Study uses sophisticated genetic engineering to improve insulin-producing beta cells

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One of the biggest mysteries about diabetes is why specialized cells in the pancreas stop secreting insulin, which the body needs in order to store glucose from food. A team from the Children's Hospital of Eastern Ontario (CHEO) Research Institute has identified a protein that inhibits insulin production in mice - work that offers a new way of understanding, and perhaps of one day treating, both Type 1 and Type 2 diabetes.

A study to be published today in the leading international journal *Cell Metabolism* describes how a research group led by Dr. Robert Screaton, who holds the Canada Research Chair in Apoptotic Signaling at the University of Ottawa, used sophisticated genetic engineering to remove or 'knock out' the Lkb1 gene from beta cells of laboratory mice. The result was an increase in both the size and number of beta cells, as well as greater amounts of insulin stored and released by the cells.

Importantly, the improved beta cell function lasted for at least five months, even in mice fed a high-fat diet designed to mimic the high caloric intake associated with Metabolic Syndrome and Type 2 diabetes in humans.

"We were surprised by the impressive accumulation of Lkb1 in beta cells of diabetic mice, which suggested that Lkb1 might contribute to their impaired function. After removal of the Lkb1 gene, the beta cells grow larger, proliferate more, and secrete more insulin. It's a one-stop shop for the much needed insulin", said Dr. Screaton.

"The knockout mice on a high-fat diet have lower blood glucose. If this observation is confirmed in humans, it may give us another clue into the development of Type 2 diabetes, and perhaps new treatment options".

"Type 1 and 2 diabetes, already common diseases, are showing disturbingly steady growth in incidence. The two conditions are among Canada's, and indeed the globe's, greatest health challenges," said Dr. Alex MacKenzie, CEO of the CHEO Research Institute and a physician who treats children with diabetes at CHEO. "The findings of Dr. Screaton's team introduce a novel and unanticipated potential therapeutic avenue for this costly and serious condition. It is some of the most important work to come out of our institute."

Source: Children's Hospital of Eastern Ontario Research Institute