HIV infection prematurely ages humans by an average of five years

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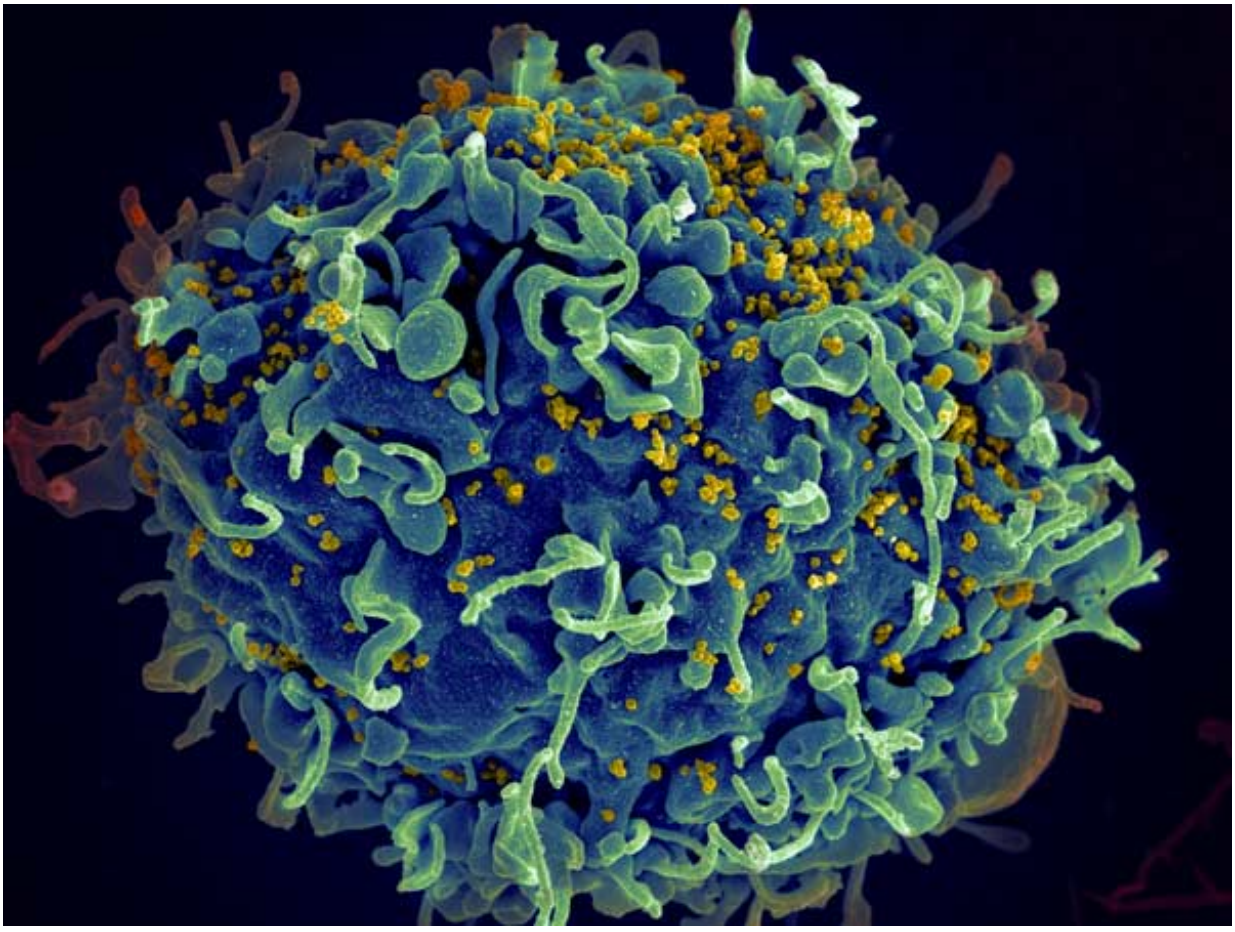

HIV (yellow) infecting a human immune cell. Credit: Seth Pincus, Elizabeth Fischer and Austin Athman, National Institute of Allergy and Infectious Diseases, National Institutes of Health

Thanks to combination antiretroviral therapy, many people with HIV can be expected to live decades after being infected. Yet doctors have observed that these patients often show signs of premature aging. Now a study published April 21 in *Molecular Cell* has applied a highly accurate biomarker to measure just how much HIV infection ages people at the biological level—an average of almost 5 years.

"The medical issues in treating people with HIV have changed," says Howard Fox, a Professor in the Department of Pharmacology and Experimental Neuroscience at the University of Nebraska Medical Center and one of the authors of the new study. "We're no longer as worried about infections that come from being immunocompromised. Now we worry about diseases related to aging, like cardiovascular disease, neurocognitive impairment, and liver problems."

The tool used in the new study looks at epigenetic changes in people's cells. Epigenetic changes affect the DNA, but not the DNA sequence. Once they occur, they are passed down from one generation of cell to the next, influencing how genes are expressed. The particular epigenetic change used as a biomarker in this research was methylation, the process by which small chemical groups are attached to DNA. Methylation of DNA can impact how genes get translated into proteins.

"What we've seen in previous studies is that as we age, methylation across the entire genome changes," says Trey Ideker, a Professor of Genetics in the Department of Medicine at the University of California San Diego and the study's other corresponding author. "Some people call it entropy or genetic drift. Although we're not sure of the exact mechanism by which these epigenetic changes lead to symptoms of aging, it's a trend that we can measure inside people's cells."

The 137 patients included in the analysis were enrolled in CHARTER (the CNS Antiretroviral Therapy Effects Research study), a long-term

study aimed at monitoring HIV-infected individuals who are being treated with combination antiretroviral therapy. Subjects who were chosen didn't have other health conditions that could skew the results. 44 HIV-negative control subjects were also included in the initial analysis. An independent group of 48 subjects, both HIV positive and negative, was used to confirm the findings.

In addition to the discovery that HIV infection led to an average advance in biological aging of 4.9 years, the researchers note that such a change correlates with an increased risk of mortality of 19%.

"We set out to look at the effects of HIV infection on methylation, and I was surprised that we found such a strong aging effect," Ideker says.

"Another thing that was surprising was that there was no difference between the methylation patterns in those people who were recently infected [less than five years] and those with chronic infection [more than 12 years]," Fox adds.

The investigators say it's possible drugs could eventually be developed to target the kinds of epigenetic changes observed in the study. But the more immediate implications are much simpler: they note that people infected with HIV should be aware that they're of greater risk for age-related diseases and work to diminish those risks by making healthy lifestyle choices regarding exercise, diet, and drug, alcohol, and tobacco use.

More information: *Molecular Cell*, Gross et al: "Methylome-wide analysis of chronic HIV infection reveals five-year increase in biological age and epigenetic targeting of HLA" DOI: 10.1016/j.molcel.2016.03.019

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