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NEWS

The Wilf Family Cardiovascular Research Institute

Rebuilding the Human Heart

he Montefiore Einstein Center for Heart and Vascular Care offers comprehensive cardiovascular care, including complex, high-risk procedures such as heart valve repair, aneurysm surgery and heart transplants. Pioneering research by co-director Robert E. Michler, M.D., right, helped gain U.S. Food and Drug Administration approval for use of robotic surgery (see sidebar, next page) in mitral valve repair and coronary bypass surgery.

Dr. Michler wears many hats besides his surgical scrub cap. He's also a basic researcher, a principal investigator and a popular Einstein professor who passes on today's medical wisdom to tomorrow's doctors.

The mother of all heart cells Heart transplants can save lives, but nearly half of all recipients die within 10 to 12 years, their transplanted hearts having succumbed to rejection, atherosclerosis or muscle damage. As professor and chairman of the department of surgery and of the department of cardiovascular and thoracic surgery at Einstein and

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Newsletter for the Wilf Family Cardiovascular Research Institute



MESSAGE FROM THE DIRECTOR



RICHARD N. KITSIS, M.D. Director, Wilf Family Cardiovascular Research Institute Dr. Gerald and Myra Dorros Professor of Cardiovascular Disease

his issue of the Wilf Family Cardiovascular Research Institute newsletter highlights the work of Dr. Robert Michler, professor and chair of the department of surgery and of the department of cardiovascular and thoracic surgery. Over the six years Rob has been at Einstein and Montefiore, he's had a huge impact on basic and translational cardiovascular research and on the delivery of surgical care to patients. The article highlights his clinical and teaching activities as well as his novel and exciting research into cardiac stem cell biology. In addition, we get a glimpse of the extensive humanitarian activities of Rob and his wife, Sally, in bringing advanced cardiac surgical procedures to needy children in the Caribbean and South America. Rob is truly a physician-scientist with a mission.

This issue of the newsletter also features the research and clinical activities of Drs. David Spray, Bin Zhou and Daphne Hsu. Their important contributions range from international health to heart development and pediatric heart disease right here in the Bronx.

At this time, we also want to welcome our newest faculty member, Dr. Evripidis Gavathiotis, a highly talented structural biologist and chemist. Dr. Gavathiotis is creating new molecules that will retard or stimulate cell death, to be used in treating cardiovascular disease and cancer, respectively. A future issue of this newsletter will provide expanded coverage of his work.

And, finally, I want to remind our friends and supporters that we are forming a Cardiovascular Research Visiting Committee. You'll find details on page 4.



Rebuilding the Human Heart (continued from page 1)

Montefiore, and the Samuel Belkin Professor, Dr. Michler is studying stem cells as a way to repair and prolong the life of transplanted hearts and hearts damaged by heart attacks.

In a study of dogs given heart transplants, Dr. Michler and his team removed heart stem cells from the dogs' native hearts, cultured them in the lab and then injected them into the coronary arteries of the transplanted foreign hearts. "The stem cells targeted areas of rejection and injury within the donor transplanted hearts and formed new native blood vessels and muscle cells," says Dr. Michler.

He and colleagues recently identified a population of human cardiac stem cells—those expressing receptors for insulin-like growth factor-1—that work well in regenerating diseased heart muscle.

Working through the National Heart, Lung and Blood Institute (NHLBI), Dr. Michler, a funded National Institutes of Health investigator, is now leading an effort to begin human trials using stem cells. "In less than 10 years, stem cells could be used to counteract heart-muscle damage," he predicts.

On the surgical front

Patients needing mitral valve repair will benefit from three five-year NHLBI-supported studies for which Dr. Michler, Montefiore surgeon-inchief, is principal investigator. The mitral valve controls blood flow between the left atrium and left ventricle. When it doesn't close—often as a result of ischemia (poor blood supply to the heart)—the resulting backflow is called mitral valve regurgitation.

Study #1 compares coronary artery bypass grafting with and without mitral valve repair in patients who have coronary artery disease and "moderate" ischemic mitral regurgitation.

Study #2 compares whether mitral valve repair or mitral valve replacement works better in patients who have coronary artery disease and "severe" chronic mitral regurgitation caused by ischemia.

Study #3 compares mitral valve surgery alone with mitral valve surgery plus surgery to ablate (interrupt) faulty electrical impulses leading to atrial fibrillation.

Around the globe

For Dr. Michler, fixing hearts is truly an international endeavor. He and his wife, Sally, are founders of Heart Care International, a not-for-profit foundation that sends teams of cardiologists, heart surgeons and medical support staff to developing countries to teach and perform heart surgery and catheterbased interventions, mainly on children. They've made many trips to Guatemala, El Salvador, the Dominican Republic and Peru. "Our goal is to work with the same medical teams in each country year after year," says Dr. Michler. This was the first year that Heart Care International travelled to Peru-and, in another first, two Einstein medical students joined the team.





Q: How is robotic heart surgery performed?

A: It's carried out by a surgeon seated at a console near the patient. First, a probe containing a tiny video camera is threaded into the patient's chest cavity and transmits images to a binocular screen viewed by the surgeon. Watching the image, the surgeon then manipulates robotic "arms" to which scissors and forceps are attached. The surgeon can rotate the instruments a full 360 degrees and the camera magnifies everything 10-fold, allowing for precise surgical maneuvers.

In Pursuit of a Parasite



The bite of South America's Pampas bug takes only minutes, but it can result in a lifelong ailment known as Chagas disease. Discovered by Brazil-

ian physician Carlos Chagas, M.D., the disease is caused by the single-celled parasite *Trypanosoma cruzi* that the bloodsucking Pampas bug transmits. Chagas disease is a major cause of heart failure in Mexico and Central and South America.

David C. Spray, Ph.D., professor in the Dominick P. Purpura Department of Neuroscience and the department of medicine (cardiology), and his colleagues are probing how *T. cruzi* causes heart failure. After analyzing chagasic mouse hearts, they reported last year in



the Journal of Infectious Diseases that genes responsible for inflammation and fibrosis (scarring)—two major causes of heart failure—are upregulated (i.e., become more active) when the parasite is present. Earlier this year, in the journal *Cell Cycle*, the Einstein researchers published findings that point to a treatment strategy for Chagas: They reported that many of the genes upregulated in Chagas disease returned to normal activity when bone marrow stem cells were transplanted into mice with chagasic hearts.

A Healthy Heart from the Start



Bin Zhou, M.D., Ph.D., associate professor in the departments of genetics, of pediatrics and of medicine (cardiology), explores molecular mechanisms

that affect heart development and heart disease. To aid in this work, Dr. Zhou's group has developed several genetic mouse models for studying gene function in the developing heart and following birth. "The genetic tools can help us understand how genes influence heart development and diseases such as coronary heart disease," he says.

In 2010, he co-authored a paper in *Nature* describing the important role of a protein involved in remodeling chromatin—the combination of DNA, histone and other proteins that makes up chromosomes. Using his genetically altered mice, Dr. Zhou and colleagues reported that this chromatinremodeling protein, called Brg1, plays a critical role in controlling the growth of the heart during embryonic development—and in causing heart disease later on: When cardiac stresses reactivate the gene for Brg1 in adulthood, cardiac hypertrophy results. The study showed that preventing this "re-expression" of the Brg1 gene helps to decrease hypertrophy, suggesting a strategy for preventing or treating the condition.



To learn more about the Wilf Family Cardiovascular Research Institute, please visit the institute's website at www.einstein.yu.edu/centers/ cardiovascular-research.

FASCINATING FACTS

- Each day the average heart beats (expands and contracts) 100,000 times and pumps about 2,000 gallons of blood.
- In a 70-year lifetime, an average human heart beats more than 2.5 billion times.
- If all of the blood vessels in your body were laid end to end, they'd extend for about 60,000 miles enough to circle the earth more than twice.

updates

Healing the Tiniest Hearts



Daphne T. Hsu, M.D., professor in the department of pediatrics (cardiology) and division chief of pediatric cardiology at Einstein and Montefiore, has

treated more than 1,000 children with heart failure and cared for 320 children who have received heart transplants. "I love caring for the sickest children," explains Dr. Hsu, co-director of the Pediatric Heart Center of the Children's Hospital at Montefiore. "You need to act quickly and do it well—and you become a part of their lives forever." Dr. Hsu came to Montefiore in 2007 to build the pediatric heart program; since 2009, 16 children have successfully received new hearts. The center is a collaborative effort between Montefiore and Einstein. Colleagues in pediatric cardiac surgery, cardiology, genetics, obstetrics, neonatology, intensive care and anesthesia work together to offer state-of-the-art care. Dr. Hsu's team participates in NIH-funded research into best treatments for children with heart failure and complex heart disease.

Dr. Hsu teaches at Einstein in the department of pediatrics (cardiology) and commends Einstein for bringing "the best research to the bedside."

NOTABLE GIFTS AND GRANTS

The Wilf Family Cardiovascular Research Institute gratefully acknowledges the generosity of the individuals and organizations whose support is critical to advancing our mission.

The Estate of Beatrice Steinhauser recently made a bequest to Einstein of approximately \$689,000. In accordance with Mrs. Steinhauser's wishes, part of the gift has been designated for cardiovascular disease research. Some of the funds will be used to purchase equipment for researchers at the Wilf Family Cardiovascular Research Institute and in the Cardiac Physiology and Surgery Core. The gift also will support the research of Nikolaos G. Frangogiannis, M.D., the Edmond J. Safra/Republic National Bank of New York Chair in Cardiovascular Medicine.

Two Wilf Family Cardiovascular Research Institute scientists have received **NIH** grants in support of their work:

- Nicholas E.S. Sibinga, M.D., researches the fat1 cadherin in atherosclerotic vascular disease. Cadherins are "calcium-dependent adhesion" proteins that ensure cell binding and appear to affect heart-muscle health.
- Richard N. Kitsis, M.D., received a grant to support high-throughput screening for small molecules that reduce heart-muscle damage.

VISITING COMMITTEE FORMING

Einstein is forming a Visiting Committee on Cardiovascular Research. The committee will be composed of donors who wish to become more involved with and gain a deeper understanding of cardiovascular disease research at Einstein. Committee members will meet with leading Einstein faculty several times a year and learn about the latest developments in cardiovascular medicine. They will have opportunities to talk with our researchers about issues, concerns and cardiovascular topics in the news. To learn more or to get involved, please contact Christie Hubbard at 718.430.4171 or christie.hubbard@ einstein.yu.edu.

FOR MORE INFORMATION

For more information or to learn more about supporting the work of the Wilf Family Cardiovascular Research Institute at Albert Einstein College of Medicine, please contact Glenn Miller, associate dean for institutional advancement, at 718.430.2411 or glenn.miller@einstein.yu.edu.

EVENTS



Robert E. Michler, M.D., right, with Overseers Marilyn and Stanley M. Katz at Palm Beach Country Club.

Robert E. Michler, M.D., surgeon-inchief, professor and chair of the departments of surgery and of cardiovascular and thoracic surgery and the Samuel Belkin Professor, spoke about the benefits of research at two events held in Florida this past spring: a luncheon hosted by Einstein Overseers **Marilyn and Stanley M. Katz** at Palm Beach Country Club and a reception co-hosted by Overseers **Karen Mandelbaum** and **Sue-ann Friedman** at Ms. Mandelbaum's home. Dr. Michler, co-director of the Montefiore Einstein Center for Heart and Vascular Care and an internationally recognized heart surgeon, is known for his pioneering minimally invasive and robotic surgery techniques with heart patients and his exploration of the use of stem cells for myocardial regeneration (see story on page 1).

The events were part of "Einstein in Florida 2011," an educational outreach program for friends and supporters of the medical school.

THE WILF FAMILY CARDIOVASCULAR RESEARCH INSTITUTE

OUR MISSION:

- To better understand cardiovascular disease—the world's number-one killer
- To translate this knowledge into novel treatments to relieve suffering and improve human health

ADMINISTRATION

Director Richard N. Kitsis, M.D.