

# Pinpointing the molecular mechanisms of ageing

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Although each and every one of us goes through it, ageing is a poorly understood process. Researchers have used a biomarker called the epigenetic clock to identify a gene that is closely linked to ageing in humans. The study, published in *Genome Biology*, shows that the epigenetic clock could be a good tool for improving our understanding of the molecular mechanisms behind ageing.

Researchers at EMBL's European Bioinformatics Institute (EMBL-EBI), the Babraham Institute and collaborators have used the [epigenetic clock](#) to explore the molecular mechanisms that may drive ageing in humans. They found one gene, called NSD1, that seems to be closely linked to the process. This type of research could advance our understanding of ageing.

There are different ways of measuring an organism's age. Chronological age is a measure of how long an organism has been alive, while [biological age](#) is a measure of how well the organism is functioning on a molecular level.

One useful tool for measuring biological age is the epigenetic clock, proposed first by Trey Ideker, and independently by Steve Horvath in 2013.

## What is an epigenetic clock?

An epigenetic clock is a [mathematical model](#) that predicts age by measuring DNA methylation levels in different sites across the genome. DNA methylation is a process by which [methyl groups](#) are added to the DNA molecule, which can modify the function of a gene without changing its underlying DNA sequence. DNA methylation is essential for the healthy growth and development of cells and it is affected by lifestyle and environmental factors.

Epigenetic clocks can be used to estimate the biological age of a tissue, cell type or organ. By comparing 'DNA methylation age' or biological age with [chronological age](#) in different tissues, scientists can gain insights into how ageing works, the factors influencing it, and how ageing is linked to cancer, obesity, Alzheimer's disease and many other conditions.

## A promising tool

The researchers examined different datasets—many of them publicly available—of people with [developmental disorders](#), to see whether there were any associations between specific [genes](#) and an acceleration of biological age. They found that individuals with a mutation in gene NSD1 had an accelerated biological age according to the epigenetic clock, meaning they were ageing faster at a molecular level.

"The epigenetic clock is the most accurate tool available to measure the [ageing process](#) in humans," explains Daniel Elías Martín-Herranz, who recently completed his Ph.D. at EMBL-EBI. "We wanted to 'peer inside' and better understand how it works. Specifically, we wanted to see if we could identify [specific genes](#) or proteins from the epigenetic machinery that accelerate or slow down the ageing process. The fact that we found one gene that, when mutated, results in a significant acceleration of biological age is very encouraging. It shows that the epigenetic clock is a promising tool for understanding ageing and that we may unravel the molecular mechanisms that control its ticking rate.

"There is a lot of potential for such studies, but it's also worth noting that they are not possible without access to relevant public datasets. We would like to thank our collaborators who made the data available to us."

Professor Wolf Reik from the Babraham Institute agrees. "Following on from the work with the mouse epigenetic ageing clock two years ago, this paper continues the productive collaboration between the Babraham Institute and EMBL-EBI on mammalian ageing," he says. "It's exciting to see that genes can be identified that may underlie an epigenetic ageing program and that they can make molecular sense. The gene identified here is implicated in ageing in other organisms, and in the regulation of the epigenome during the ageing process."

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