

# New type 2 diabetes biomarker identified

February 8 2016

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Researchers from the Hospital del Mar Medical Research Institute (IMIM) have found an epigenetic mechanism implicated in the regulation of blood sugar. The study, published in the journal *Molecular Human Genetics*, reveals that the methylation of the TXNIP gene is associated with diabetes mellitus type 2 and, in particular, average blood glucose levels. These results, replicated in two patient cohorts, could help to both identify patients at risk of developing diabetes and control treatment response, as well as generating possible future therapies for this disease, one of the major cardiovascular risk factors in the population.

The work was coordinated by Carolina Soriano, from the Neurovascular research group at the IMIM, and Jordi Jiménez Conde, from the same group and a neurologist at the Hospital del Mar, in collaboration with the IMIM's Cardiovascular Epidemiology and Genetics group.

The aim of the study was to determine the association between type 2 diabetes and DNA methylation. Methylation is an epigenetic process that modifies DNA, altering the structure of a gene but not modifying its basic sequence. "Unlike genetics, where all the cells of a single organism share the same DNA that remains unchanged throughout life, epigenetics, and methylation in this case, the best studied epigenetic mechanism, is dynamic and adjusts according to our lifestyle. It is a mechanism that can be associated with risk modulation in diverse pathologies, including diabetes", indicates Carolina Soriano.

The researchers looked at methylation in the blood samples of a cohort

of 355 stroke patients using a state-of-the-art technique that allows them to study more than 450,000 methylation points in the genome. In addition, the study compared the methylation profiles of diabetics and non-diabetics as well as their levels of glycosylated haemoglobin, a biomarker that indicates blood [glucose levels](#) over the past 3 months. "In both analyses we detected that the TXNIP gene was hypomethylated (low level of genomic methylation) in patients with diabetes and, in particular, in those with poor control over their glucose levels. In addition, an in silico analysis (computer simulation) revealed that the hypomethylation position is located in a regulating region of the gene, which is why it has an effect on the expression", explained the researcher.

## **A potential therapeutic target**

The study was subsequently replicated in two cohorts from independent populations, with 167 and 645 patients respectively, confirming the relationship between TXNIP methylation, diabetes and glucose level dysfunction. "The methylation of this gene could be used as an early biomarker of dysfunction in the control of glucose levels. We are currently studying the implications and specific role of this gene in diabetes. In the future it could provide a possible therapeutic target for treating diabetes or controlling glucose concentrations", states the scientist.

Type 2 diabetes is a chronic illness characterised by the presence of elevated [blood glucose levels](#). It accounts for between 80 and 90% of [diabetes](#) cases and is one of the major cardiovascular risk factors. If not treated appropriately it can lead to very serious complications including strokes, heart attacks, neuropathy and blindness. The results of this study could aid in the early detection of this disease as well as helping assess the effectiveness of both treatments and lifestyle changes that the patients can make to control it.

**More information:** Soriano C, Jiménez-Conde J, Giralt E, Mola M, Vivanco R, Ois A, Rodríguez-Campello A, Cuadrado E, Sayols-Baixeras S, Elosua R, Roquer J, on behalf of the GENESTROKE Consortium. Epigenome-wide association study identifies TXNIP gene associated with Type 2 diabetes mellitus and sustained hyperglycemia. *Hum Mol Genet* 2015

Provided by Hospital del Mar Medical Research Institute

Citation: New type 2 diabetes biomarker identified (2016, February 8) retrieved 19 May 2024 from <https://medicalxpress.com/news/2016-02-diabetes-biomarker.html>

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