## Is Your DNA Clock Running Fast? You May Die Sooner Than Later

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University of Edinburgh researchers find that the difference between actual age and DNA methylation age is predictive of all-cause mortality in later life. [©illarionova/Fotolia]

Chemical changes to DNA that accumulate over a lifetime amount to a kind of biological clock. By analyzing these changes, scientists based at the **University of Edinburgh** found that if "biological clock age" exceeds actual chronological age, earlier death is more likely.

The chemical changes that the scientists used to predict people's ages are epigenetic in nature. That is, they do not alter DNA's underlying code of base sequence. Rather, they consist of methylation marks, which are characterized by the addition of a methyl group to a cytosine nucleotide primarily at cytosine-phosphate-guanine (CpG) sites.

**DNA methylation**, which alters the degree to which genes are active, plays an essential role in development, and it may vary over the course of one's life. For example, the degree to which DNA is methylated may depend on lifestyle and environmental factors, as well as genetic variation.

Although various factors contribute to variations in DNA methylation, the University of Edinburgh researchers, in collaboration with researchers in Australia and the United States, were able to conclude that "DNA methylation-derived measures of accelerated ageing are heritable traits that predict mortality independently of health status, lifestyle factors, and known genetic factors."

This finding emerged from a study of four independent cohorts of older people. Overall, nearly 5,000 people had their biological clock ages, or DNA methylation ages, determined from blood samples. Follow-up periods lasted as long as 14 years.

The results of this work appeared online January 30 in Genome Biology, in an article entitled, "DNA methylation age of blood predicts all-cause mortality in later life." The article cited patterns in terms of  $\Delta_{age}$ , the difference between DNA methylation age and chronological age.

"A 5-year higher  $\Delta_{age}$  is associated with a 21% higher mortality risk, adjusting for age and sex," wrote the authors. "After further adjustments for childhood IQ, education, social class, hypertension, diabetes, cardiovascular disease, and APOE e4 status, there is a 16% increased mortality risk for those with a 5-year higher  $\Delta_{age}$ ."

"The same results in four studies indicated a link between the biological clock and deaths from all causes," said lead author Riccardo Marioni, Ph.D., of the University of Edinburgh's Centre for Cognitive Ageing and Cognitive Epidemiology. "At present, it is not clear what lifestyle or genetic factors influence a person's biological age. We have several follow-up projects planned to investigate this in detail."

"This new research increases our understanding of longevity and healthy **aging**," added principal investigator Ian Deary, Ph.D., also from the Centre for Cognitive Ageing and Cognitive Epidemiology. "It is exciting as it has identified a novel indicator of aging, which improves the prediction of lifespan over and above the contribution of factors such as smoking, diabetes, and cardiovascular disease."