

Why is type 2 diabetes an increasing problem?

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Contrary to a common belief, researchers have shown that genetic regions associated with increased risk of type 2 diabetes were unlikely to have been beneficial to people at stages through human evolution.

Type 2 diabetes is responsible for more than three million deaths each year and this number is increasing steadily. The harmful genetic variants associated with this common disease have not yet been eliminated by [natural selection](#).

To try to explain why this is, geneticists have previously hypothesised that during times of 'feast or famine' throughout [human evolution](#), people who had advantageous or 'thrifty' genes processed food more efficiently. But in the modern developed world with too much food, these same people would be more susceptible to type 2 diabetes.

"This thrifty gene theory is an attractive hypothesis to explain why natural selection hasn't protected us against these harmful variants," says Dr. Yali Xue, lead author of the study from the Wellcome Trust Sanger Institute. "But we find little or no evidence to corroborate this theory."

The team tested this theory by examining 65 [genetic regions](#) that were known to increase type 2 diabetes risk, the most detailed study of its kind.

If these harmful variants were beneficial in the past, the team would expect to see a genetic imprint of this in the DNA around the affected

regions. Despite major developments in tests for positive selection and a four-fold increase in the number of genetic variants associated with diabetes to work with, they found no such imprint.

"We found evidence for positive selection in only few of the 65 variants and selection favoured the protective and risk alleles for type 2 diabetes in similar proportions," notes Dr. Qasim Ayub, first author from The Wellcome Trust Sanger Institute, "This is no more than what we would expect to find for a random set of genomic variants."

This finding poses an intriguing and still unanswered question: if the harmful genetic variants that are associated with [type 2 diabetes](#) were not beneficial in the past, then why have they not been eliminated?

"Geneticists have been able to identify multiple genetic risk variants for many common diseases, such as type 2 [diabetes](#)," says Professor Mark McCarthy, co-author from the University of Oxford. "However, the big challenge, if we are to use this information to improve human health, lies in understanding how it is that these differences in DNA sequence lead to an altered risk of disease. Understanding how variants that appear, in the current environment, to have largely harmful consequences, have become so frequent will be an important step on this path towards better treatment and prevention"

More information: Qasim Ayub, Loukas Moutsianas, Yuan Chen, Kalliope Panoutsopoulou, Vincenza Colonna, Luca Pagani, Inga Prokopenko, Graham R.S. Ritchie, Chris Tyler-Smith, Mark I. McCarthy, Eleftheria Zeggini,¹ and Yali Xue. (2013) 'Revisiting the thrifty gene hypothesis via 65 loci associated with susceptibility to type 2 diabetes' Advanced online publication in *American Journal of Human Genetics* 09 Jan.

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