

# Massive genetic study shows how humans are evolving

Analysis of 215,000 people's DNA suggests variants that shorten life are being selected against.

Bruno Martin

06 September 2017



Ira Block/NGC

Human populations are evolving to improve fitness in unexpected ways.

A huge genetic study that sought to pinpoint how the human genome is evolving suggests that natural selection is getting rid of harmful genetic mutations that shorten people's lives. The work, published in *PLoS Biology*<sup>1</sup>, analysed DNA from 215,000 people and is one of the first attempts to probe directly how humans are evolving over one or two generations.

To identify which bits of the human genome might be evolving, researchers scoured large US and UK genetic databases for mutations whose prevalence changed across different age groups. For each person, the parents' age of death was recorded as a measure of longevity, or their own age in some cases.



A radical revision of human genetics

“If a genetic variant influences survival, its frequency should change with the age of the surviving individuals,” says Hakhamanesh Mostafavi, an evolutionary biologist at Columbia University in New York City who led the study. People who carry a harmful genetic variant die at a higher rate, so the variant becomes rarer in the older portion of the population.

Mostafavi and his colleagues tested more than 8 million common mutations, and found two that seemed to become less prevalent with age. A variant of the *APOE* gene, which is strongly linked to Alzheimer's disease, was rarely found in women over 70. And a mutation in the *CHRNA3* gene associated with heavy smoking in men petered out in the population starting in middle age. People without these mutations have a survival edge and are more likely to live longer, the researchers suggest.

This is not, by itself, evidence of evolution at work. In evolutionary terms, having a long life isn't as important as having a reproductively fruitful one, with many children who survive into adulthood and birth their own offspring. So harmful mutations that exert their effects after reproductive age could be expected to be 'neutral' in the eyes of evolution, and not selected against.

But if that were the case, there would be plenty of such mutations still kicking around in the genome, the authors argue. That such a large study found only two strongly suggests that evolution is “weeding” them out, says Mostafavi, and that others have probably already been purged from the population by natural selection.



Genomics is failing on diversity

### **Links to longevity**

Why these late-acting mutations might lower a person's genetic fitness — their ability to reproduce and spread their genes — remains an open question.

The authors suggest that for men, it could be that those who live longer can have more children, but this is unlikely to be the whole story. So scientists are considering two other explanations for why longevity is important. First, parents surviving into old age in good health can care for their children and

grandchildren, increasing the later generations' chances of surviving and reproducing. This is sometimes known as the 'grandmother hypothesis', and may explain why humans tend to live long after menopause.

Second, it's possible that genetic variants that are explicitly bad in old age are also harmful — but more subtly — earlier in life. "You would need extremely large samples to see these small effects," says Iain Mathieson, a population geneticist at the University of Pennsylvania in Philadelphia, so that's why it's not yet possible to tell whether this is the case.

The researchers also found that certain groups of genetic mutations, which individually would not have a measurable effect but together accounted for health threats, appeared less often in people who were expected to have long lifespans than in those who weren't. These included predispositions to asthma, high body mass index and high cholesterol. Most surprising, however, was the finding that sets of mutations that delay puberty and childbearing are more prevalent in long-lived people.

To see a genetic link to delayed childbearing is intriguing, says Jonathan Pritchard, a geneticist at Stanford University in California. The link between longevity and late fertility has been spotted before, but those studies could not discount the effects of wealth and education, because people with high levels of both tend to have children later in life. The latest genetic evidence makes Pritchard think there is an evolutionary trade-off between

fertility and longevity, which had previously been studied only in other animals. "To actually find this in humans is really pretty cool," he says. "I think it's a really nice study."

Studying ongoing evolution in humans is notoriously difficult. Scientists who want to observe selection directly would need to measure the frequency of a mutation in one generation, and then again in all that generation's children and, better still, grandchildren, says Gil McVean, a statistical geneticist at the University of Oxford, UK. "That would be very hard to do well," he says. "You would need vast samples".

#### Related stories

- Scientists track last 2,000 years of British evolution
- Gene variants linked to success at school prove divisive
- Genetic secrets of the healthy elderly unveiled

[More related stories](#)

#### Related stories

- Scientists track last 2,000 years of British evolution
- Gene variants linked to success at school prove divisive
- Genetic secrets of the healthy elderly unveiled

[More related stories](#)

*Nature* doi:10.1038/nature.2017.22565

## References

---

1. Mostafavi, H. *et al.* *PLoS Biol.* **15**, e2002458 (2017).