Blazing a New Trail in the Treatment of Heart Disease

An injectable nanoparticle that delivers HMG-CoA reductase inhibitors, or statins, which directly inhibit atherosclerotic plaque inflammation could represent a new frontier in the treatment of heart disease. This novel approach is being developed by researchers at Icahn School of Medicine at Mount Sinai, who have seen promising results in mice models and plan to translate their findings to humans within the next few years.

The researchers found that administering injections of the statin nanodrug at a low dose over a three-month period significantly inhibited plaque progression, while the administration of four high-dose injections over the course of a week eradicated 90 percent of the inflammation in advanced atherosclerotic plaques. The results were published in the January 20, 2014, edition of Nature Communications.

A Leader in Cardiovascular Care for HIV Patients

What started as a casual observation among physicians almost a decade ago—that patients with HIV tend to develop hypertension and have a greater risk of heart attacks than the general population—has become a formal area of study and treatment within the Mount Sinai Health System.

Under the direction of Merle Myerson, MD, EdD, Director of the St. Luke’s Roosevelt Center for Cardiovascular Disease Prevention, and Director of the Cardiology Section of the Spencer Cox Center for Health, patients with HIV are being closely monitored and treated for heart disease and stroke. In fact, cardiovascular care has become increasingly critical to the overall health of HIV patients, as more of them live well into their 70s and 80s.
The goal to treating heart disease is targeting inflammation,” says the study’s senior investigator Willem Mulder, PhD, Associate Professor of Radiology and Director of the Nanomedicine Program in the Translational and Molecular Imaging Institute at Icahn School of Medicine at Mount Sinai. “But anti-inflammatory drugs have a lot of side effects. When you put the statin in a nanoparticle and deliver it directly to the site, you prevent it from going elsewhere and creating problems.”

Despite the widespread use of oral statins and preventive strategies to control smoking and high-cholesterol diets, atherosclerotic diseases continue to be a major cause of death and disability worldwide. Even when treatment goals are met, patients have a high risk of a recurring heart attack within the first few years.

The new delivery strategy is based on reconstituted high-density lipoprotein (rHDL) nanoparticles. Orally prescribed statins, which are the current standard of care, are limited by a couple of factors, according to Dr. Mulder. “They reduce lipid levels but don’t resolve inflammation in the vessel wall because their effect is limited by absorption in the liver and by concerns over doses that are too high and cause hepatotoxicity and myopathy.”

Dr. Mulder, who is working with Zahi A. Fayad, PhD, Professor of Radiology and Medicine (Cardiology), and Director of the Translational and Molecular Imaging Institute, says their team is examining the results of combining ingested statins with injected nanoparticles. They are also trying to find compounds that have a longer lasting effect. So far, one important finding was that the rHDL nanoparticle was not seen as a foreign invader by the body’s immune system.

“Levels of inflammation spike after a heart attack, which is why up to 50 percent of patients may suffer another heart attack, some while in the hospital or just after discharge,” says Dr. Fayad. A vital time to prevent the onset of inflammation and stabilize the body through nanotherapy would be immediately following a heart attack or stroke. Nanotherapy could also be used to prevent heart attacks from occurring the first time.

The team also includes researchers at the Academic Medical Center in Amsterdam, Holland, where Dr. Mulder has a secondary affiliation as Professor of Cardiovascular Nanomedicine.

**Expertise in Mitral Valve Repair**

Mitral Valve Prolapse (MVP) is a common heart valve abnormality that affects up to 5 percent of the U.S. population. The mitral valve controls the flow of blood from the lungs to the main pumping chamber of the heart. MVP results from a degeneration of valve structure that leads to a regurgitation of blood backwards that can result in heart enlargement and weakening, as well as fatigue and shortness of breath.

Women are twice as likely as men to develop the condition. Children can also be affected. MVP is often asymptomatic and detected during a routine checkup when the physician hears a murmur or clicking sound in the patient’s chest. Most cases are mild and require no treatment, but important steps should be taken when the patient’s case is more serious. The optimal treatment is to repair the damaged mitral valve, although many patients still undergo a replacement with an animal or mechanical valve.

David H. Adams, MD, Marie-Josée and Henry R. Kravis Professor of Cardiothoracic Surgery at Icahn School of Medicine at Mount Sinai, is a world leader in the field of heart valve surgery. He and his team have published benchmark papers documenting repair rates of more than 99 percent for degenerative mitral valve disease, which are among the highest in the world.

As Program Director of The Mount Sinai Hospital’s Mitral Valve Repair Reference Center, Dr. Adams leads a team that performs the most operations for MVP in the region, operating weekly on patients from across the United States. Last year, they performed more than 400 mitral valve operations, and are recognized by their peers for their leadership in the field. Dr. Adams and his team coordinate several live mitral surgery courses at Mount Sinai annually, and in 2013 hosted more than 150 surgeons from around the world who came to learn from their experience.

Dr. Adams says the Reference Center’s team approach is the key to its success. “Our teams in the clinic, operating room, intensive care unit, and Cardiothoracic Surgery step-down unit all share equally in the success of this program,” he says. The expertise of Mount Sinai’s imaging teams from the departments of Anesthesiology and Cardiology also contribute to the high level of repair at Mount Sinai.
Michael P. Mullen, MD, directs the Mount Sinai Health System’s six outpatient HIV clinics throughout Manhattan. They treat approximately 10,000 HIV patients, making it one of the largest health programs of its kind in the country, and the largest in New York State, with the most diverse population. According to the New York City Department of Health and Mental Hygiene, the city remains the epicenter of the U.S. HIV epidemic with 72 of every 100,000 New Yorkers infected, versus 23 per 100,000 people nationally.

“Having HIV should be recognized as a risk factor for cardiovascular disease the way it is with diabetes,” says Dr. Myerson. “Today, there are no medical guidelines that tell us how cholesterol should be handled for patients living with HIV. There is a lot more that we have to know.”

HIV patients are believed to be at greater risk for cardiovascular disease for several reasons. The antiretroviral medications they take, particularly protease inhibitors, are believed to adversely affect lipid levels. Patients with HIV also tend to smoke cigarettes at a higher proportion than the general population, and they are now living to an age where heart disease is more prevalent.

Dr. Myerson has set up a program where patients with severe heart failure and coronary artery disease can be closely monitored through frequent doctor and nurse-practitioner visits, so that interventions can take place before patients seek emergency care. Her team has been able to reduce frequent emergency room visits and hospital admissions.

“Mount Sinai is uniquely poised to be a leader in preventing cardiovascular disease in HIV patients,” says Dr. Myerson. This is due to the Health System’s expertise in heart disease treatment and prevention, and its large and diverse HIV patient population, which allows for high-quality research.

Vivek Reddy, MD, center, with Brian H. Kopell, MD, right, and Eric Oermann, MD, PGY1 Neurosurgical Resident, implant a new cranial nerve stimulation device for heart failure, a procedure now in clinical trial at Mount Sinai.

Approximately 6 million Americans are affected by heart failure, which occurs when the heart is too weak to effectively pump and circulate blood throughout the body. Any number of conditions, such as weakened heart muscle and damaged vessels, can lead to heart failure. Prescription drugs may help manage some symptoms but do not always succeed at relieving all symptoms or preventing heart failure deterioration.

Studying a Novel Device for Heart Failure

The Mount Sinai Hospital is one of three institutions in New York State, and one of one hundred in the nation, selected to study the safety and effectiveness of an implantable cranial nerve stimulation device for heart failure patients with debilitating fatigue, shortness of breath, and heart arrhythmias.

Specifically, the clinical trial will study a novel device known as CardioFit®, which involves implanting a pacemaker-sized stimulator under the skin of the chest to help stimulate the vagus nerve on the right side of the neck. The large vagus nerve runs from the brain stem down to the abdomen and is responsible for regulating multiple bodily functions, including heart rate. A lead from the device to the vagus nerve delivers mild electrical pulses in an effort to reduce heart rate, stress, and workload on the cardiac muscle and ultimately improve overall heart function.

“Vagus nerve stimulation may be the therapy we have long been waiting for to bring relief to heart failure patients with chronic symptoms and protect them, as well, from dangerous and potentially fatal arrhythmias,” says Vivek Reddy, MD, Director of Arrhythmia Services at The Mount Sinai Hospital, who is leading the research. “I am excited to be working with our heart failure and neurosurgery colleagues to offer this potentially transformative therapy to our patients.”

The study will compare the benefits of vagus nerve stimulation, in combination with medications, to the standard therapy of medication. “We will also investigate vagus nerve stimulation therapy’s ability to reduce hospitalization, a major issue for heart failure patients, as well as its capability to reduce mortality in this high-risk population,” says Ajith P. Nair, MD, Director of the Pulmonary Hypertension Program in the Advanced Heart Failure and Transplantation Program at Mount Sinai Heart.

A key member of the team is Brian H. Kopell, MD, Director of the Center for Neuromodulation. “At Mount Sinai, we have successfully used vagus nerve stimulation for refractory epilepsy in patients with uncontrollable seizures, and to treat patients with major depression, who do not have good responses to medication therapy,” says Dr. Kopell. “We now want to see what clinical benefits are possible for heart failure.”

The clinical trial, known as INOVATE-HF (Increase of Vagal Tone in Chronic Heart Failure) is enrolling up to 650 patients in the United States and Europe.
February is **Heart Health Month**, and the Mount Sinai Health System is sponsoring a number of activities to educate faculty, staff, employees, and the community about cardiovascular disease.

### Love Your Heart Wellness Fair

Physician talks, exercise training, food demonstrations, relaxation techniques, smoking-cessation programs, and more

**Tuesday, February 4**  
5 – 7:30 pm  
Mount Sinai Beth Israel  
Phillips Ambulatory Care Center  
Second Floor

### Salud con Sabor Latino

A Spanish-language nutrition workshop and food demonstration

**Monday, February 3**  
5:30 – 7 pm  
Mount Sinai St. Luke’s Cafeteria

Sponsored by Women’s Heart NY, a multisite comprehensive heart program comprised of Mount Sinai Health System staff. To learn more, visit [www.WomensHeartNY.com](http://www.WomensHeartNY.com).

### Heart Healthy Smoothie Station

Enjoy fresh smoothies, and learn why they are nutritious.

**Monday, February 24**  
9 – 11 am  
Mount Sinai Roosevelt Cafeteria

### Community Health Fair and “Wear Red Day”

Complimentary blood pressure, cholesterol, and glucose testing; nutrition and diet counseling; diabetes education; heart-healthy cooking; stress management and yoga; and more

**Friday, February 7**  
10:30 am – 2 pm  
The Mount Sinai Hospital  
Guggenheim Pavilion Atrium

Sponsored by Mount Sinai Heart, and the departments of Community and Government Affairs, Clinical Nutrition, and Nursing. Go to [www.mountsinai.org/heart](http://www.mountsinai.org/heart) to learn more.

### Grand Rounds Nursing

“Heart to Heart with Women from the Heart”

**Wednesday, February 12**  
Noon  
The Mount Sinai Hospital  
Stern Auditorium

### Community Health Talk

“Saving Hearts by Eating Right”

**Friday, February 28**  
2 – 3 pm  
Stanley Isaacs Neighborhood Center, Inc.  
415 East 93rd Street

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**Mount Sinai Heart’s Cardiac Care Unit Awarded for Excellence**

The Mount Sinai Hospital Cardiac Care Unit (CCU) was awarded a 2014 Beacon Award for Excellence from the American Association of Critical-Care Nurses (AACN), the leading society of acute- and critical-care nurses.

Mount Sinai Heart was recognized for its success in several key areas, among them: appropriate staffing and staff engagement, effective communication, evidence-based practices, and outcomes measurement.

“Our CCU team is a true partnership of nurses, staff, and doctors working collaboratively each and every day, and our goal is always the best clinical care possible for our patients,” says Beth Oliver, DNP, RN, Vice President, Clinical Operations at Mount Sinai Heart.

“Congratulations to the CCU team for its hard work and outstanding commitment to excellence in patient care,” adds Valentin Fuster, MD, PhD, Director of Mount Sinai Heart and Physician-in-Chief at The Mount Sinai Hospital.