Detecting Diabetes the Metabolomic Way

The Diabetes Research Center (DRC) welcomes endocrinologist Irwin J. Kurland, M.D., Ph.D. (pictured at right), a nationally recognized expert in metabolic biology. He was recruited from Stony Brook University to direct Einstein’s new Metabolomics and Stable Isotope Core Facility, located in the Michael F. Price Center for Genetic and Translational Medicine/Harold and Muriel Block Research Pavilion.

What is metabolomics? This emerging discipline is a sophisticated way of assessing metabolism—the sum of all chemical reactions occurring in a person’s body. These reactions—digesting food so it can be stored as energy, for example—leave behind “fingerprints” in the form of chemical by-products, or metabolites, in amounts so small that only recently could they be detected.

Metabolomics uses highly sensitive instruments to detect and measure these metabolites. Subtle abnormalities in those levels can signal the early stages of certain diseases long before symptoms are evident.

Dr. Kurland uses metabolomics to

continued on page 2
I’m pleased to announce several new developments at Einstein’s Diabetes Research Center.

Over the past two years, we’ve recruited a number of investigators to Einstein to head up new laboratories. These investigators conduct research on a wide variety of diabetes-related topics, including glucose metabolism and insulin secretion in type 2 diabetes, the autoimmunity of type 1 diabetes and behavioral factors that keep people from sticking with their diabetes therapies. One of these investigators, Irwin Kurland, M.D., Ph.D., is featured on the cover of this newsletter, and the work of other new investigators is described on the facing page.

We’ve also increased our research support, with new and newly reorganized core services. This includes expanding our Physiology Core staff expertise and creating the new Metabolomics Core, which provides synergy with the Physiology Core for metabolite profiling; adding cutting-edge assay systems; and incorporating the services of the Analytical Imaging Facility (light and electron microscopy), the Flow Cytometry Facility (cell analysis and sorting) and the newly established Einstein Epigenomics Facility (DNA modification and gene-expression profiling).

Finally, we’ve substantially increased our collaborations with neighboring institutions in the New York metropolitan area. Several exciting new studies with faculty at Mount Sinai Medical School and Columbia University are now under way, and we’re also organizing junior-faculty seminars and mentorship programs with these institutions. Our goal is to form strong partnerships to address the major health problems and quality-of-life issues caused by diabetes and related disorders.

**Detecting Diabetes continued**

A study “metabolic flexibility”—the body’s ability to match its energy requirements to its energy intake as it switches between using carbohydrates immediately after meals and metabolizing fats after fasting overnight. Healthy people can readily make this switch; often those who have trouble doing so are obese and are predisposed to developing diabetes, he says.

A former engineer who began his career designing satellites and lasers at Hughes Aircraft in California, Dr. Kurland focuses on a symptomless but important condition known as pre-diabetes. When people have pre-diabetes, their blood glucose (sugar) levels are slightly elevated but not yet in the diabetic range. Nevertheless, even the “slightly abnormal” blood glucose levels found in pre-diabetes are far from harmless. Over the years, they can contribute to long-term damage to the heart and circulatory system. And equally important, pre-diabetes all too often leads to full-blown type 2 diabetes.

Pre-diabetes is surprisingly common in the United States; the American Diabetes Association estimates that 57 million people are affected. But a major problem is diagnosing it—something that the standard test for diabetes can’t do. In that test, people drink a glucose solution; then, two or more hours later, the level of glucose in their blood is measured. Normally, the body’s release of insulin in response to a glucose “meal” will rapidly lower glucose levels in the blood. A test result showing an abnormally high glucose level indicates insulin resistance (the body’s failure to respond properly to the insulin it produces)—the hallmark of type 2 diabetes. But the test isn’t sensitive enough to detect subtle delays in the pancreas’s normally rapid release of insulin right after a meal containing glucose or other carbohydrates. Dr. Kurland’s metabolomics expertise allows him to detect these subtle glitches in the body’s insulin response.

Dr. Kurland has developed and patented a pre-diabetes test that uses glucose tagged with stable, non-radioactive isotopes. By measuring the isotope pattern in the glucose response, the test picks up subtle metabolic abnormalities that can occur within minutes of a meal.

Dr. Kurland notes that his test wouldn’t be needed if people avoided becoming overweight, the main culprit in pre-diabetes and type 2 diabetes. The solution, he says, is a balanced diet and regular exercise.

While we clean up our shopping lists and lace up our walking shoes, investigators under Dr. Kurland’s direction at the Metabolomics and Stable Isotope Core Facility will continue to research ways to detect, prevent or reverse diabetes.

Dr. Kurland is also profiled in the Summer/Fall 2009 issue of EINSTEIN Magazine.

**Q: Why are so many Americans developing type 2 diabetes?**

**A:** Type 2 diabetes—now the sixth-leading cause of death in the United States—is becoming more common for several reasons, including decreased physical activity and the aging of the population. But the most important reason for the rise in type 2 diabetes is our “overweight epidemic”; more than two-thirds of American adults are overweight or obese. Just why obesity or being overweight causes diabetes remains unknown. One possibility: eating too much may trigger an inflammatory response that provokes insulin resistance, which ultimately causes type 2 diabetes. (See the article on the facing page about Dr. Olefsky’s 2009 Rifkin Visiting Professor lecture.)
**NEW FACULTY**

Claire C. Bastie, Ph.D.
Dr. Bastie studies the metabolism of fat and glucose. She works with knockout mouse models (mice in which certain genes have been intentionally inactivated). Dr. Bastie recently identified a novel signaling pathway involved with increased calorie burning and insulin sensitivity.

Dongsheng Cai, Ph.D.
Dr. Cai is studying the brain’s involvement in diabetes, obesity, cardiovascular disease and other metabolic disorders. In previous research, he discovered that the cell-signaling pathway in the hypothalamus known to be associated with inflammation is also involved in food intake.

Jeffrey Gonzalez, Ph.D.
Dr. Gonzalez studies why patients don’t stick with prescribed treatments. He is developing ways to help chronically ill patients—particularly those with diabetes—adhere to their treatment regimens. In recent studies, he found that depression can lead to poor treatment compliance among diabetics.

Colette Knight, M.D.
Dr. Knight is examining whether resveratrol, the highly publicized antioxidant in red wine, improves glucose metabolism. She has already found that resveratrol helps protect against metabolic slowdowns that accompany aging.

Matthew Levy, Ph.D.
Dr. Levy uses novel techniques for uncovering basic biological interactions important in diabetes. For example, his lab is creating aptamers (the nucleic-acid equivalent of antibodies) that bind to specific key receptors on the surface of pancreatic beta cells—the insulin-making cells that are destroyed in type 1 diabetes. Use of these aptamers could help researchers monitor the progression of type 1 diabetes in experimental animals.

Dr. Gonzalez studies why patients don’t stick with prescribed treatments. He is developing ways to help chronically ill patients—particularly those with diabetes—adhere to their treatment regimens. In recent studies, he found that depression can lead to poor treatment compliance among diabetics.

Colette Knight, M.D.
Dr. Knight is examining whether resveratrol, the highly publicized antioxidant in red wine, improves glucose metabolism. She has already found that resveratrol helps protect against metabolic slowdowns that accompany aging.

Matthew Levy, Ph.D.
Dr. Levy uses novel techniques for uncovering basic biological interactions important in diabetes. For example, his lab is creating aptamers (the nucleic-acid equivalent of antibodies) that bind to specific key receptors on the surface of pancreatic beta cells—the insulin-making cells that are destroyed in type 1 diabetes. Use of these aptamers could help researchers monitor the progression of type 1 diabetes in experimental animals.

**ON THE WEB**

To learn more about the Diabetes Research Center, please visit its website at www.einstein.yu.edu/diabetes

**Diabetes Hot Spot: The Bronx**

With nearly 12 percent of its young adults affected by diabetes, the Bronx ranks as a diabetes “hot spot.” In response, Einstein’s Diabetes Research Center (DRC) and Montefiore’s Clinical Diabetes Center (CDC) have developed many diabetes-management programs, including “Bronx HbA1c: Bring It Down for Health.” This collaboration between the DRC and the New York City Department of Health is supported by a grant from the NIH. The name refers to a test that people with diabetes should take every three to six months. The HbA1c test measures the amount of glucose bound to the hemoglobin in red blood cells—an indication of how well people have controlled their blood sugar over the preceding three or four months. Bilingual health educators regularly call diabetes patients whose HbA1c results are elevated and encourage them to adhere to their treatment regimens.

**Comparing Diabetes Therapies**

The Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) study, a DRC initiative in collaboration with the Montefiore CDC, assessed the best treatments for patients with type 2 diabetes and stable heart disease. The results, published in the New England Journal of Medicine, showed no significant difference in the rate of death, heart attacks or strokes in patients who controlled blood glucose with insulin versus insulin-sensitizer medications. Surprisingly, angioplasty or stenting did not change outcomes, implying that these common procedures rarely help. Some patients with type 2 diabetes and advanced heart disease did benefit from medical therapy plus prompt bypass surgery.

**Internationally Renowned Type 2 Diabetes Expert Speaks at Einstein**

Jerrold M. Olefsky, M.D., whose research advances have helped reveal the cause of type 2 diabetes, spoke at Einstein in April as the 2009 Harold Rifkin lecturer.

Dr. Olefsky is professor of medicine, associate dean for scientific affairs and director of the University of California Los Angeles/San Diego Diabetes Center. He has published more than 450 scientific studies and received numerous important awards. Dr. Olefsky’s research has defined the basic genetic and cellular mechanisms underlying insulin resistance and identified it as a primary cause of type 2 diabetes. More recently, he showed that overeating can activate the immune system, resulting in inflammation that encourages insulin resistance.

The Rifkin two-day series of basic and clinical lectures is sponsored annually by the DRC in memory of Harold Rifkin, M.D., a clinical professor with a nearly 50-year association with Einstein and Montefiore Medical Center. Dr. Rifkin served as president of both the American Diabetes Association and the International Diabetes Federation, and he edited the first of many editions of Diabetes Mellitus: Theory and Practice. His extraordinary intellect, charismatic teaching and advocacy for patient care and research were widely recognized.
our donors

NOTABLE GIFTS AND GRANTS

The Albert Einstein Diabetes Research Center gratefully acknowledges the generosity of the following donors, whose support is critical to advancing the mission of the DRC.

Judy R. Rosenberg was one of a pioneering group of women who, beginning in 1953, helped turn the dream of a medical school at Yeshiva University into reality. A passionate supporter of the College of Medicine until her death in 2008, Judy served on the Einstein Board of Overseers for 30 years and was a founder of Einstein’s National Women’s Division.

Judy and her husband, Alfred, were Benefactors of the College of Medicine, and they endowed the position of Faculty Scholar in Diabetes Research at Einstein. In 1996, following Alfred’s death, Judy established the Judy R. and Alfred A. Rosenberg Professorial Chair in Diabetes Research. The Rosenberg Chair is an enduring testament to their steadfast commitment to advancing diabetes research at Einstein. Dr. Jeffrey E. Pessin, director of the Diabetes Research Center, is the current Rosenberg Professorial Chair.

The Skirball Foundation has contributed $1 million in support of research at Einstein’s Jack D. Skirball Institute for Nutrient Sensing in Diabetes and Obesity. The Skirball Institute, established in 2003 with an initial gift of $1.5 million from the Foundation, has helped make it possible for Gary Jordan Schwartz, Ph.D., professor in the departments of medicine and neuroscience at Einstein, to discover the biological mechanism used by the brain to sense when hunger has been satisfied.

The Foundation’s most recent gift is supporting a multidisciplinary research initiative led by Dr. Schwartz. In collaboration with other Einstein senior investigators—in the areas of diabetes, obesity, developmental neurobiology, reproductive biology and behavioral medicine—Dr. Schwartz is developing a technique to curb a person’s appetite by triggering the brain’s “hunger shutoff switch.” The resulting weight loss may help prevent the onset of type 2 diabetes. Dr. Schwartz’s innovative appetite-curbing technique is slated for clinical trials later this year.

EVENTS

Diabetes “Visiting Committee” Forming This Fall

We are pleased to announce that Einstein is forming a Visiting Committee for the Diabetes Research Center. The committee will be composed of supporters who wish to be more deeply involved with diabetes research at Einstein. Members will have the opportunity to meet leading faculty members and learn about the latest research developments. The first meeting of the Visiting Committee will be held this fall. For more information, please contact Ira Lipson, Director of Institutional Advancement, at 718.430.2371 or ira.lipson@einstein.yu.edu.

To learn more about supporting the work of the DRC, please contact:

Glenn Miller
Associate Dean for Institutional Advancement
Albert Einstein College of Medicine
Jack and Pearl Resnick Campus
1300 Morris Park Avenue, Mazer 726
Bronx, NY 10461
718.430.2411
glenn.miller@einstein.yu.edu

DIABETES RESEARCH CENTER

Our mission:
• To support and conduct basic and clinical research related to diabetes and its causes, treatment and complications
• To encourage research that will rapidly lead to diabetes therapies, especially in minority and underserved populations

ADMINISTRATION

Director
Jeffrey Pessin, Ph.D.

Co-Director
Norman Fleischer, M.D.

Associate Directors
Michael Brownlee, M.D.
Streamson Chua, M.D., Ph.D.
Gary Schwartz, Ph.D.
Elizabeth Walker, Ph.D., R.N.

Administrator
Aneleen Dizon, M.P.A.