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Largest genome-wide study reveals genes driving obesity

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This is an image of a weight scale. Credit: CDC/Debora Cartagena

In obesity, some people store fat evenly throughout the body while others store fat around the abdomen. Storing fat around the abdomen places some obese individuals at an increased risk of developing diabetes and cardiovascular disease.

New research findings indicate that particular genes are associated with

driving different types of obesity and that these genetic factors will be key to improving treatments options and prevention strategies in future.

The largest ever study of the genetics behind obesity has identified 140 locations across the genome that may play an important role in obesity and fat distribution, many of which have never been identified before.

Researchers at the Diabetes Complications Research Centre (DCRC) at UCD Conway Institute and UCD School of Medicine & Medical Science participated in this international collaboration to analyse the DNA of nearly 340,000 people recruited from around the world.

The GIANT consortium (Genetic Investigation of Anthropometric Traits) and collaborators recently published findings of two studies in articles in the scientific journal *Nature*. They suggest that the genetic markers for obesity as measured by body mass index (BMI – ratio of weight and height) are quite different to those markers that predict fat distribution around the body, as measured by waist-to-hip ratio.

"We found that the genetic factors predictive of how we distribute our body fat involve genes linked to fat cell development, blood vessel formation, skeletal growth, glucose control, and insulin resistance", explained Dr Eoin Brennan, postdoctoral researcher with Professor Catherine Godson and named author on the article.

"Genetic factors that predict a high BMI suggest an important role for the brain and central nervous system in controlling obesity, including genes involved in how we regulate our appetites."

The findings also indicate that there are major differences between men and women in the genetic regulation of fat distribution. These data suggest that personalising future treatments for obesity will require considering both metabolic and neurological aspects.

"Taken together, these studies suggest that there are different genetic mechanisms driving the different types of obesity, and by understanding the biology better, we'll eventually be able to get better treatments and better prevention", said Dr Brennan.

Professor Carel le Roux, an obesity expert working within the DCRC but not associated with these studies commented, 'This work may be part of the breakthrough required for us as clinicians to understand that obesity is a chronic and complex disease caused by brain dysfunction although characterised by excess body fat. Obesity has enormous impacts on the individual, on healthcare systems and the national economy. However, by using data such as provided in these papers, we may in future bring a personalised medicine approach to patients that will improve their outcomes."

By knowing what these genetic features are, researchers can now move ahead with mapping the vital signalling pathways and cellular networks implicated in obesity.

The DCRC team provided genetic data from DNA samples of patients with diabetes and obesity within their GENIE (Genetics of Nephropathy: an International Effort) consortium collection. In parallel activities funded by the US Ireland R&D partnership, the DCRC are using a similar approach to investigate genetic determinants of diabetic kidney disease and renal failure. DCRC research has revealed several associations between genetic variants and kidney disease and current investigations are focused on the functional significance of such changes on signalling networks in the kidney.

More information: "New genetic loci link adipose and insulin biology to body fat distribution." *Nature*. 2015 Feb 12; 518(7538):187-96. www.nature.com/nature/journal/ … ull/nature14132.html

"Genetic studies of body mass index yield new insights for obesity biology." *Nature*. 2015 Feb 12; 518(7538):197-206.
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