MedicalXpress

Hopkins team discovers sweet way to detect prediabetes

July 8 2010

Having discovered a dramatic increase of an easy-to-detect enzyme in the red blood cells of people with diabetes and prediabetes, Johns Hopkins scientists say the discovery could lead to a simple, routine test for detecting the subtle onset of the disease, before symptoms or complications occur and in time to reverse its course.

Pilot studies, published online April 22 in Diabetes, show the enzyme O-GlcNAcase is up to two to three times higher in people with diabetes and prediabetes than in those with no disease: "That's a big difference, especially in an enzyme that's as tightly regulated as this one is," says Gerald Hart, Ph.D., the DeLamar Professor and director of biological chemistry at the Johns Hopkins School of Medicine.

Building on their previous research, which showed how an abundant but difficult-to-detect sugar switch known as O-GlcNAc (pronounced oh-GLICK-nack) responded to nutrients and stress, the Hopkins team knew this small molecule was elevated in the red cells of patients with diabetes. "The question was whether the elevation happened in the earliest stages of diabetes and therefore might have value as a diagnostic tool," Hart said.

To find out, Kyoungsook Park, a graduate student of biological chemistry working in Hart's lab, focused on levels of O-GlcNAcase, an enzyme that removes O-GlcNAc in red cells. O-GlcNAc modifies many of the cell's proteins to control their functions in response to nutrients and stress. Nutrients, such as glucose and lipids, increase the extent of O-

GlcNAc modification of proteins affecting their activities. When the extent of O-GlcNAc attached to proteins becomes too high, as occurs in diabetes, it is harmful to the cell.

First, Park purified human red blood cells by depleting them of their main constituent, hemoglobin. The samples had been collected by two sources — the National Institute of Diabetes, Digestive and Kidney Diseases, or NIDDK, and Johns Hopkins Diabetes Center in collaboration with Christopher D. Saudek, M.D. — and characterized as normal (36 samples), prediabetes (13 samples) and type 2 diabetes (53 samples) according to traditional tests that require patient fasting. Defined as normal hemoglobin A1c with impaired fasting glucose, prediabetes is an intermediate state of altered glucose metabolism with a heightened risk of developing type 2 diabetes and other associated complications.

Then, she measured and compared the amount of the enzyme protein within the red cells associated with the sugar molecule, O-GlcNAc.

"When I checked the enzyme levels and saw how dramatically different they were between the prediabetic cells and the controls, I thought I did something wrong," Park says. "I repeated the test five times until I could believe it myself."

Hart speculates that in diabetes and prediabetes, it's not a good thing for the increased amount of sugar to be attached to proteins, so the cell is responding by elevating the enzyme that gets rid of it.

"This is an example of how basic research is directly affecting a serious disease," Hart says, adding that his team's pilot studies encourage further investigation of a method that potentially could fill the void that currently exists for an easy, accurate routine test for prediabetes. "Only a much larger clinical trial will determine if, by measuring O-GlcNAcase,

we can accurately diagnose prediabetes."

More information: Diabetes: diabetes.diabetesjournals.org/

Provided by Johns Hopkins Medical Institutions