MedicalXpress

Novel drug target linked to insulin secretion and type 2 diabetes treatment

May 26 2014

A signal that promotes insulin secretion and reduces hyperglycemia in a type 2 diabetes animal model is enhanced by the inhibition of a novel enzyme discovered by CHUM Research Centre (CRCHUM) and University of Montreal researchers. The team is part of the Montreal Diabetes Research Center and their study, published recently in *Cell Metabolism*, was directed by researchers Marc Prentki and Murthy Madiraju.

Insulin is an important hormone in our body that controls glucose and fat utilization. Insufficient insulin release by the beta-cells of the pancreas and interference with the action of insulin lead to type 2 diabetes. The secretion in the blood of insulin is dependent upon the utilization of glucose and fat by the beta-cells and the production of a novel signal that they discovered named monoacylglycerol.

"Despite significant research on the mechanisms implicated in insulin secretion, the signal molecules involved in this process remained enigmatic; the identification of these signals is necessary to develop better therapeutics against diabetes," explains Marc Prentki, Director of the Montreal Diabetes Research Centre and Professor at the University of Montreal. Marc Prentki holds the Canada Research Chair in Diabetes and Metabolism.

"When sugar is being used by the insulin secreting pancreatic beta-cell, it produces monoacylglycerol, a fat-like signal and this is associated with insulin release into blood; we found that the production of

monoacylglycerol is essential for glucose-stimulated insulin secretion by the beta-cell," says Murthy Madiraju, Researcher at the CRCHUM.

Importantly, the research team discovered that an enzyme called alpha/beta hydrolase domain-6 (in short ABHD6) breaks down monoacylglycerol and thus negatively controls insulin release. These researchers said that "an ideal drug for type-2 diabetes would increase insulin levels in blood by enhancing the beta cells response to glucose only when it is elevated and also increase the sensitivity of body tissues to insulin; this is precisely what ABHD6 inhibition does and thus we have identified a unique new target for type 2 diabetes."

The research team is currently in the process of discovering new and potent blockers of ABHD6 that do not show any unwanted toxicity and which can be developed as potential drugs for type 2 diabetes. These studies are being done in collaboration with AmorChem Financial, Inc., and its subsidiary NuChem Therapeutics, Montreal.

More information: Paper: http://www.cell.com/cell-metabolism/abstract/S1550-4131(14)00166-1

Provided by University of Montreal