'Jumping gene' diminishes the effect of a new type 2 diabetes risk gene

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Research led by the German Institute of Human Nutrition (DIfE) has identified a new gene associated with diabetes, together with a mechanism that makes obese mice less susceptible to diabetes.

A genomic fragment that occurs naturally in some mouse strains diminishes the activity of the risk gene Zfp69. The researchers also found that the corresponding human gene (ZNF642) is especially active in overweight individuals with diabetes. The results of the study, which also involved scientists from the University of Leipzig and the German Cancer Research Center in Heidelberg, are published July 3 in the open-access journal PLoS Genetics.

According to the World Health Organization (WHO), around 1.6 billion people are overweight worldwide. The number of people with type 2 diabetes has increased accordingly to 230 million. The risk of developing type 2 diabetes is approximately 50% hereditary, but is also dependent on nutrition and lifestyle factors.

In the present study, the researchers compared the genomes of different mouse strains. Some mouse strains were obese but had no strikingly elevated blood glucose levels and were less susceptible to diabetes. Other strains developed a severe malfunction of fat and glucose metabolism as they continued to gain weight, causing these mice to rapidly develop type 2 diabetes.

According to the study, this difference is due to a small fragment of

genetic information: a so-called "jumping gene" or "transposon" of viral origin, localized in a non-coding segment of the gene Zfp69, whose effect it diminishes. Without this genetic fragment, the risk gene is fully active and, in combination with obesity, leads to high blood sugar levels and malfunction of fat metabolism. The gene is also active in the fat tissues of overweight people suffering from diabetes - more so than in healthy individuals.

"Our data suggest that the protein product of the risk gene in obese individuals enhances the storage of fat in fat cells. As a result, excessive fat accumulates in the liver and this in turn contributes to the development of diabetes," explains Stephan Scherneck, first author of the study.

"We have therefore discovered a new diabetes gene of similar importance in mice and humans," says Hans-Georg Joost, head of the study and scientific director of DIfE, "as well as a mechanism that has not been described before in connection with the heredity of diabetes and obesity."

These data show the importance of studying in detail not only genes themselves but also transposons in their vicinity.

Joost continued, "This transposon is quite active and almost completely "turns off" the Zfp69 gene. We have found indications that it is also active in other mouse genes. Since the human genome is full of such fragments, it is quite possible that they play a greater role than previously assumed."

More information: Scherneck S, Nestler M, Vogel H, Blüher M, Block M-D, et al. (2009) Positional Cloning of Zinc Finger Domain Transcription Factor Zfp69, a Candidate Gene for Obesity-Associated Diabetes Contributed by Mouse Locus Nidd/SJL. *PLoS Genet* 5(7):

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