

# Gene mutation evolved to cope with modern high-sugar diets

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The gene variant became more common in humans after cooking and farming became widespread, and might now help people avoid diabetes, according to the findings published in *eLife*.

"We found that people differ in how efficiently their bodies can manage [blood sugar levels](#), resulting from an evolutionary process that seems to have been brought about by changing diets," said the study's lead author, Professor Frances Brodsky, Director of UCL Biosciences.

The researchers were investigating the CLTCL1 gene, which directs production of the CHC22 protein that plays a key role in regulating a [glucose](#) transporter in our fat and [muscle cells](#).

After people eat, the hormone insulin reacts to higher levels of blood glucose by releasing the transporter to remove glucose from the blood, taking it into muscle and fat tissue. Between meals, with the help of the CHC22 protein, the glucose transporter remains inside muscle and fat so that some [blood sugar](#) will continue to circulate.

The research team, consisting of specialists in [population genetics](#), [evolutionary biology](#), ancient DNA and cell biology, analysed [human genomes](#) as well as those of 61 other species, to understand how the gene producing CHC22 has varied throughout evolutionary history.

In humans, by looking at the genomes of 2,504 people from the global 1000 Genomes Project, they found that almost half of the people in many ethnic groups have a variant of CHC22 that is produced by a mutated gene, which became more common as people developed cooking and farming.

The researchers also looked at genomes of ancient humans, and found that the newer variant is more common in ancient and modern farming populations than in hunter-gatherers, suggesting that increased consumption of carbohydrates could have been the selective force driving the genetic adaptation.

By studying cells, the researchers found that the newer CHC22 variant is

less effective at keeping the glucose transporter inside muscle and fat between meals, meaning the transporter can more readily clear glucose out of the blood. People with the newer variant will therefore have lower blood sugar.

"The older version of this genetic variant likely would have been helpful to our ancestors as it would have helped maintain higher levels of blood sugar during periods of fasting, in times when we didn't have such easy access to carbohydrates, and this would have helped us evolve our large brains," said first author Dr. Matteo Fumagalli, who began the study at UCL before moving to Imperial College London.

"In more recent years, with our high-carb diets that often provide us too much sugar, the newer variant may be advantageous," Dr. Fumagalli added.

The researchers say that while this genetic variant does not play a direct role in the development of diabetes, having the older variant may make people more likely to develop diabetes, and it may also exacerbate insulin resistance involved in diabetes.

"People with the older variant may need to be more careful of their carb intake, but more research is needed to understand how the genetic variant we found can impact our physiology," added Professor Brodsky.

Co-author Professor Mark Thomas (UCL Genetics, Evolution & Environment) added: "Our analyses strongly suggest that we have found yet another example of how prehistoric changes in dietary habits have shaped human evolution. Understanding how we have adapted to these changes doesn't only inform us about why people lived or died in the past, but also helps us to better understand the relationship between diet, health and disease today."

**More information:** Matteo Fumagalli et al, Genetic diversity of CHC22 clathrin impacts its function in glucose metabolism, *eLife* (2019). [DOI: 10.7554/eLife.41517](https://doi.org/10.7554/eLife.41517)

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