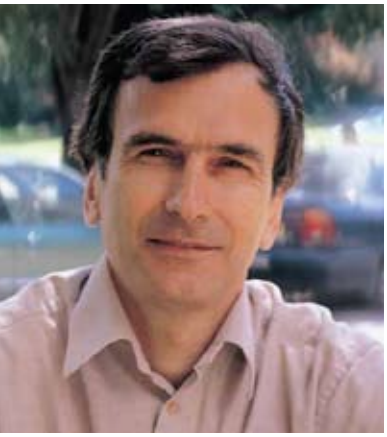
AMERICAN COMMITTEE FOR THE WEIZMANN INSTITUTE OF SCIENCE
SCIENCE FOR THE BENEFIT OF HUMANITY

Issue No. 25

WEIZMANN*views*

THE DIABETES AND OBESITY CONNECTION

More than 220 million people around the world suffer from diabetes, a chronic condition in which abnormally high levels of glucose (sugar) circulate in the blood. Type 2 diabetes, the most common form of the disease, develops when the body cannot adequately produce, or improperly uses, insulin, a hormone that regulates blood sugar levels. People with type 2 diabetes are at an increased risk for many serious health problems, including heart disease, blindness, and kidney damage. Notably, according to the National Institutes of Health, more than 85 percent of those with type 2 diabetes are overweight.



Prof. Michael Walker

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"Most researchers believe that the rising rate of obesity is the driving force behind the epidemic of type 2 diabetes," says Prof. Michael Walker of the Weizmann Institute of Science's Department of Biological Chemistry. "Our challenge is to understand why obese individuals have a much higher risk of developing diabetes."

To unravel this connection, Prof. Walker studies the insulin-producing beta cells in the pancreas. These cells are attuned to changes in blood sugar levels and—when they are functioning correctly—respond to after-meal surges with a sharp increase in insulin production. Prof. Walker is examining the unique properties of these cells and trying to find out why an excess of body fat can impair their function. "Our philosophy is that the better we understand how the beta cell works, the better our chances of understanding what goes wrong in disease and, ultimately, coming up with novel treatments," he says.

In 2005, Prof. Walker and colleagues made an important discovery about a protein called GPR40 that is produced in the beta cell and sits on its surface, acting as a sensor for fatty acids (specifically, a type known as long-chain fats) in the bloodstream. The researchers found that when fat is present in the blood in addition to sugar, the GPR40 receptor is activated and causes an even higher spike in insulin output. Frequent overstimulation of the pancreatic beta cells, in turn, can lead to persistently elevated insulin levels, possibly triggering the onset of diabetes.

"These problems arise in obese individuals because they have elevated levels of fat in their bloodstream," explains Prof. Walker. "Our hope is that by further studying the GPR40 receptor, we may ultimately be able to develop drugs that block its action and interfere with the progression of diabetes," he says.

Prof. Walker's team is also studying an additional receptor in the pancreatic beta cell. Called GPR41, it acts as a sensor for another type of fat: the short-chain fatty acid. "We don't know much about GPR41 yet, but we believe that it's likely to be playing an important role in controlling normal metabolism, and may be involved in the diabetic state as well," says Prof. Walker.

Another project in Prof. Walker's lab involves finding new ways to induce embryonic stem cells to develop efficiently into insulin-producing pancreatic beta cells. In type 1 diabetes, also known as "juvenile diabetes," the pancreas produces little or no insulin because the immune system has destroyed the beta cells. However, in the future, it may be possible to generate fully functioning beta cells in large numbers in the lab and transplant them into diabetic patients. "If we can do that, the patient will essentially be cured and won't have to worry about injecting insulin several times a day. The transplanted cells do the work of the missing beta cells," says Prof. Walker, who is collaborating on this research with Dr. Yoav Soen of the Department of Biological Chemistry. "In Israel," Prof. Walker adds, "we are able to pursue this research much more freely than in many other countries. We have access to many different lines of embryonic stem cells."

In the future, it may be possible to generate fully functioning pancreatic beta cells in large numbers in the lab and transplant them into patients with type 1 diabetes—essentially curing the disease.

Born and raised in Glasgow, Scotland, Prof. Walker received his MSc and PhD degrees in life sciences from the Weizmann Institute's Feinberg Graduate School. After completing postdoctoral work and serving as an adjunct assistant professor at the University of California, San Francisco, he joined the Institute's faculty in 1987. "This is a wonderful environment in which to do research because it's very collaborative," he says. "A lot of our work is technology-driven, and we have great support services and infrastructure for that here at Weizmann."

Prof. Walker says he feels optimistic that basic research can eventually lead to new treatments—and even cures—for both type 1 and type 2 diabetes. "On the one hand, diabetes is an enormous challenge," he says. "But on the other, we're living through an unprecedented revolution in biology, and are able to do things biologists would not have believed possible 20 years ago."

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Prof. Michael Walker's research is supported by the Helen and Martin Kimmel Institute for Stem Cell Research; the Florence Blau, Morris Blau & Rose Peterson Fund; the Andrew D. Friedland Memorial Fund; the Benjamin and Seema Pulier Charitable Foundation, Inc.; and Judith Benattar, Canada.

Prof. Walker is the incumbent of the Marvin Myer & Jenny Cyker Professorial Chair for Diabetes Research.