Obesity genes probably didn't evolve to help us survive famine

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Genes that helped our ancestors store fat in times of famine may have been useful, but whether they cursed future generations with a predisposition toward obesity is a little more controversial. This popular "thrifty gene hypothesis" has had its critics, but with a study published September 22 in *Cell Metabolism*, there is now evidence that nearly all the common obesity-related genes show no properties of traits that

evolved because they provide an adaptive advantage.

"This is probably the hardest evidence so far against the thrifty gene hypothesis—our ambition here is for people to entertain a wider range of ideas about where the genetic basis of complex diseases, like obesity, comes from," says John Speakman, a biologist at the Chinese Academy of Sciences Institute of Genetics and Developmental Biology in Beijing, who co-authored the piece with Guanlin Wang, one of his PhD students at the Chinese Academy of Sciences. "The process of evolution is a lot more complex than just the spread of favorable traits by natural selection, and the thrifty gene is like an emblem of this older way of thinking about evolutionary aspects of medicine."

The thrifty gene hypothesis, originally proposed by James Neel in 1962, suggests that the effective elimination of famine in developed countries means that gene variants that were once favorable for storing fat instead could cause widespread obesity. The question arises, however, as to why everyone didn't inherit these favorable traits if selection has been acting for millions of years on our ancestors.

Addendums to the hypothesis have tried to remedy this problem, stating that famines are relatively new (since the dawn of agriculture), so human populations haven't had a chance to catch on, or that obesity is a secondary trait of another that would have encouraged survival, such as an ability to stay warm.

Speakman and Wang's study challenges the thrifty gene hypothesis and its addendums by finding that only 9 out of 115 genes known to be associated with obesity showed evidence of being under positive selection. (Moreover, of those 9 genes, only 4 showed evidence of selection favoring obesity, while in the other 5, selection had favored leanness.) The data were gathered from publically available databases such as the HapMap consortium and 1000 Genomes project.

"Supporters of the thrifty gene idea predicted that the advent of genomic technologies and the ability to find signatures of positive selection would prove the thrifty gene idea correct," Speakman say. "Our work failed to find such strong signatures."

One limitation of the study is that the current model for positive selection may have limited the research, so that Speakman and Wang were only able to detect "hard sweeps" of genetic selection, focusing on the characteristic reductions in genetic diversity around a single selected mutation. BMI is also not the perfect indicator of obesity, and so results could differ based on more accurate measurements. Further study is necessary to replicate the findings in other datasets and analytical tools.

More information: Guanlin Wang et al, Analysis of Positive Selection at Single Nucleotide Polymorphisms Associated with Body Mass Index Does Not Support the "Thrifty Gene" Hypothesis, *Cell Metabolism* (2016). DOI: 10.1016/j.cmet.2016.08.014

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