

New research links genes to a longer human lifespan

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A group of genes that play an essential role in building components of our cells can also impact human lifespan, finds a new study led by UCL researchers.

The [genes](#) have previously been found to extend lifespan in small organisms, such as making [fruit flies](#) live 10% longer, but this is the first time scientists have demonstrated a link in people as well, as they report in a new *Genome Research* paper.

Co-lead author Dr. Nazif Alic (UCL Institute of Healthy Ageing) said, "We have already seen from extensive previous research that inhibiting certain genes involved in making proteins in our cells, can extend lifespan in model organisms such as yeast, worms and flies. However, in humans, loss of function in these genes has been seen to cause diseases, such as developmental disorders known as ribosomopathies.

"Here, we have found that inhibiting these genes may also increase longevity in people, perhaps because they are most useful early in life before causing problems in late life."

The genes are involved in the protein synthetic machinery of our cells, which is essential for life, but the researchers say it may be that we do not need as much of its effect late in life. The genes appear to be an example of antagonistic pleiotropy, where genes that shorten our lives are selected for in evolution if they help us early in life and through our child-bearing years.

The researchers reviewed [genetic data](#) from previous studies involving 11,262 people who had lived an exceptionally [long life](#), to an age above the 90th percentile of their cohort. They found that people with reduced activity of certain genes were more likely to live very long lives. The genes are linked to two RNA polymerase enzymes (Pols) that transcribe ribosomal and transfer RNAs, namely Pol I and Pol III, as well as the expression of ribosomal protein genes.

The scientists found evidence that the genes' effects were linked to their expression in specific organs, including abdominal fat, liver, and [skeletal](#)

[muscle](#), but also found that the effect on longevity went beyond just associations with any specific age-related diseases.

The findings add to the evidence that drugs such as rapamycin, an immune regulator which acts to inhibit Pol III, may be helpful to promote healthy lifespan.

Professor Karoline Kuchenbaecker (UCL Genetics Institute) said, "Aging research in model organisms, such as flies, and in humans are often separate efforts. Here we are trying to change this. In flies we can experimentally manipulate aging genes and investigate mechanisms. But ultimately, we want to understand how aging works in humans. Bringing the two fields together using methods such as Mendelian Randomization has the potential to overcome the limitations of both fields."

More information: Sara Javidnia et al, Mendelian randomization analyses implicate biogenesis of translation machinery in human aging, *Genome Research* (2022). [DOI: 10.1101/gr.275636.121](https://doi.org/10.1101/gr.275636.121)

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