The Curious Case of Adiponectin

Why do some people have heart attacks while others don’t? A major culprit is the highly individualized pattern of fat buildup in our blood vessels—the result of what we eat, what we do and our personal palette of body chemicals governing fat buildup (plaque). One of these signature substances is adiponectin, a bioactive hormone that our fat cells secrete into the bloodstream.

In animals, adiponectin inhibits plaque formation in arteries, helps hold down inflammation in blood vessel walls and also boosts insulin sensitivity (helping clear vessel-damaging sugars from the blood).

Earlier studies had shown that in younger people, a high adiponectin level was a sign of overall good health. In 2004, for example, a major epidemiology study linked high levels of adiponectin to reduced heart-attack risk in healthy middle-aged (continued on page 2)

Jorge Kizer, M.D., studies molecules that influence cardiovascular health.
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men. Soon adiponectin was viewed as a biological marker of good cardiovascular health for everyone.

So in 2008, Einstein’s Jorge Kizer, M.D., received a surprise after seeing the results of his analyses of nearly 1,400 elderly people participating in the National Institutes of Health–funded Cardiovascular Health Study. He noticed that those with the highest adiponectin levels had higher rates of heart disease than people with lower levels. Soon Dr. Kizer, director of clinical cardiovascular research in Einstein’s department of medicine, found himself drawn into the scientific debate dubbed the “adiponectin paradox.”

Good or Bad?

These findings led Dr. Kizer and colleagues to pursue an investigation in the Cardiovascular Health Study cohort, where adiponectin was measured in almost 4,800 participants. This follow-up study was the largest to date examining the relationship between adiponectin and fatal events in older men and women (65 to 100 years old). The findings suggested an ideal level of adiponectin—not too high, not too low—for elderly people with no cardiovascular disease, heart failure or atrial fibrillation (irregular heartbeat).

“The highest risk of death was associated with the highest and lowest blood levels of adiponectin, while those in the middle had the lowest risk of death,” explains Dr. Kizer, an associate professor of medicine (cardiology) and of epidemiology & population health.

Further findings added a twist to the curious case of adiponectin: in older people with heart failure or atrial fibrillation, only the highest levels were dangerous.

It turns out that in older people, increases in adiponectin reflect generally worsening health. Levels rise after a heart attack or as heart failure develops and also following other physical insults, including unintentional weight loss, muscle wasting and declining kidney function. “The sicker you are, the stronger the association between high adiponectin levels and risk of dying,” says Dr. Kizer.

The adiponectin story highlights the complex ways in which biological molecules can act as markers and determinants of disease. Dr. Kizer and others will continue to research adiponectin’s mechanisms—and what they mean for health as we age.

Beyond Adiponectin

Like other Einstein researchers, Dr. Kizer has several research interests and clinical responsibilities:

• He studies molecules that form as a result of chronically high sugar and oxidant levels and their role in heart and kidney disease.
• He investigates noninvasive imaging of the heart and arteries in the early detection of cardiovascular disease and in evaluating risk.
• He collaborates with other Einstein researchers on how HIV ages the cardiovascular system.
• As an attending physician in medicine at Montefiore, the University Hospital and academic medical center for Einstein, Dr. Kizer studies STEMI (ST segment elevation myocardial infarction) and works to build Montefiore’s STEMI registry.

Q&A

Q: What is the Goldilocks principle?

A: It refers to an amount that’s not too much, not too little, but just right. Take alcohol: Moderate drinkers live longer than teetotalers or those who drink to excess. Other examples include salt, exercise, body weight and—as described above—adiponectin levels in older people. Sometimes, the middle of the road is the place to be.
Arteriosclerosis and Transplants
Nicholas E. S. Sibinga, M.D.
Associate Professor of Medicine (Cardiology)
Associate Professor of Developmental and Molecular Biology
Albert Einstein College of Medicine
Attending Physician (Cardiology)
Montefiore Einstein Center for Heart and Vascular Care

Patients who receive organ transplants need clear, healthy arteries to supply blood and nutrients to their new organs. Unfortunately, a transplanted organ’s blood vessels often thicken, threatening the long-term success of the transplant. This thickening is called transplant-associated arteriosclerosis. It can have two causes: immune cells that invade the vessel and abnormal growth of vascular smooth muscle cells, which form the walls of blood vessels.

Working with a group led by E. Richard Stanley, Ph.D., Dr. Sibinga and his team showed that CSF-1, a molecule that regulates the activity of certain immune cells, caused mouse arteries to become dangerously thick by triggering smooth muscle cells to proliferate. The artery thickening slowed when CSF-1 was absent. The research suggests that inhibiting CSF-1 activity could combat the life-threatening artery thickening that often accompanies a heart transplant. The study appeared in a 2013 edition of Arteriosclerosis, Thrombosis and Vascular Biology.

Growing Blood Vessels
Bin Zhou, M.D., Ph.D.
Professor of Genetics
Professor of Pediatrics
Professor of Medicine (Cardiology)
Albert Einstein College of Medicine

When the coronary arteries become blocked or otherwise diseased, heart muscle dies (which we call a myocardial infarction, or heart attack). Dr. Zhou’s research may yield a way to replace diseased arteries with brand-new ones.

Dr. Zhou and his team had previously found that, during fetal development, the coronary arteries originate in a network of primitive blood vessels in heart muscle. Further research has shed light on how this happens. The researchers found that a molecule called Vegfr1, produced in the endocardium, or innermost lining of the heart, is required for the normal development of coronary arteries. When the researchers removed Vegfr1 from the endocardium of mouse embryo hearts, they saw a surge in molecules that promote coronary vessel growth plus earlier-than-normal coronary angiogenesis. The findings may lead to ways of “coaxing” endocardial cells to build new coronary arteries. The study was published in a 2013 edition of PLOS ONE.

Predicting Heart Failure Survival
Daniel M. Spevack, M.D.
Associate Professor of Clinical Medicine
Albert Einstein College of Medicine
Medical Director
Noninvasive Cardiology
Montefiore Medical Center

Most diagnostic tests used to evaluate heart function focus on the heart’s ability to squeeze. Measuring the heart’s ability to expand and fill with blood is more difficult. But a key way of doing so—measuring the left ventricular end diastolic pressure-volume relationship (LV-EDPVR)—requires a procedure so invasive and complex that it’s rarely used.

In a large recent study of patients with congestive heart failure, Dr. Spevack and his colleagues found they could fine-tune echocardiography, an imaging technology that is not invasive (no insertion of instruments into the body), to predict accurately which heart failure patients were most likely to survive. The findings, published in a 2013 issue of the Journal of Cardiac Failure, offer clinicians a noninvasive way to assess heart attack damage in their patients.

UPDATE: Latino Heart Health
Mario J. Garcia, M.D., co-director of the Montefiore Einstein Center for Heart and Vascular Care, was a keynote speaker at the fourth annual Tu Corazón Latino Health Summit, a conference dedicated to Latino cardiovascular health. The conference featured leaders from fields including medicine, the media, nutrition, culinary arts and public policy. It was sponsored by the American Heart Association/American Stroke Association and Montefiore and was held in November 2013 at the Bronx Museum of the Arts.

“Diseases of the heart are the number-one health threat we face as Latinos, and research shows we lack awareness,” said Dr. Garcia, a professor of medicine and of radiology and the Pauline Levitt Chair in Medicine at Einstein. “By combining our medical knowledge and research with Latino leadership, we can make people more aware of cardiovascular health.”
In January 2014, the Montefiore Einstein Center for Heart and Vascular Care presented “A Practical Approach to Electrophysiology,” a continuing-education symposium for physicians, physician assistants, nurse practitioners, registered nurses and fellows. Einstein faculty included Einstein’s Mario J. Garcia, M.D., center co-director and chief of cardiology at Einstein and Montefiore, and Luigi Di Biase, M.D., Ph.D., an associate professor of medicine (cardiology), who served as symposium director. Both are Wilf Institute members.

Conference attendees gained knowledge about:

- catheter-based therapies as an alternative to traditional drug treatment in managing atrial and ventricular arrhythmias;
- novel anticoagulants and their role in treating atrial fibrillation; and
- the role of new device therapies for preventing thromboembolism in patients with underlying atrial fibrillation.

Einstein and Montefiore Collaborate on Symposium for Physicians and Clinicians

Top, an electrocardiogram of a normal heartbeat; bottom, an ECG showing atrial fibrillation.

Notable Grants

Bin Zhou, M.D., Ph.D., a professor of genetics, of pediatrics and of medicine (cardiology), has received a grant from the National Heart, Lung and Blood Institute (NHLBI) to study the mechanisms of coronary ostium (opening) formation and coronary artery patterning (growth of branches).

Thomas V. McDonald, M.D., a professor of medicine (cardiology) and of molecular pharmacology, and attending cardiologist in the department of medicine at Montefiore and co-director of the Einstein-Montefiore Cardiogenetics Clinic, has received an NHLBI grant to investigate cardiac mechanisms that may lead to new diagnostic and therapeutic approaches to hereditary and acquired arrhythmia syndromes.

For more Information

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

Office of Institutional Advancement
Albert Einstein College of Medicine
Jack and Pearl Resnick Campus
1300 Morris Park Avenue
Harold and Muriel Block Building
Room 726
Bronx, NY 10461
718.430.2411
institutionaladvancement@einstein.yu.edu
www.einstein.yu.edu/donors/