New genes discovered for adult BMI levels

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A large international study has identified three new gene variants associated with body mass index (BMI) levels in adults. The scientific consortium, numbering approximately 200 researchers, performed a meta-analysis of 46 studies, covering gene data from nearly 109,000 adults, spanning four ethnic groups.

In discovering intriguing links to lipid-related diseases, type 2 diabetes and other disorders, the IBC 50K SNP Array BMI Consortium's study may provide fundamental insights into the biology of adult obesity. Scientists from the Center for Applied Genomics at The Children's Hospital of Philadelphia led the study, using the CardioChip, a gene array containing probes for some 50,000 genetic variants across 2,100 genes relevant to cardiovascular and metabolic functions.

The study appeared online Sept. 21 in Human Molecular Genetics.

"BMI is a widely used measure of obesity, which affects one third of U.S. adults, and approximately half a billion people worldwide," said first author Yiran Guo, Ph.D., of Children's Hospital, who led the meta-analysis. "Previous studies have shown that genetics plays an important role in obesity, and this study expands our knowledge of BMI genetics."

The researchers first analyzed a dataset of approximately 51,000 individuals of European ancestry (EA) to discover initial gene signals, and then performed replication studies in another 27,000 EA subjects, as well as 14,500 additional EA individuals. Further analyses of data from approximately 12,300 African Americans, 2,600 Hispanics and 1,100

East Asians strengthened the team's findings.

The researchers uncovered three novel signals, from the genes TOMM40-APOE-APOC1, SREBF2 and NTRK2) that were significantly associated with BMI in adults. All had previously been linked to other important disorders. The APOE locus is well known to be involved in blood lipid regulation and circulation, and plays an important role in Alzheimer's disease. The SREBF2 gene is in the same family as SREBF1, linked to type 2 diabetes in another CardioChip study. Finally, NTRK2 codes for a receptor of the BDNF protein, which is known to be related to BMI and is associated with the eating disorder anorexia.

Anorexia is a special interest of Guo, who holds a Davis Foundation Postdoctoral Fellowship in Eating Disorders. Guo added that the large dataset from the previous studies allowed the researchers "to enhance our understanding of BMI genetics, as well as the interplay between genetic variants and metabolic disorders such as obesity, type 2 diabetes and lipid-related conditions."

Guo also noted that the team was able to test for conditional associations within genes—-independent signals from within the same gene locus. In particular, the researchers discovered that two genes, BDNF and MC4R, each harbor two independent signals for BMI. Both genes were among eight genes previously associated with BMI that the current study was able to replicate, including FTO, SH2B1 and COL4A3BP-HMGCR.

Guo concluded that "while the individual effects of each gene may be small, they may provide fundamental clues to the biology of adult obesity." He added that further studies will investigate gene-gene interactions for the same trait.

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