

Friday » August
17 » 2007

Diabetes breakthrough

Toronto scientists cure disease in mice

Tom Blackwell

National Post

Friday, December 15, 2006

In a discovery that has stunned even those behind it, scientists at a Toronto hospital say they have proof the body's nervous system helps trigger diabetes, opening the door to a potential near-cure of the disease that affects millions of Canadians.

Diabetic mice became healthy virtually overnight after researchers injected a substance to counteract the effect of malfunctioning pain neurons in the pancreas.

"I couldn't believe it," said Dr. Michael Salter, a pain expert at the Hospital for Sick Children and one of the scientists. "Mice with diabetes suddenly didn't have diabetes any more."

The researchers caution they have yet to confirm their findings in people, but say they expect results from human studies within a year or so. Any treatment that may emerge to help at least some patients would likely be years away from hitting the market.

But the excitement of the team from Sick Kids, whose work is being published today in the journal *Cell*, is almost palpable.

"I've never seen anything like it," said Dr. Hans Michael Dosch, an immunologist at the hospital and a leader of the studies. "In my career, this is unique."

Their conclusions upset conventional wisdom that Type 1 diabetes, the most serious form of the illness that typically first appears in childhood, was solely caused by auto-immune responses -- the body's immune system turning on itself.

They also conclude that there are far more similarities than previously thought between Type 1 and Type 2 diabetes, and that nerves likely play a role in other chronic inflammatory conditions, such as asthma and Crohn's disease.

The "paradigm-changing" study opens "a novel, exciting door to address one of the diseases with large societal impact," said Dr. Christian Stohler, a leading U.S. pain specialist and dean of dentistry at the University of Maryland, who has reviewed the work.

"The treatment and diagnosis of neuropathic diseases is poised to take a dramatic leap forward because of the impressive research."

About two million Canadians suffer from diabetes, 10% of them with Type 1, contributing to 41,000 deaths a year.

Insulin replacement therapy is the only treatment of Type 1, and cannot prevent many of the side effects, from heart attacks to kidney failure.

In Type 1 diabetes, the pancreas does not produce enough insulin to shift glucose into the cells that need it. In Type 2 diabetes, the insulin that is produced is not used effectively -- something called insulin resistance -- also resulting in poor absorption of glucose.

The problems stem partly from inflammation -- and eventual death -- of insulin-producing islet cells in the pancreas.

Dr. Dosch had concluded in a 1999 paper that there were surprising similarities between diabetes and multiple sclerosis, a central nervous system disease. His interest was also piqued by the presence around the insulin-producing islets of an "enormous" number of nerves, pain neurons primarily used to signal the brain that tissue has been damaged.

Suspecting a link between the nerves and diabetes, he and Dr. Salter used an old experimental trick -- injecting capsaicin, the active ingredient in hot chili peppers, to kill the pancreatic sensory nerves in mice that had an equivalent of Type 1 diabetes.

"Then we had the biggest shock of our lives," Dr. Dosch said. Almost immediately, the islets began producing insulin normally "It was a shock ? really out of left field, because nothing in the literature was saying anything about this."

It turns out the nerves secrete neuropeptides that are instrumental in the proper functioning of the islets. Further study by the team, which also involved the University of Calgary and the Jackson Laboratory in Maine, found that the nerves in diabetic mice were releasing too little of the neuropeptides, resulting in a "vicious cycle" of stress on the islets.

So next they injected the neuropeptide "substance P" in the pancreases of diabetic mice, a demanding task given the tiny size of the rodent organs. The results were dramatic.

The islet inflammation cleared up and the diabetes was gone. Some have remained in that state for as long as four months, with just one injection.

They also discovered that their treatments curbed the insulin resistance that is the hallmark of Type 2 diabetes, and that insulin resistance is a major factor in Type 1 diabetes, suggesting the two illnesses are quite similar.

While pain scientists have been receptive to the research, immunologists have voiced skepticism at the idea of the nervous system playing such a major role in the disease. Editors of Cell put the Toronto researchers through vigorous review to prove the validity of their conclusions, though an editorial in the publication gives a positive review of the work.

"It will no doubt cause a great deal of consternation," said Dr. Salter about his paper.

The researchers are now setting out to confirm that the connection between sensory nerves and diabetes holds true in humans. If it does, they will see if their treatments have the same effects on people as they did on mice.

Nothing is for sure, but "there is a great deal of promise," Dr. Salter said.

© National Post 2006

CLOSE WINDOW

Copyright © 2007 CanWest Interactive, a division of [CanWest MediaWorks Publications, Inc.](#) All rights reserved.