

New genomic technique reveals obesity gene variants

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Obesity is highly heritable, but so far genetic association studies have only explained a small fraction of this heritability. Now, in a study published in BioMed Central's open access journal *Genome Biology*, researchers have identified DNA variants in two nervous system genes that are associated with an excessively high BMI.

Kelly Frazer and colleagues from UC San Diego, Scripps Translational Science Institute and Sanofi-Aventis used a new approach that is likely to become popular in searching for hidden [heritability](#): the resequencing of a candidate area of the genome in a large number of individuals followed by screening for [genetic markers](#) within this region that are associated with the disease or condition in question.

Frazer said, "We sequenced two intervals encoding the enzymes FAAH and MGLL which modulate the levels of endocannabinoids present in the brain and peripheral tissues that are involved in the regulation of [energy balance](#) and appetite. The level of these endocannabinoids is high in obese patients, and thus these two enzymes provide strong candidates to examine for a genetic association with [BMI](#)".

In these two genes, the researchers were able to identify four regions associated with BMI: the FAAH promoter, MGLL promoter, MGLL intron 2, and an enhancer in the MGLL intron 3. Further testing of one of these regions revealed rare variants that were associated with increased levels of endocannabinoids in the plasma, which is consistent with previous findings.

According to Frazer, "This is one of the first studies to use the new sequencing technologies to link rare and low frequency variants to a complex trait such as obesity and will be of particular interest to understand more comprehensively the role of inheritance in obesity, a rapidly rising serious health issue across the world".

More information: Population sequencing of two endocannabinoid metabolic genes identifies rare and common regulatory variants associated with extreme obesity and metabolite level, Olivier Harismendy, Vikas Bansal, Gaurav Bhatia, Masakazu Nakano, Michael Scott, Xiaoyun C Wang, Colette Dib, Edouard Turlotte, Jack C Sipe, Sarah S Murray, Jean-Francois Deleuze, Vineet Bafna, Eric J Topol and Kelly A Frazer, *Genome Biology* (in press), genomebiology.com/

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