The expression “the cure is worse than the disease” is especially apt when it comes to heart attack: how the heart heals (remodels) can cause more damage than the heart attack itself. Molecular signals govern cardiac repair, and cardiologist Nikolaos G. Frangogiannis, M.D., wants to learn what those signals do.

His research focuses on the inflammation of heart muscle following a heart attack. Inflammation is a normal response after a heart attack, since it destroys dead tissue and promotes healing. But when inflammation persists, healthy collagen that provides structural support to heart cells is broken down and replaced by scar tissue. Excessive scarring (fibrosis) during the healing process can lead to cardiomyopathy (an enlarged and weakened heart), irregular heartbeat and heart failure.

Animal studies conducted by Dr. Frangogiannis, professor of medicine (cardiology) and the Edmond J. Safra/Republic National Bank of New York Chair in Cardiovascular Medicine, suggest that overproduction of TGF-β (transforming growth factor beta)—a protein that helps regulate immune and inflammatory responses as well as tissue repair—causes heart cells to pump out excessive
Heart disease is the world’s leading killer, mainly because of heart failure, which is often the result of past heart attacks. In the United States someone has a heart attack every 37 seconds. We cardiologists have gotten better at treating heart attacks, so the risk of suffering a fatal heart attack has decreased. Ironically, our success in treating heart attacks has allowed more survivors to develop heart failure.

Much of the research at the Wilf Family Cardiovascular Research Institute involves preventing and treating heart failure and heart attack. A major focus of the work of Dr. Nikolaos Frangogiannis is the heart muscle scarring that heart attack victims experience. Dr. Frangogiannis is a worldwide leader in understanding how scarring of the heart starts and how it can be stopped.

At Einstein, we try hard to recruit the very best scientists and clinicians. We attracted Dr. Frangogiannis from the famous unit at Baylor College of Medicine in Houston last year. He says Dr. Frangogiannis, who came to Einstein from Baylor College of Medicine in Houston last year. He hopes to begin a study this year to develop a simple blood test that can identify patients who have high levels of TGF-β and are at increased risk for scarring caused by severe inflammation. His work could lead to personalized post–heart attack treatment strategies that will control levels of TGF-β and other mediators as the heart heals.

“It’s important to block inflammation at the right time. We don’t want to block inflammation globally, as with corticosteroids, because inflammation does help with the repair process,” says Dr. Frangogiannis, who came to Einstein from Baylor College of Medicine in Houston last year. He hopes to begin a study this year to measure blood levels of TGF-β and other inflammatory mediators in heart attack patients from Montefiore, the University Hospital and academic medical center for Einstein, and see if those initial levels correlate with poor healing and heart failure in the months and years following the heart attacks.

Dr. Frangogiannis explains that adverse remodeling after a heart attack can result from defects in genes that help resolve inflammation. Certain common conditions, such as diabetes or high blood cholesterol, may also be associated with defective resolution of inflammation or with an impaired repair response. People with diabetes, for instance, tend to have overactive fibrotic responses.

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Q: Are drugs that block inflammation effective in reducing damage after a heart attack?

A: Inflammation consists of many pathways; some are important for repairing the heart, while others may damage the heart by causing fibrosis (scarring). “One of the goals of our research is developing strategies that block specific inflammatory pathways involved in heart remodeling and the fibrotic process,” says Dr. Frangogiannis. Broad spectrum anti-inflammatory drugs are not specific enough to be useful in repairing the heart. However, some other drugs routinely administered to heart attack patients may act by improving cardiac healing. For example, ACE (angiotensin-converting enzyme) inhibitors, prescribed when the pumping ability of a patient’s heart muscle is significantly impaired, appear to curb fibrosis to some degree.
Can Heavy Be Healthy?

Many heavyset people show no signs of high blood pressure, high cholesterol or diabetes, but are they as healthy as they seem? Using data from the Women’s Health Initiative Observational Study, a team led by Rachel P. Wildman, Ph.D., formerly associate professor of epidemiology & population health, and Sylvia Wassertheil-Smoller, Ph.D., professor of epidemiology & population health, head of the division of epidemiology and the Dorothy and William Manealoff Foundation and Molly Rosen Chair in Social Medicine, found that overweight and obese women often have elevated inflammatory markers (such as C-reactive protein) that, over many years, increase risk for heart disease. The study was published in a 2011 issue of Obesity.

Prostaglandins and Blood Pressure

Victor L. Schuster, M.D., professor of medicine (nephrology) and of physiology & biophysics, chair of the department of medicine at Einstein and at Montefiore and holder of the Ted and Florence Baumritter Chair in Medicine, and his colleagues are investigating prostaglandins—a family of important body chemicals—and their role in controlling blood pressure. A protein called the prostaglandin transporter (PGT) plays a vital role in reducing levels of a prostaglandin called PGE2. Dr. Schuster and his team reported in a 2011 issue of the Journal of Pharmacology and Experimental Therapeutics that a PGT inhibitor called T26A injected into rats blocks PGE2 metabolism and dilates blood vessels, shedding more light on how PGT works. The research could lead to novel medicines to lower blood pressure.

Blocking Blood-Vessel Cell Death

A protein called apoptosis repressor with caspase recruitment domain (ARC) protects against several forms of heart muscle cell death during a heart attack. But ARC isn’t a good guy in all situations. Working with researchers from Johns Hopkins University School of Medicine, Einstein’s Richard N. Kitsis, M.D., professor of medicine (cardiology) and of cell biology, and Chang-Fu Peng, M.D., formerly assistant professor of medicine, have shown for the first time that ARC is also expressed in the smooth muscle cells of lung arteries and plays an essential role in a condition known as pulmonary hypertension—high blood pressure exerted in the arteries of the lungs. ARC appears to support cell proliferation that thickens the blood vessels, leaving a smaller channel and raising pulmonary blood pressure to potentially lethal levels. The study was published in Circulation, the journal of the American Heart Association, in December 2011. In addition, working in the Kitsis lab, Christina Medina-Ramirez, Ph.D., a recent graduate of Einstein’s Sue Golding Graduate Division of Biomedical Sciences, and colleagues showed that ARC plays important roles in the development and metastasis of breast cancers. The study was published in Cancer Research in December 2011.

DID YOU KNOW?

Myth: Thin people don’t get high cholesterol.
Fact: Though heavyset people are more likely to have elevated cholesterol levels, anyone can have this dangerous health problem, including normal-weight and thin people. In fact, people who don’t worry about their weight may be less aware of how much saturated and trans fat they eat. Everyone should have cholesterol checked regularly; how often depends on age, gender, past cholesterol levels or other risk factors.

updates

New Faculty

The Wilf Family Cardiovascular Research Institute welcomes Evripidis Gavathiotis, Ph.D., assistant professor of biochemistry and of medicine, who was recruited to Einstein in 2011 from the Dana Farber Cancer Institute. Dr. Gavathiotis’ research centers on a molecule called BAX, which plays a key role in driving cell death when a heart attack or stroke deprives cells of oxygen. Dr. Gavathiotis has identified several “trigger points” at which BAX is activated. “For patients who have suffered a heart attack, we’re looking for a drug that would inactivate BAX and prevent cell death,” he says.

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.
LEGACY: EDMUND H. SONNENBLICK, M.D.

Edmund H. Sonnenblick, M.D., Einstein’s first chief of cardiology, was a pioneer of modern cardiovascular science and medicine. Dr. Sonnenblick joined the Einstein faculty in 1975 as chief of the division of cardiology and served in that role until 1996, when he was named Distinguished University Professor. He died in 2007, soon after learning that the American Heart Association would honor him with its prestigious Research Achievement Award.

Edmund Sonnenblick was one of the first scientists to recognize that the heart is governed by physiologic rules similar to those that regulate the body’s other muscles. His research into the structure and function of heart muscle cells helped provide the physiologic foundation for understanding how the heart works. He and Einstein’s William Frishman, M.D., pioneered the use of beta blockers for heart failure. His work also helped lead to the development of ACE inhibitors—one of the main classes of antihypertensive drugs. And together with Einstein’s James Scheuer, M.D., now University Chair and Distinguished Professor Emeritus of Medicine, and Leslie A. Leinwand, Ph.D., formerly professor of microbiology & immunology, of genetics and of medicine, Dr. Sonnenblick created one of the first molecular cardiology programs in the country.

“Ed Sonnenblick was a towering figure in both clinical cardiology and cardiovascular research,” says Dr. Kitsis. “He possessed an extraordinary intellect as well as being a warm and approachable human being. He trained literally hundreds of cardiology fellows and led by example.”

Dr. Sonnenblick was the inaugural holder of the Edmond J. Safra/Republic National Bank of New York Chair in Cardiovascular Medicine, which was established by Edmond J. Safra, a distinguished Benefactor of Einstein and of Yeshiva University. Honorary Einstein Overseer Charles A. Krasne, a longtime supporter of medical research and education programs at the College of Medicine and Einstein Benefactor, recalls Dr. Sonnenblick fondly. “I was privileged to know Ed Sonnenblick for many years, and he holds a special place in my thoughts,” says Mr. Krasne. “He was not only a brilliant scientist—he was a devoted and exceptional physician, as well as a close friend. He leaves a great legacy.”

In April of this year, world-class heart failure researcher Thierry LeJemtel, M.D., professor of medicine at Tulane University and medical director of heart transplantation at Tulane University Hospital, was the featured speaker at a lecture Einstein named in Dr. Sonnenblick’s honor.

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 Ira Lipson, director of institutional advancement, at 718.430.2371 or ira.lipson@einstein.yu.edu.

FOR MORE INFORMATION

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.