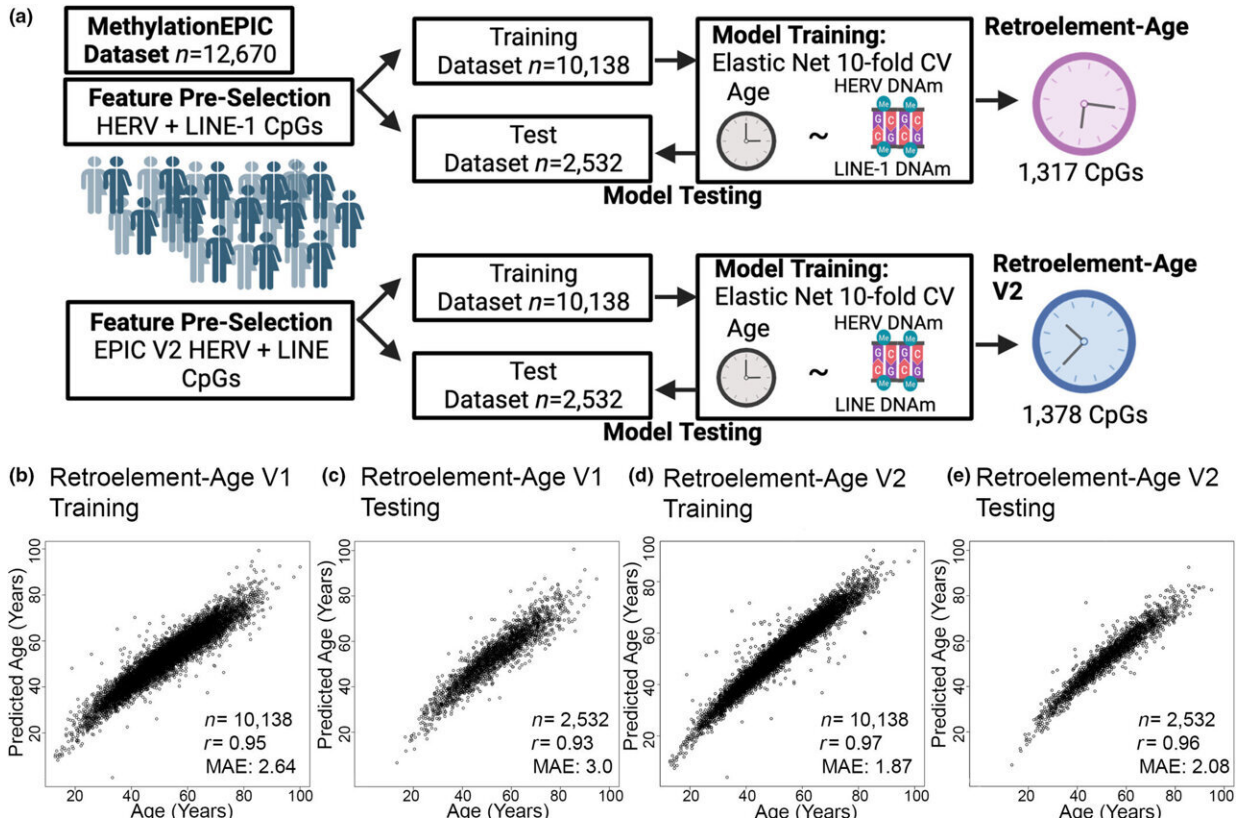
Study finds potential link between DNA markers and aging process

August 19 2024



Construction of Composite Retroelement-Age and Retroelement-Age V2 Epigenetic Clocks. Credit: *Aging Cell* (2024). DOI: 10.1111/acel.14288

Researchers at Weill Cornell Medicine and the epigenetics company TruDiagnostic have uncovered DNA markers associated with

retroelements, remnants of ancient viral genetic material in our genes that act as highly accurate epigenetic clocks predicting chronological age. The results support the idea that certain retroelements in the human genome may be involved in aging.

Retroelements have been known to impact gene regulation, gene expression, genomic stability and the trajectory of various human diseases, but their potential as biomarkers for aging had been largely unexplored.

The study, published in *Aging Cell*, concluded that these retroelement clocks embedded in the human genome capture unique signals of aging not previously recognized by other clocks that measure chronological age.

Most aging clocks estimate a person's biological age based on patterns of epigenetic markers—chemical tags called methyl groups that are attached to DNA and affect how genes are expressed. The pattern of methylation on retroelements seems to change as people age, causing some genes to be more active, which may lead to genomic instability, inflammation and age-related diseases.

Aging is a complex process influenced by genetic, environmental and epigenetic factors, with researchers pursuing reliable markers that can predict biological age—a snapshot of a person's age at the biochemical level that impacts health and overall well-being. On the other hand, chronological age represents the number of years a person has lived. Depending on the individual, the two may not correlate.

Building an aging clock based on retroelements

Researchers used a machine learning model from TruDiagnostic to analyze epigenetic data from 12,670 individuals with ages ranging from

12 to 100. Using the resulting DNA methylation patterns of retroelements, specifically human endogenous retrovirus (HERV) and long interspersed nuclear elements (LINEs), they developed a composite retroelement-age clock called "Retro-Age."

"Now, with Retro-Age, we have greater insight and a fresh perspective into the aging process and a potentially powerful tool to predict biological age," said first author Dr. Lishomwa Ndhlovu, the Herbert J. and Ann L. Siegel Distinguished Professor of Medicine and professor of immunology in medicine in the Division of Infectious Diseases at Weill Cornell Medicine.

The researchers found that the Retro-Age clock remained accurate when testing various human tissues, complemented existing epigenetic clocks and even extended to other mammalian species. Their findings point to the possibility that retroelement activity might be a fundamental aspect of aging across different species.

Turning back the clock: The impact of environmental factors

The researchers also found that the DNA methylation patterns they observed were not only predictive of age but also responsive to outside factors like antiretroviral therapy taken by people living with HIV. HIV infection accelerates epigenetic aging, while antiretroviral therapy appears to reverse the clock to some degree. This suggests that retroelement activity is influenced by both the infection and its treatment, affecting the biological aging process in people living with HIV.

"The reactivation of specific retroelements increases with age, potentially leading to biological hallmarks of aging such as

inflammation, cellular senescence and genomic instability," said corresponding author Dr. Michael Corley, assistant professor of immunology in medicine in the Division of Infectious Diseases at Weill Cornell Medicine.

"Our findings indicate that retroelement clocks capture previously undetected facets of biological aging and may open the door to future treatments for these and other age-related conditions."

Monitoring the activity of retroelements could help track the effectiveness of anti-aging therapies, health outcomes in aging populations and the impact of lifestyle changes on biological aging, said the researchers.

Drs. Ndhlovu and Corley plan to explore new treatments or therapeutic interventions for age-related diseases by targeting the epigenetic states of specific retroelements in the human genome. This approach, they noted, may eventually reverse or mitigate the biological effects of aging, improving an individual's health span and lifespan.

More information: Lishomwa C. Ndhlovu et al, Retro-age: A unique epigenetic biomarker of aging captured by DNA methylation states of retroelements, *Aging Cell* (2024). DOI: 10.1111/acel.14288

Provided by Weill Cornell Medical College