Medical Xpress

DNA variant affects diabetes risk and treatment response

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A DNA variant near a digestive enzyme does not only affect risk of developing diabetes but also affects the response to treatment, an international consortium of researchers including the University of Dundee has found.

The study found that healthy volunteers with this DNA variant had an up to forty percent higher insulin response after stimulation with the hormone GLP-1, a likely explanation as to why they have a reduced chance of developing type 2 diabetes.

"It was already known that subjects carrying this variant have a reduced chance of developing type 2 diabetes," according to Dutch scientist Dr Leen 't Hart from Leiden University Medical Center, Leiden, The Netherlands, who is the lead author on the paper. "What we have been able to show is why they are less likely to develop type 2 diabetes

GLP-1 (Glucagon-like peptide-1) is a hormone that is produced by the gut in response to a meal. One of its functions is to stimulate insulin secretion from the pancreas so that the elevated glucose levels after a meal rapidly return to normal.

While the patients with the DNA variant were shown to be less likely to develop type 2 diabetes, it was also found that they actually respond worse to treatment with a novel class of drugs that improve GLP-1 function, called DPP4-inhibitors. These drugs, such as Sitagliptin and Vildagliptin, are being increasingly used to treat diabetes. It is not yet

known how the DNA variant affects response to these drugs but researchers said it might be due to the observed increased activity of chymotrypsin in the intestines.

The research study was carried out by a consortium of researchers from the Netherlands, Germany, Denmark, Sweden and the United Kingdom and the results are published in the scientific journal *Diabetes*.

Professor Ewan Pearson, of the University of Dundee, said, "These novel findings provide new clues to better diabetes prevention and treatment. This will be the subject of future experiments aiming to personalise treatment of diabetes, which is targeting specific treatments to an individual based upon his or her genetic features."

Provided by University of Dundee

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