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NEWS

The Wilf Family Cardiovascular Research Institute



Success Against Heart Failure

Heat failure—the weakening of the heart’s pumping ability—can result from heart-muscle damage caused by a heart attack. The right treatment can prevent further damage, improve the heart’s pumping power and possibly even restore heart health. But receiving optimal treatment can be a challenge. Of the approximately one million Americans hospitalized each year for heart failure, one in five returns to the hospital within a month.

Physician-scientist Ileana L. Piña, M.D., M.P.H., above, a professor of medicine (cardiology) and of epidemiology & population health at Einstein, wants to succeed where the system so far has failed. “We’re trying to find the best way to bring these patients safely home, get them well medicated and keep them out of the hospital with a good quality of life,” says Dr. Piña, also associate chief in the division of cardiology at the Montefiore Einstein Center for Heart & Vascular Care.

The Exercise Effect

Dr. Piña’s research focuses on exercise training for treating heart failure. As an investigator for the HF-ACTION (Heart Failure—A Controlled Trial Investigating Outcomes of Exercise Training) study of the National Heart, Lung and Blood Institute, she and her colleagues found that heart-failure patients who

MESSAGE FROM THE DIRECTOR



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

Albert Einstein College of Medicine is known for its strength in basic cardiovascular research. Thanks to our affiliation with Montefiore, Einstein's University Hospital and academic medical center, we're also leaders in putting knowledge into the hands (or hearts) of those who need it. Consider the work of physician-scientist Ileana Piña, featured in our cover story. Her research not only helps heart-failure patients get better but helps them gain access to the best possible care. Her approach has helped patients in the Bronx and may have nationwide or even worldwide consequences.

In this issue of the newsletter, we also spotlight the clinical research of Dr. Sylvia Wassertheil-Smoller, who has identified prestroke factors that increase mortality from stroke. Her work suggests that improving nutrition, increasing physical activity and quitting smoking may be critically important in older women.

Finally, the scientists at the Wilf Family Cardiovascular Research Institute continue to examine cardiac life and death at the molecular and cellular levels. This issue of the newsletter includes a summary of a study by the Wilf Institute's Dr. Nick Frangogiannis, who explores the molecular connections between diabetes and heart disease.

None of this research could have advanced without the generosity of individuals, organizations and the Wilf family. We remain extremely grateful for their support.

Richard N. Kitsis

Success Against Heart Failure *(continued from page 1)*

completed a 12-week exercise program were 11 percent less likely to be rehospitalized, and their average medical costs were \$5,320 lower than those treated with medication alone. Based on these findings, Medicare recently changed its reimbursement rules to cover cardiac rehabilitation programs for heart-failure patients. The new coverage will "encourage patients to join a formal program so they feel safe and secure, and then they can continue at home," says Dr. Piña. "The fewer hospitalizations for patients will save money, and their quality of life will improve."

Women are twice as likely as men to develop heart failure after a heart attack or bypass, yet they're less likely to be referred to

"Heart failure is a team-care syndrome," says Dr. Piña.

a cardiac rehabilitation program or to complete an exercise training program. Why?

"There wasn't as much evidence that exercise training benefited women with heart failure compared with men—mainly because of the small numbers of women in trials and the lack of baseline data," says Dr. Piña. Women made up 28 percent of the 2,331 patients in HF-ACTION. After comparing

women who underwent exercise training with women who didn't, Dr. Piña and her colleagues found a significant 26 percent reduction in all-cause death or all-cause hospital stays in women who exercised; this was the first analysis to report such results. "Exercise training for women with heart failure appears to be a useful addition to medical therapy," says Dr. Piña.

New Discharge Strategies

Tightening up overall management is also essential. Dr. Piña was a co-author of an Institute for Healthcare Improvement and American College of Cardiology study that identified hospital strategies in addition to exercise that could help reduce 30-day readmission rates for heart-failure patients. Among the most effective were avoiding medication errors, arranging follow-up appointments before discharge and making sure the patient's primary physician received discharge notes or electronic summaries.

"Heart failure is a team-care syndrome," says Dr. Piña. At Montefiore, that team includes nurse practitioners and pharmacists who optimize drug dosages and make sure patients know how to take their medications; nutritionists who teach low-sodium cooking; physical therapists who encourage patients to enroll in supervised rehabilitation programs; and behavioral modification experts who help patients stop smoking, lose weight and follow their doctors' instructions.

cardiovascular



Q: What's the biggest misconception about heart failure?

A: Many people believe that exercise will harm the heart. But studies show that exercise is safe and beneficial, even for a patient with an implantable cardioverter-defibrillator. In a large study of exercise in patients with heart failure, there were no abnormal firings with exercise. Efforts to improve the heart's pumping ability typically begin with drugs—ACE inhibitors, beta blockers or other medications. "Once patients feel better—the energy rises with time—I encourage them to get active slowly, starting with easy walking or stretching," says Dr. Piña. "From there, a steady increase in exercise duration and intensity will bring the benefits."

discoveries

from the Wilf Family Cardiovascular Research Institute

Diabetes and Heart Failure

Nikolaos G. Frangogiannis, M.D.
Professor of Medicine (Cardiology)
Professor of Microbiology &
Immunology
Edmond J. Safra/Republic National
Bank of New York Chair in
Cardiovascular Medicine
Albert Einstein College of Medicine



People with diabetes are at increased risk for death. This is due in part to diabetic cardiomyopathy, a heart-failure syndrome characterized by

thickening (fibrosis) of the heart muscle.

Dr. Frangogiannis and colleagues hypothesized that a protein called thrombospondin 1 (TSP-1), overexpressed in the heart tissue of diabetes patients, may play a role. They created a diabetic mouse model with the gene that codes for TSP-1 knocked out. The TSP-1 knockout mice had less cardiac fibrosis and more myocardial vessels than diabetic mice expressing TSP-1, which was good. But they also had dilated left ventricles and modest systolic dysfunction. The researchers will now try to develop drugs that selectively mimic the beneficial effects of TSP-1 loss. The study was published in *Circulation Research*.

Stopping Cell Death

Richard N. Kitsis, M.D.
Director, Wilf Family Cardiovascular
Research Institute
Professor of Medicine (Cardiology)
Professor of Cell Biology
Dr. Gerald and Myra Dorros Chair in
Cardiovascular Disease
Albert Einstein College of Medicine



Whether a cell lives or dies depends on a complex interplay of signals between the cell and its environment. One molecule affecting cell

survival is ARC (apoptosis repressor with CARD [caspase recruitment domain]), which inhibits apoptosis—one of two forms of cell death. Apoptosis is a highly regulated process in which the cell shrinks and becomes fragmented, and the pieces are swallowed by neighboring cells. Necrosis, the other form of cell death, involves cell swelling and results in inflammation.

Necrosis was long thought to be unregulated. But the Kitsis group has now found that ARC inhibits necrosis as well as apoptosis, adding to the evidence that necrosis is indeed as well regulated as apoptosis. The findings were published in *Cell Death and Differentiation*.

Stroke Contributors

Sylvia Wassertheil-Smoller, Ph.D.
Distinguished University Professor
Emerita of Epidemiology &
Population Health
Albert Einstein College of Medicine



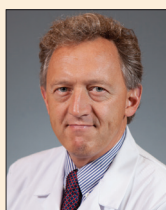
Collaborating with researchers around the country, Dr. Sylvia Wassertheil-Smoller has finished a long-term study on lifestyle factors associated with

mortality and recovery from stroke in older women. The study, a project of the Women's Health Initiative, collected data on prestroke lifestyle factors and health outcomes.

The overall mortality rate from stroke was 35 percent. Prestroke factors that increased mortality included low body mass index, smoking, diabetes and physical inactivity. Surprisingly, being overweight or obese before stroke lowered the mortality rate by 30 percent when compared with being normal weight. These findings suggest that improving nutrition, increasing physical activity and quitting smoking may be important ways to reduce mortality and morbidity from stroke in older women. The study was published in the *Journal of the American Geriatrics Society*.

update

Welcome



The Wilf Family Cardiovascular Research Institute welcomes new member Ulrich P. Jorde, M.D., vice chief of the division of cardiology at Einstein and Montefiore, and an attending physician and section head of Heart Failure,

Cardiac Transplantation & Mechanical Circulatory Support at Montefiore. Dr. Jorde comes to us from Columbia University, where he was an attending

physician and medical director of the mechanical circulatory support program at New York–Presbyterian Hospital/Columbia University Medical Center and a professor of medicine at the Columbia University College of Physicians and Surgeons. He is already familiar with Einstein, having completed his cardiology fellowship here in the late 1990s. Dr. Jorde has published extensively on heart failure and mechanical circulatory support, with more than 100 publications in peer-reviewed journals.

notable grants

RECENT GRANTS

Faculty Awards

Ana Maria Cuervo, M.D., Ph.D.

Modulating autophagy to treat cardiovascular disease
Fondation Leducq

Nikolaos G. Frangogiannis, M.D.

Chemokines in healing myocardial infarction
National Institutes of Health
2R01HL076246-11
03/10/2015 – 1/31/2019

Evrpidis Gavathiotis, Ph.D.

BAX as a small molecule therapeutic target for myocardial infarction
American Heart Association
Winter 2015 Collaborative Sciences Award

Robert C. Kaplan, Ph.D.

Role of innate immunity in HIV-related vascular disease: Biomarkers and mechanisms
National Institutes of Health
1R01HL126543-01
09/15/2014 – 05/31/2018

Bernice E. Morrow, M.D.

22q11.2 deletion syndrome: Novel approaches to understand cardiopharyngeal pathogenesis
Fondation Leducq

Nicholas E. S. Sibinga, M.D.

Allograft inflammatory factor-1 in atherosclerosis
National Institutes of Health
1R01HL128066-01
3/16/2015 – 2/28/2019

Colony-stimulating factor-1 in graft vascular disease

National Institutes of Health
1R01HL127700-01A1
6/30/2015 – 6/30/2019

Richard N. Kitsis, M.D.

Linking cell death and mitochondrial quality control mechanisms in heart disease

National Institutes of Health
1R01HL128071-01
4/1/2015 – 2/28/2019

A new molecular pathway for diabetic cardiomyopathy

National Institutes of Health
1R01HL130861-01
09/01/2015 – 08/31/2020

Modulating autophagy to treat cardiovascular disease
Fondation Leducq

BAX as a small molecule therapeutic target for myocardial infarction
American Heart Association
Winter 2015 Collaborative Sciences Award

Thomas V. McDonald, M.D.

Large-scale functional phenotyping of ion channel arrhythmia genomic variants
National Institutes of Health
1R21HL120782-01A1 (R21/R33)
08/07/2014 – 06/30/2016

Graduate Student Awards

Dulguun Amgalan (Kitsis lab)

BAX as a small molecule therapeutic target for myocardial infarction
American Heart Association
Predoctoral fellowship

Prameladevi Chinnasamy (Sibinga lab)

Allograft inflammatory factor-1 in atherosclerosis
American Heart Association
Predoctoral fellowship

Marika Osterbur (McDonald lab)

Extra-coding features of mRNA are essential for hERG channel function
National Institutes of Health
F30 HL126283-01A1
(Dates pending)

FOR MORE INFORMATION

To learn about supporting the work of the Wilf Family Cardiovascular Research Institute, please contact:

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ON THE WEB

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



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.