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Chromosomal Variants Help Explain Why People With Obesity Often Develop Diseases Such as Asthma and Diabetes

The link between obesity and other diseases may be found in chromosomal inversions

Barcelona, 28 May 2020 - People who are obese often have comorbid conditions, for example hypertension, asthma, diabetes or depression. While the authors of many epidemiological studies have postulated an association between these diseases and obesity, until now **it was not known whether obesity was a cause or a consequence of these comorbidities or the result of shared genetic conditions**. Now, a study led by the Barcelona Institute for Global Health (ISGlobal), a centre supported by the "la Caixa" Foundation, has identified several chromosomal alterations that explain the tendency for obesity to be associated with certain other diseases. The research, recently published in the *American Journal of Human Genetics*, is the result of a collaboration with Pompeu Fabra University (UPF) in Barcelona, the University of Adelaide, the Estonian Genome Centre and the Barcelona Supercomputing Centre.

Analysing data from **over 400,000 individuals**, the researchers identified **chromosomal inversions responsible for shared susceptibility to obesity and certain related diseases**. "Chromosomal inversions are rearrangements that cause a segment of DNA to be reversed end to end, that is, the fragment is arranged in the opposite direction to the linear sequence of the reference DNA segment," explains **Juan Ramón González**, first author and coordinator of the study and head of the Bioinformatic Research Group in Genetic Epidemiology (BRGE) at ISGlobal. "These types of mutations can alter the function of several genes located in or near the inverted regions. This is why inversions make certain people more susceptible to diseases that often **occur concomitantly**, such as obesity and hypertension, for example".

The findings of this study indicate that certain inversions often found in the population are more frequent in **people who are obese and have at least one of the diseases typically associated with excess body weight**. In fact, the research team identified **three chromosomal inversions** that are common in people who have **obesity and asthma, obesity and hypertension**, or **obesity and depression**.

"This is the first study to thoroughly assess the role played by common inversions in human traits", explains **González**, who, together with his team, has invested ten years of intense work in the development of the **bioinformatic tools** that have made it possible to study these kinds of variations, which were—until now—impossible to analyse on a large scale.

Obesity and Diabetes

One of most interesting findings was the increased frequency in obese and diabetic people of an **inversion located on chromosome 8**: "We observed this phenomenon in the large population cohort of the UK biobank and validated it in the largest global diabetes consortiums (70KforT2D)," specifies, González. "In fact, we went a step further and established the **possible molecular mechanisms** by which this inversion can link the two diseases". According to the article, this chromosomal inversion can change gene

expression or alter the effect certain genetic variants have on the expression of genes, which are key to obesity and **insulin regulation**, ultimately causing diabetes.

Obesity is a complex disease that is becoming increasingly prevalent in society and the accompanying conditions have a very negative impact on the quality of life and life expectancy of those affected. González concludes, "Our results shed light on the complex relationships between obesity and its comorbidities and define a **causal pathway** linking chromosomal inversions and conditions, such as diabetes, that are prevalent in people who are obese".

Reference

Juan R González, Carlos Ruiz-Arenas, Alejandro Cáceres, Ignasi Morán, Marcos López-Sánchez, Lorena Alonso, Ignacio Tolosana, Marta Guindo-Martínez, Josep M Mercader, Tonu Esko, David Torrents, Josefa González, Luis A Pérez-Jurado. *Polymorphic inversions underlie the shared genetic susceptibility of obesity-related diseases*. *American Journal of Human Genetics,* Mayo 2020. DOI: 10.1016/j.ajhg.2020.04.017

About ISGlobal

The Barcelona Institute for Global Health, ISGlobal, is the fruit of an innovative alliance between the "la Caixa" Foundation and academic and government institutions to contribute to the efforts undertaken by the international community to address the challenges in global health. ISGlobal is a consolidated hub of excellence in research that has grown out of work first started in the world of health care by the Hospital Clínic and the Parc de Salut MAR and in the academic sphere by the University of Barcelona and Pompeu Fabra University. The pivotal mechanism of its work model is the transfer of knowledge generated by scientific research to practice, a task undertaken by the institute's Education and Policy and Global Development departments. ISGlobal has been named a Severo Ochoa Centre of Excellence and is a member of the CERCA programme of the Generalitat de Catalunya.

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