

Finding genes that expand waistlines

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Figure 1: Success or failure in battling weight gain can partly depend on the ancestry of your genes. Credit: iStockphoto/wakila

Some common genetic variants associated with obesity in east Asians have been identified by two international research teams involving RIKEN researchers. Yukinori Okada and Toshihiro Tanaka at the RIKEN Center for Genomic Medicine in Yokohama, Japan, co-led the first study, and Tanaka co-led the second in an international collaborative consortium, the Asian Genetic Epidemiology Network (AGEN).

By analyzing data from over 62,000 east Asian individuals, the researchers found two of the variants, or single nucleotide polymorphisms (SNPs), in the KLF9 and MSTN genes. KLF9 encodes a transcription factor that activates expression of genes involved in

numerous physiological processes, including one that is involved in fat cell differentiation and implicated in [obesity](#). Mutations in MSTN are known to cause decreases in body fat. Further analysis revealed that the newly identified SNPs interact with each other, suggesting that MSTN regulates the effects of KLF9 on body mass index (BMI), a common measure of obesity.

In the second study, the researchers performed a meta-analysis on data from eight genome-wide association studies, including approximately 2.4 million SNPs in the genomes of nearly 28,000 east Asians. This revealed SNPs in three well-known genes, FTO, SEC16B and MC4R, which geneticists have previously found to be associated with BMI.

In an analysis of data from approximately 55,000 additional east Asian individuals, Okada, Tanaka and colleagues focused on 798 SNPs that they found were associated with BMI, and 50 additional SNPs linked to BMI in earlier studies. By combining these data sets, they confirmed that SNPs in six genes previously associated with obesity in Europeans are significantly associated with BMI in east Asians.

The researchers also identified three previously unknown variations that are significantly associated with BMI, located in or near the CDKAL1, PCSK1 and GP2 genes, all of which encode enzymes involved in metabolism.

Of all the variants identified, the FTO variant was most strongly associated with BMI, accounting for nearly 0.2% of the variation in the study population. This and nine other genes strongly associated with BMI account for nearly 0.9% of the individual variation between them, while all 22 of the [genes](#) identified together explained 1.18% of the individual variation in east Asians.

Large-scale studies such as these provide valuable information about the

genetic bases of obesity. As well as identifying genetic variants that are important in east Asians, they allow for comparisons with European individuals. "We will continue [to clarify the function] of these SNPs, which might lead to a better understanding of metabolic syndromes," says Tanaka.

More information: Okada, Y., et al. Common variants at CDKAL1 and KLF9 are associated with body mass index in east Asian populations. [Nature Genetics](#) 44, 302 - 306 (2012).

Wen, W., et al. Meta-analysis identifies common variants associated with body mass index in east Asians. [Nature Genetics](#) 44, 307 - 311 (2012).

Provided by RIKEN

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