October in San Francisco. The 77 accepted abstracts were featured as oral presentations and posters, covering a wide range of topics, including spinal surgery and trauma, intracerebral hemorrhage, skull base tumors, glioblastoma, pediatric epilepsy, and neurocritical care, as well as socioeconomic issues related to neurosurgical treatment. At the 2018 CNS meeting, the Department placed third, with 35 accepted abstracts. “Our trainees are strongly supported to perform research by Neurosurgery Vice Chair and Residency Program Director J Mocco, MD, MS. They are extremely active in exploring ways to work with faculty to improve how we treat neurological diseases and conditions, and the number of accepted abstracts we had at this year’s CNS meeting is a testament to that,” says Joshua B. Bederson, MD, Leonard I. Malis, MD/Corinne and Joseph Graber Professor of Neurosurgery, and Chair of Neurosurgery, Mount Sinai Health System.

A Fun Day to Support Children and Families

More than 1,200 Mount Sinai faculty, staff, patients, families, and friends enjoyed a fun-filled day at a private performance of the Big Apple Circus on Sunday, November 10, at Damrosch Park at Lincoln Center. The event was hosted by the Mount Sinai Children’s Center Foundation (CCF), which has supported children and families served by Mount Sinai Kravis Children’s Hospital for 33 years. It is the largest fundraiser for the Jack and Lucy Clark Department of Pediatrics, and proceeds provide critical support for the Child Life and Creative Arts Therapy Program; seed funding for exceptional junior physician-scientists; and support for the Program for Underserved Children. The benefit was chaired by Sara and Nathaniel Zilkha and honored CCF Co-Chair Vicki Panzier Gross and Karen M. Wilson, MD, MPH, the Debra and Leon Black Professor and Division Chief of General Pediatrics at the Icahn School of Medicine at Mount Sinai. “I am so thankful to the CCF for all of its support,” said Dr. Wilson.

A Thank You to Clinical Trial Participants

Physician-scientists from Mount Sinai Beth Israel and The Michael J. Fox Foundation highlighted new treatments and research in Parkinson’s disease during a “Thankfest” symposium and lunch in October. The event was held to recognize the valuable contributions of 60 special attendees—patients who volunteer to participate in clinical trials to advance understanding of Parkinson’s disease.

“Clinical trials are in a very exciting new phase of targeted treatments that include correcting specific genetic causes,” says Susan Bressman, MD, a renowned Parkinson’s disease clinician and researcher. Dr. Bressman is the Mirken Family Professor of Neurology and Director of the Movement Disorders Center. “The only way we will know if these approaches work is by testing them in patients,” says Dr. Bressman. “The process depends on the altruism of patients, and they deserve giant kudos.”
The Mount Sinai Health System
And Mount Sinai Heart Celebrate
National Wear Red Day

No appointment is necessary. There will be free blood pressure, cholesterol, glucose, and body mass index testing; nutrition and diet counseling; heart-healthy cooking demonstrations; and more!

**Mount Sinai Brooklyn**
11 am – 2 pm
3201 Kings Highway
Between East 32nd Street and New York Avenue
Main Lobby

**The Mount Sinai Hospital**
11 am – 2 pm
1468 Madison Avenue
100th Street
Guggenheim Pavilion Atrium

**Mount Sinai St. Luke’s**
11 am – 2 pm
1111 Amsterdam Avenue
114th Street
Babcock Lobby

**Mount Sinai South Nassau**
11 am – Noon
One Healthy Way
Atrium, Ground Floor

**Mount Sinai-Union Square**
11 am – 1 pm
10 Union Square East
Between 14th and 15th Streets
Atrium, Second Floor

**Mount Sinai West**
11 am – 1 pm
1000 10th Avenue
Between 58th and 59th Streets
Lobby

**Mount Sinai Queens**
11:30 am – 1:30 pm
25-10 30th Avenue
Mount Sinai Queens Pavilion
Lobby

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**Research Study on Body Shape, Fat, and Health in Women**

Researchers at the Diabetes, Obesity and Metabolism Institute are seeking healthy volunteers between 18 and 40 years of age with apple- or pear-shaped bodies for a study on fat and health in women. The study requires up to three visits to the clinical research unit at Mount Sinai St. Luke’s. Participants will donate blood and fat samples, which will be taken by a trained medical professional. Participants will be compensated for their time (up to $450) upon completion of the study. For more information, contact Gyu Ho (Kyle) Lee gyuho.lee@mssm.edu, or call 212-241-3108.

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**Heart-to-Heart Grand Rounds**

Top female cardiologists, cardiac surgeons, and nurse practitioners from the Mount Sinai Health System will lead informative conversations about women’s heart health.

**Mount Sinai St. Luke’s**
Tuesday, February 11
2 – 3 pm
Muhlenberg Auditorium

**The Mount Sinai Hospital**
Friday, February 14
Noon – 1 pm
Hatch Auditorium