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Chromosomal abnormalities may explain increased cancer risk in type 2 diabetes

Certain chromosomal abnormalities of the preleukemic type appear to be over-represented in patients with type 2 diabetes (T2D) who are suffering from vascular complications. This finding may provide a partial explanation for the higher rates of cancer-related mortality observed among patients with this type of diabetes. These results were obtained by a French-British-Qatari research group coordinated by Professor Philippe Froguel in the Laboratoire Génomique et maladies métaboliques (CNRS/Université Lille 2/Institut Pasteur de Lille), working in collaboration with teams attached to INSERM, AP-HP (Paris Public Hospitals) Paris Diderot and Paris-Sud universities[1]. Their work was published on July 14, 2013 on the *Nature Genetics* website.

There are more than 200 million diabetics worldwide, and one in three suffer from vascular or nerve complications. In 2012, two studies published in *Nature Genetics* showed that large chromosomal clonal mosaic events (CMEs)[2] affecting large portions of chromosomes (or even their totality), could be observed in the DNA of blood or saliva cells from some ageing individuals. These studies also suggested that CMEs could predict the risk of cancer, and notably leukemia, in these individuals. The incidence of CMEs is indeed negligible among people below the age of 50 years, while they affect 2% of those over 70, in whom they markedly increase the risk of cancers, notably of a hematological type.

Furthermore, type 2 diabetes (T2D) is a disease that accelerates ageing and its concomitant conditions. T2D is thus characterized by a marked increase in the cancer risk, and particularly hematological cancers such as leukemia.

Philippe Froguel's team has been studying T2D for several years. The researchers have been focusing on whether, like ageing, T2D causes the appearance of CME chromosomal abnormalities in blood cells. To achieve this, they have been using an inexpensive gene analysis technology based on DNA arrays (measuring just a few square centimeters) onto which nearly half a million DNA mutations are loaded. Each array thus allows for complete “dissection” of the genome of an individual.

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1 This work was carried out by the Franco-British-Qatari team coordinated by Professor Philippe Froguel from the Laboratoire Génomique et maladies métaboliques (CNRS/Université Lille 2/Institut Pasteur de Lille) and Imperial College London, in collaboration with teams attached to INSERM, AP-HP (Paris Public Hospitals) and Paris Diderot and Paris-Sud universities. This work also formed part of the EGID project (European Genomic Institute for Diabetes, CNRS/INSERM/Université Lille 2/Institut Pasteur de Lille/CHRU Lille).

2 The term “mosaic” abnormalities refers to abnormalities present in some cells or tissues in an individual (these abnormalities are not found in all cells and all tissues): this is mainly the case of chromosomal abnormalities acquired over time.

Using this method, the scientists evaluated the presence of CMEs in the DNA of blood from 7437 individuals aged over 50 years, including 2208 patients with T2D. They found that the incidence of CME carriers was four times higher among T2D patients than in the controls. In addition, the team confirmed a significant effect of age on the presence of CMEs. More precisely, they showed that diabetic CME carriers suffered from much more severe T2D – presence of vascular complications (affecting the eyes, kidneys or heart) – than non-carriers. Although weighing less than non-carriers, 70% of diabetics carrying CME presented T2D-related micro- and/or macro-vascular complications. The presence of certain CME-type chromosomal abnormalities may therefore partly explain the high incidence of cancers in patients with type 2 diabetes.

This study may have far-reaching clinical implications, notably regarding the detection of precancerous states in some diabetics. A CME genetic analysis using DNA arrays could thus be proposed, mainly in patients with severe T2D associated with early-onset vascular complications.

Bibliography

Association between large detectable clonal mosaicism and type 2 diabetes with vascular complications. Amélie Bonnefond, Boris Skrobek, Stéphane Lobbens, Elodie Eury, Dorothée Thuillier, Stéphane Cauchi, Olivier Lantieri, Beverley Balkau, Elio Riboli, Michel Marre, Guillaume Charpentier, Loïc Yengo & Philippe Froguel. *Nature Genetics*. 14 July 2013. DOI : 10.1038/ng.2700

Contact information

Researcher l Philippe Froguel l T +33 (0)3 20 87 79 54 / 79 11 l p.froguel@imperial.ac.uk
CNRS Press officer l Priscilla Dacher l T +33 (0)1 44 96 46 06 l priscilla.dacher@cnrs-dir.fr