Digesting milk in Ethiopia: A case of multiple genetic adaptations

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A genetic phenomenon that allows for the selection of multiple genetic mutations that all lead to a similar outcome—for instance the ability to digest milk—has been characterised for the first time in humans.

The phenomenon, known as a 'soft selective sweep', was described in the population of Ethiopia and reveals that individuals from the Eastern African population have adapted to be able to digest milk, but via different mutations in their genetic material.

A team of geneticists from UCL, University of Addis Ababa and Roskilde University have shown that five different alleles are found in the Ethiopian population that cause adult lactase production, one of

which is newly confirmed. Their study is published in The *American Journal of Human Genetics*.

Professor Dallas Swallow, from the Department of Genetics, Evolution and Environment, senior author of the paper said: "Our genetic make-up determines our ability to digest milk into adulthood. Just over a third of the global population have inherited genes that allow us to make lactase, the enzyme that digests milk, as adults.

"This study shows that several different genetic changes that allow our bodies to make lactase have emerged independently. Changes to our lifestyle over the past 10,000 years—including diet, altitude acclimatisation and infectious disease resistance—will likely have caused many genetic adaptations of this kind."

We need lactase when we are babies to digest our mother's milk, so in babies large amounts of lactase enzyme are expressed by our genes. When we are older we no longer rely on our mother's milk for essential nutrients, so in most humans manufacture of the lactase enzyme stops through de-activation of the corresponding gene.

However, subtle mutations in the regulatory region of the gene in some individuals cause lactase to carry on being expressed into adulthood. Different mutations are likely to affect lactase expression using slightly different mechanisms. This parallel selection of different gene mutations that have the same phenotypic effect - in this case lactase persistence - is known as a soft selective sweep.

Soft selective sweeps have not been so clearly described before in humans, one reason being that variations caused by soft selective sweeps are more likely to be caused by genetic mutations in regulatory sequences, rather than mutations found in coding regions of genes.

Most statistical methods that analyse genetic variation assume we are looking for only one variation as the cause of genetic adaptation. But, in soft selective sweep patterns, more than one genetic variation is selected in parallel, which makes them more difficult to detect.

Dr Bryony Jones, also from the UCL Department of Genetics, Evolution and Environment, and lead author of the paper said: "Such variations have so far been very poorly studied and it will be important for them to be better characterised to understand better the relationship between historic adaptation and 21st century disease susceptibility."

Only in the last 5-10,000 years have humans started drinking the milk of other animals, following advances in our ability to herd animals. In times of plenty, being able to drink the milk of other animals would not have given a particular advantage to those with lactase persistence.

However, in situations where food sources became scarce, individuals capable of producing lactase as adults would be able to drink the milk of their animals, increasing their chances of survival.

Ethiopia has been subject to frequent droughts that contribute to famine. Individuals who can digest milk are more likely to increase their chance of survival under these conditions.

Dr Jones explained: "Ethiopia has been a cross-roads of human migrations in the last five thousand years since the lactase persistence genes are likely to have come under selection.

"Our studies on other African and Middle Eastern populations show quite different geographic distributions, with overlap in Ethiopia, suggesting that their origins are all different, but determining where these were and how they spread is likely to be difficult."

Professor Swallow said: "The combination of mutation, large effective population size, migration and selection has been shown to be important in generating this kind of pattern of diversity, namely parallel selection of multiple alleles of similar function, a so-called soft selective sweep."

More information: 'Diversity in lactase persistence alleles in Ethiopia; signature of a soft selective sweep' is published online on the 29th of August in The *American Journal of Human Genetics*.

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