

Researchers identify gene that regulates glucose levels

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In an effort to understand how genes work, a collaborative study which includes the University of Southern California (USC) has identified a gene that regulates glucose levels. The results, which will be published in the July issue of the *Journal of Clinical Investigation* and is currently available online, may provide further understanding of the underlying causes of diabetes.

"Elevations of blood glucose are diagnostic of diabetes. This finding demonstrates there are gene variants that are important for day-to-day regulation of glucose, but they do not appear to play a significant role in disease risk," says Richard M. Watanabe, Ph.D., associate professor of preventive medicine and physiology & biophysics at the Keck School of Medicine of USC and co-senior author of the paper.

The study determined that this variant is not associated with an increased risk for type 2 diabetes.

"The identification of these variants increases our basic biologic knowledge about regulation of glucose and may also be useful in future genetic studies to help discriminate between genetic variants that do or do not contribute to disease susceptibility," continues Watanabe.

The study examined genetic information from more than 24,000 people. Researchers scanned the genomes of more than 5,000 participants by combining the genome-wide association (GWA) findings from the Finland-United States Investigation of Non-insulin-dependent Diabetes

Mellitus (FUSION) study and the SardiNIA study of aging.

The results determined that a gene on chromosome 2 that encodes for the enzyme glucose-6-phosphatase catalytic 2 (G6PC2) is associated with fasting glucose levels.

"G6PC2 is primarily expressed in the beta-cells of the pancreas and is responsible for converting glucose-6-phosphate back to glucose," says Watanabe. "Genetic variation of G6PC2 may be responsible for reducing insulin secretion and causing the glucose concentration to increase."

Glucose concentrations increased with each additional copy of the higher frequency variant of the gene. Watanabe adds that chronically higher levels of glucose may be a precursor for type 2 diabetes. The critical role of beta-cell function in the development of type 2 diabetes have also been demonstrated through previous studies by Richard N. Bergman, Ph.D., professor of physiology and biophysics and Thomas A. Buchanan, M.D. professor of endocrinology at the Keck School of Medicine of USC.

To validate the findings, the results were compared to a second set of FUSION participants in addition to individuals from six other studies of Northern European descent.

According to Buchanan, a co-author of the paper, the finding points to the importance of studying not just diseases like diabetes, but also the regulation of phenotypes like blood glucose.

"Genetics is identifying a whole new set of genes, proteins and pathways that are related to diabetes and blood sugar control. Our next challenge is to figure out how these genes work," says Buchanan.

Source: University of Southern California

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