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Genetic breakthrough explains dangerously high blood glucose levels

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Canadian, French and British researchers have identified a DNA sequence that controls the variability of blood glucose levels in people. This is a potentially significant discovery because high blood glucose levels in otherwise healthy people often are indications of heart disease and higher mortality rates. The results will be published May 1 in the online version of the journal *Science*.

The research was conducted by Dr. Phillippe Froguel and colleagues at Imperial College London and le Centre national de la recherche scientifique (CNRS) in Lille, France, in collaboration with Dr. Robert Sladek, Dr. Constantin Polychronakos and their teams at McGill University and the McGill University Health Centre (MUHC) in Montreal. Dr. Ghislain Rocheleau, a post-doctoral fellow in Dr. Sladek's lab, is the study's co-first author. The scientists worked with data collected from a large genome study originally conducted for diabetes research that looked at over 390,000 different locations – or loci – on the human genome. The study's first important diabetes results were published in 2007 and received worldwide media attention.

In this study, researchers looked at the genetic code of healthy, non-diabetic individuals whose blood glucose levels were in the normal range. They discovered that a single DNA mutation within three different genes explained, in part, why some individuals have high or low blood glucose levels. The researchers believe that these genes actually affect the threshold level of glucose in the bloodstream, which triggers the secretion of insulin. The higher the threshold, the higher the

blood glucose level will rise before insulin starts to regulate it.

“These sequences explain about 5 per cent of the normal variation in blood glucose levels between otherwise healthy people,” explained Dr. Sladek, of McGill’s Faculty of Medicine, the Department of Human Genetics, the MUHC Research Institute and the McGill University and Génome Québec Innovation Centre. “Five per cent may not sound huge, but for complex traits, that’s rather a lot. By contrast, hundreds of different genes influence height.”

These findings provide important insights into the genetic mechanisms behind glucose metabolism, say the researchers, which they predict will lead to greater understanding of the genetic roots of metabolic disorders in general. “In theory, any medical test which has a genetic component can use this approach,” Sladek explained. “That brings us to the idea of ‘personalized medicine.’ Eventually, we might be able to customize treatment to an individual’s unique genetic structure.”

High blood glucose levels are also closely linked with increased risk for cardiovascular disease, and these findings hold out of the hope of discovering new management techniques and treatments. “It’s important to know that a high blood glucose level, even within the normal and non-diabetic range, is a risk factor for early mortality,” explains Dr. Philippe Froguel of Imperial College and CNRS. “Epidemiological studies have shown that 80 per cent of the risk of cardiovascular disease is related to a blood glucose level just above the average.”

“Obviously, the next step would be to get some collaborators on the heart disease side, and see whether some of these other genes might also play a role,” added Dr. Sladek.

“We are proud of this announcement, which once again confirms the scientific excellence and talent of Québec’s scientists,” said Paul

L'Archevêque, President and CEO of Génome Québec. "These findings, which are the direct result of studies co-financed by Génome Québec, clearly show the strategic role of genomics in the search for solutions to improve human health. We would also like to underline the cooperation among the institutes, an initiative that made this major advance possible. Congratulations to Dr. Sladek and his team!"

Source: McGill University