

Large-scale analysis identifies 32 genetic loci for obesity

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An international team of researchers has identified 18 new genetic loci associated with obesity assessed by BMI, and confirmed a link between obesity and 14 previously known loci. Almost 250,000 individuals were included in the analysis, which is published in the latest issue of *Nature Genetics*.

"We know that hereditary factors play a key role in the development of obesity, and thus in increasing risk of many diseases such as cardiovascular disease and diabetes," says Erik Ingelsson, professor at the Department of Medical Epidemiology and Biostatistics at Karolinska Institutet, and one of the principal investigators of the study. "What we wanted to do was to identify genes that increase the risk of obesity using large-scale methods that involved examining the entire genome in a large number of subjects."

The object of the study was to study gene variants, which is to say individual differences in genetic code. There are several millions of common variants distributed throughout the entire genome, but since many of these variants are located between two genes rather than within one gene, scientists usually talk about genetic loci rather than genes. In the present study, the researchers have charted the gene variants associated with obesity by analysing the relation between BMI (body mass index) and 2.8 million gene variants in 123,865 individuals.

The researchers then carried out a targeted follow-up of the 42 gene variants with the strongest BMI correlation in an additional 125,931



individuals, from which they were able to confirm the 14 previously known gene loci and identify 18 new loci associated with BMI. They were also able to show that certain biological mechanisms are overrepresented as regards the development of obesity, such as neuroendocrinal signal pathways involved in the regulation of appetite, and signal pathways that control the intestines and pancreas.

"We estimate that the 32 loci that we've found, together account for two to four per cent of the genetic causes of obesity, so much remains to be discovered," says Professor Ingelsson. "In learning more about how the human bodyweight is regulated, we can hopefully do something about the serious health problem that obesity poses to modern society."

The present study was conducted within the GIANT (Genetic Investigation of ANthropometric Traits) Consortium and comprises almost 100 studies with some 400 co-authors. It was coordinated by researchers from Karolinska Institutet, Oxford and Cambridge universities and the Broad Institute in Boston, USA. In the same issue of Nature Genetics, GIANT scientists publish an article describing major sex differences in how genetic factors affect the distribution of body fat. A better understanding of how fat distribution is regulated is important since the site of fat accumulation very much determines how dangerous it is for future health problems such as cardiovascular disease and type II diabetes.

More information: Speliotes EK, et al. Association analyses of 249,796 individuals reveal eighteen new loci associated with body mass index

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