Our immune systems defend us against microbes that threaten our health. But sometimes this vigilance backfires, and our tissues become targets instead. This glitch in the immune response is called autoimmunity—the body attacking itself. It can lead to autoimmune diseases, one of which is type 1 diabetes.

The culprits in type 1 diabetes are the immune system’s T cells. Instead of targeting bacteria and viruses, some T cells attack pancreatic cells, known as beta cells, that make insulin, the vital hormone that converts sugars, starches and other nutrients into energy.

People whose beta cells are destroyed by autoimmune attack develop type 1 diabetes. They require daily insulin supplements (usually by injection) to keep blood glucose under control. (People with the more common form of diabetes, known as type 2 diabetes, either don’t make enough insulin or their bodies don’t respond to the insulin that they produce. In both types, excess blood sugar forms toxic compounds that can damage tissues, leading to problems such as nerve damage, impaired vision and heart disease.)

Type 1 diabetes could be prevented if T cells could be deterred from attacking pancreatic cells. That has been the mission of Teresa P. DiLorenzo, Ph.D., associate professor in the departments of microbiology & immunol-
I’d like to share with you some of the new developments in the Albert Einstein Diabetes Research Center.

First, we’re pleased to announce an award of approximately $10 million from the National Institutes of Health that will continue funding our diabetes center for five more years. The money will support our Biomedical Research and Prevention & Control Cores, which offer important infrastructure support for nearly 90 independent investigators. These funds also provide Pilot & Feasibility grants for developing innovative approaches for understanding the basic mechanisms underlying diabetes and developing new treatments.

The investigators of the Einstein Diabetes Research Center strive to collaborate with neighboring institutions in the New York metropolitan area as well as colleagues nationwide and around the world. Last May, we hosted a New York Regional Diabetes Symposium attended by more than 200 people. The symposium featured research presentations by eight junior faculty members from Columbia University, Weill Cornell Medical College, Mount Sinai School of Medicine and Einstein. In the fall of 2009, we held a continuing medical education program for our Brazilian colleagues.

Our continued efforts to improve treatments for diabetes and eventually develop a cure require bright and resourceful investigators. This year we’ve successfully recruited two new outstanding investigators. Rubina A. Heptulia, M.D., came to us from Baylor College of Medicine and will direct our division of pediatric endocrinology, and Rajat Singh, M.B., B.S., formerly at the Einstein Liver Center, will study diabetes as an assistant professor in the departments of medicine and molecular pharmacology. We are thrilled that these exceptional individuals will be enhancing our research and patient-care efforts, and we welcome them warmly to our Diabetes Center family.

**Type 1 Diabetes (continued)**

The dendritic cells essentially “tell” T cells which proteins to zero in on when launching an immune attack. To perform this job, dendritic cells swallow a protein, digest it and then present the protein’s antigen to the T cells as if to say, “Here’s your target—attack it wherever you find it in the body.” Unfortunately, type 1 diabetes will occur if that antigen being targeted happens to belong to the pancreas’s beta cells.

What if you could fool the dendritic cells—induce them to pass along antigens that would kill the T cells rather than prime them to attack beta cells? Dr. DiLorenzo’s laboratory is manipulating dendritic cells to accomplish just that. (See sidebar below.) “Ideally,” says Dr. DiLorenzo, “we’d supply dendritic cells with antigens that would not only wipe out ‘bad’ T cells (those that destroy beta cells) but would also foster the growth of so-called regulatory T cells, which would knock out any bad T cells that might still be lurking.”

“Tolerizing” immune systems of people at risk for type 1 diabetes (e.g., due to family history) might prevent it. And since people diagnosed soon after onset of type 1 diabetes retain about 20 percent of their beta cells, tolerance therapy early on might halt diabetes in its tracks.

**STUDENT PROFILE: Jeffrey Babad**

Jeffrey Babad’s pet hamster once bit him, a childhood trauma that hasn’t deterred him from rodent research.

Jeffrey, a third-year Ph.D. student in Dr. DiLorenzo’s lab, works with mice that ordinarily develop type 1 diabetes. His goal is to “tolerize” their T cells so they won’t attack beta cells and cause diabetes.

Tolerizing occurs naturally in mice as well as men, courtesy of immune system cells called dendritic cells.

Just as dendritic cells prime some T cells to attack foreign cells, they teach others to ignore the heart, brain and other tissues. Dendritic cells engulf and digest a segment of heart protein, for example, and then present a bit of it to T cells, which learn not to attack in the same way that a dog that has swallowed a bee will avoid honeybees.

Jeffrey is delivering a similar message to T cells that would otherwise attack mouse beta cells. He starts with an antigen (small section of protein) that T cells are known to target when attacking beta cells. He attaches this antigen to an antibody, which homes in on molecules jutting from the surface of dendritic cells. Once the antibody attaches to these molecules, called DEC-205, its antigen “cargo” is ingested by dendritic cells and presented to T cells.

When the antigen was later introduced into the mice, no immune response occurred—evidence that tolerance was achieved. More research will be needed before this strategy can be tried on people, but the payoff could be significant: “We may be able to prevent type 1 diabetes from developing,” says Jeffrey.

No mouse has bitten him yet.

The researchers are also trying to make the immune system tolerate rather than attack beta-cell antigens. The strategy: Kill off the T cells responsible for the immune attack. To help them in this effort, Dr. DiLorenzo and her colleagues have enlisted other immune cells known as dendritic cells.

The researchers have identified IGRP’s antigen, the key fragment of the IGRP protein that T cells recognize. Identifying the antigens targeted by T cells might allow scientists to stop early diabetes from worsening or even prevent the disease entirely. To that end, Dr. DiLorenzo’s lab is researching strategies to short-circuit the attraction between T cells and antigens such as IGRP.

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**One-Stop Biomarker Testing**

“Share and share alike” could be the motto of Albert Einstein College of Medicine. Einstein’s 40 shared facilities and “cores” allow researchers from many departments to take advantage of expensive instrumentation and specialized expertise. Two cores essential to the work of the Diabetes Research Center (DRC) are the Hormone Assay Core (where insulin and other hormones are measured) and the Einstein-Montefiore Institute for Clinical and Translational Research’s Analytic Core (for processing DNA and analyzing levels of lipids and other biomarkers that are important in diabetes).

Within the next few months, the two cores will merge to form the state-of-the-art Biomarker Analytical Resource Center, led jointly by the two cores’ current directors: Norman Fleischer, M.D., professor in the department of medicine (endocrinology) and Jacob A. and Jeanne E. Barkey Chair in Medicine, and Daniel T. Stein, M.D., associate professor in the department of medicine (endocrinology). The center features “high-throughput robotics”—automated equipment that rapidly measures levels of numerous biomarkers in thousands of blood samples simultaneously. The center’s benefits will extend to other disciplines, such as cancer and heart disease, in which biomarker measurement is increasingly important.

**The DRC in Action!**

The effort to combat diabetes and its serious complications begins with research. Einstein’s DRC administers the Diabetes Research and Training Center, one of only five centers in the country awarded a competitive National Institutes of Health grant that funds diabetes research. DRC scientists collaborate with the Montefiore Clinical Diabetes Center, a patient-oriented program that diagnoses and treats diabetes in the Bronx, where the disease is prevalent and devastating. The Montefiore Clinical Diabetes Center has a comprehensive approach for patient care:
- The outpatient program team provides state-of-the-art care to a large population of type 1 and type 2 diabetes patients. Each year, more than 300 high-risk diabetes patients participate in workshops to learn how to manage their diabetes, courtesy of a program called the Proactive Managed Intervention System for Education in Diabetes (PROMISED).
- The inpatient program team identifies patients with diabetes who need better glycemic control and helps patients manage their diabetes after they leave the hospital.

Education and treatment programs are available at both the East (Moses) and West (Weiler) campuses.

Diabetes Research Center (DRC) are the Hormone Assay Core (where insulin and other hormones are measured) and the Einstein-Montefiore Institute for Clinical and Translational Research’s Analytic Core (for processing DNA and analyzing levels of lipids and other biomarkers that are important in diabetes).

**Fascinating Fact**

“Diabetes” is a Greek word that means “siphon.” Excessive urination is a symptom of diabetes, and the name for the disease is credited to the second-century Greek physician Aretus the Cappadocian, who wrote about patients (presumably with diabetes) who “passed water like a siphon.”

**Fat-Burning Drug Could Block Diabetes**

Those ads about burning off fat may have some validity after all. Claire Bastie, Ph.D., assistant professor in the department of medicine (endocrinology), and her team identified a chemical that blocks an enzyme called Fyn kinase. Mice that received the blocker burned more fatty acids, which could potentially prevent type 2 diabetes by leading to weight loss. Furthermore, the Fyn kinase blocker also increased insulin sensitivity—another change that makes type 2 diabetes less likely. Since humans also have Fyn kinase, Dr. Bastie’s discoveries could lead to both a new type of weight-loss drug and a new way to prevent type 2 diabetes.

The study was published in the February 2010 issue of *Cell Metabolism*.

**Anti-inflammatory Agent Shows Encouraging Results**

Salsalate is a nonsteroidal anti-inflammatory drug that is chemically similar to aspirin but less irritating to the stomach. Used for many years to treat arthritis, salsalate has recently shown promise in treating type 2 diabetes. In a three-month trial involving Einstein investigators and published in the March 2010 online issue of *Annals of Internal Medicine*, the drug significantly improved blood glucose levels in people taking it. The researchers hope for continued funding from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) so that they can carry out a larger study investigating salsalate as a diabetes treatment. The study was led by researchers at Boston’s Joslin Diabetes Center and included Einstein’s Eric J. Epstein, M.D., assistant professor in the department of medicine (endocrinology), and Jill P. Crandall, M.D., associate professor of clinical medicine, department of medicine (endocrinology).

**ON THE WEB**

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

**Discoveries**

Einstein’s Jack D. Weiler Hospital is one of several locations where patients can get information and treatment.

The new core’s automated system will dramatically improve sample turnaround times.
our supporters

NOTABLE GIFTS AND GRANTS

The Albert Einstein Diabetes Research Center gratefully acknowledges the generosity of the individuals and organizations whose support is critical to advancing its mission.

The Juvenile Diabetes Research Foundation (JDRF) has awarded $187,000 to Michael Brownlee, M.D., the Anita and Jack Saltz Chair in Diabetes Research and professor in the departments of medicine (endocrinology) and pathology. These funds, which are an extension of a 5-year grant of $5,909,781 from the JDRF, will support Dr. Brownlee’s study of a newly discovered mechanism by which diabetes damages kidneys. Diabetes is the leading cause of kidney failure in the United States and the developed world; Dr. Brownlee’s innovative research may lead to new treatments to prevent diabetic kidney disease. Dr. Brownlee is director of the JDRF International Center for Diabetic Complications Research (ICDCR), which develops effective therapies for complications caused by type 1 diabetes. The ICDCR brings together leading research groups from three continents: the United States (Albert Einstein College of Medicine), Australia (the Baker Heart Research Institute in Melbourne) and Europe (the University of Heidelberg).

EVENTS

Visiting Committee Update

The DRC held its first meeting of the newly formed Diabetes Visiting Committee on January 13 at the New York office of Einstein Overseer Benjamin Winter. DRC Director Jeffrey Pessin, Ph.D., holder of the Judy R. and Alfred A. Rosenberg Endowed Professorial Chair in Diabetes Research, described past and current research developments at the DRC. Norman Fleischer, M.D., the Jacob A. and Jeanne E. Barkey Chair in Medicine, then discussed groundbreaking work in type 1 and type 2 diabetes. Committee members shared their interests in diabetes research and discussed future activities of the group.

Diabetes has reached critical levels in the United States, and the number of U.S. patients affected is expected to double over the next 25 years. The toll on individual health is enormous. The expected cost in economic terms is estimated to be $336 billion—more than 30 percent of our nation’s overall healthcare budget.

The Diabetes Visiting Committee will greatly assist the Einstein DRC as Dr. Pessin and his colleagues address the challenges that lie ahead in combating this devastating disease. To learn more or to tell us about your interests, please contact Liz Alberti at 718.430.4178 or liz.alberti@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

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