Broader approach reveals genetic complexity behind diabetes genes

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(Medical Xpress)—Using a new method, diabetes researchers at Lund University, Sweden, have been able to reveal more of the genetic complexity behind type 2 diabetes. The new research findings have been achieved as a result of access to human insulin-producing cells from deceased donors and by not only studying one gene variant, but many genes and how they influence the level of the gene in pancreatic islets and their effect on insulin secretion and glucose control of the donor.

"With this approach, we can explain 25 per cent of variations in blood sugar levels. Previously, the best studies have explained less than three per cent", says Leif Groop from Lund University Diabetes Centre, the principal author of the study, which has been published in the journal Cell Metabolism.

The findings of the study provide greater insight into why, in cases of type 2 diabetes, the insulin-producing beta cells cease to be able to perform their function of producing sufficient insulin to keep blood sugar levels under control.

"We have linked different gene variants to their effect on donated human beta cells and have compared cells from non-diabetics and diabetics", says Professor Groop.

The research team had access to cells from 63 donors, nine of whom had had type 2 diabetes.

The starting point for the work was the 47 known gene variants that have a statistical link to diabetes.

"We used them as 'bait' to find new signal paths and chains of events where the 47 variants work together with other genes. We have to map patterns because a single gene rarely acts on its own", explains Leif Groop.

Various criteria were used to sift out the 20 strongest gene variants. The criteria included a difference between beta cells from healthy individuals and diabetics and a link to insulin secretion and blood sugar levels. The majority of the 20 variants identified were not among the 47 known risk genes.

The central aim of the study is to understand why certain gene variants raise the risk of diabetes.

"By taking a new and more holistic approach, we have gone a step further than previous projects and succeeded in linking together gene variants and their signal paths in human beta cells that cause reduced insulin secretion. The next step is to look in more detail at the way in which the strongest genes affect insulin secretion", says Leif Groop.

More information: Article: 'A Systems Genetics Approach Identifies Genes and Pathways for Type 2 Diabetes in Human Islets', Published in: *Cell Metabolism*

Provided by Lund University

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