Medical Xpress

# Experimental blood test predicts age-related disease risk in diverse populations

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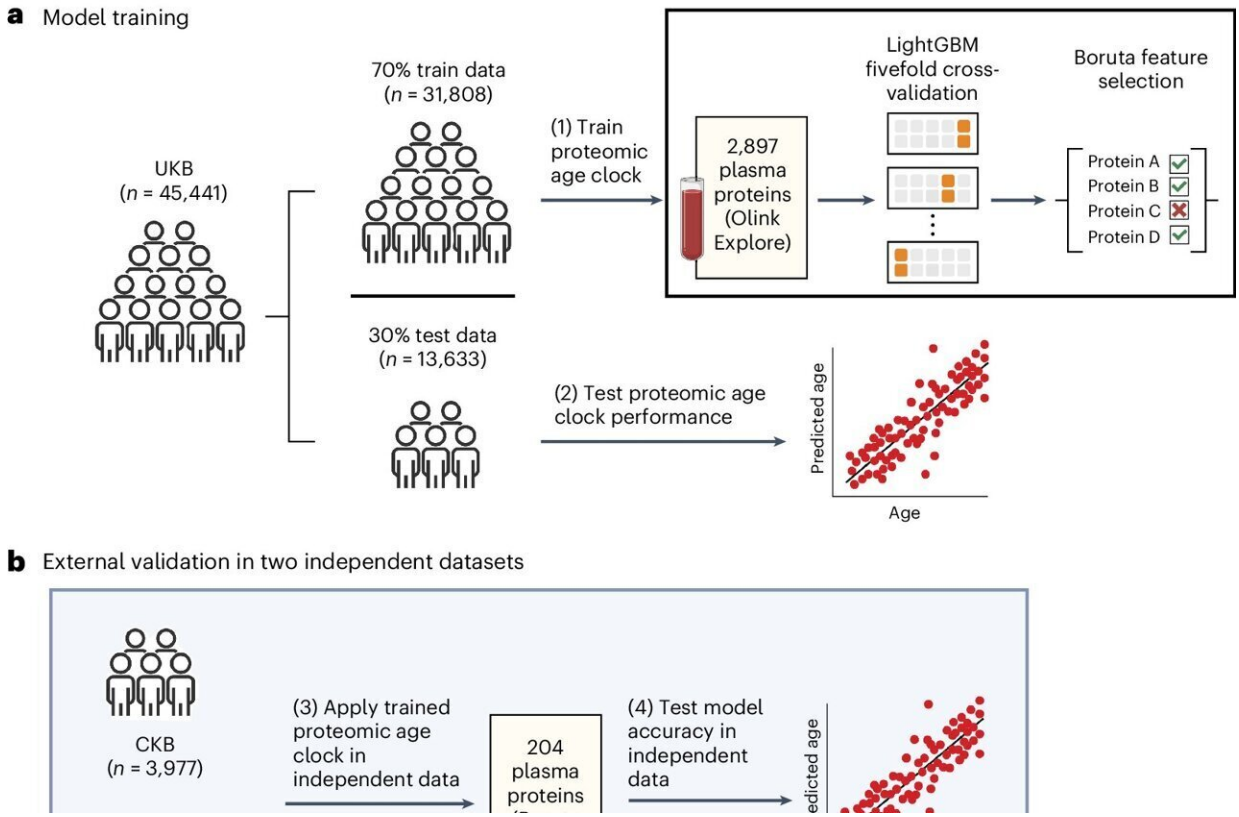


Overview of the study design and analytic approaches. Credit: *Nature Medicine* (2024). DOI: 10.1038/s41591-024-03164-7

Researchers have developed a machine learning-powered blood test that analyzes more than 200 proteins to gauge a person's rate of biological

aging, which the team says can be used to estimate the person's risk of developing 18 major age-related diseases and of dying prematurely from any cause.

The work helps validate the use of the proteome—the entire set of proteins present in the body at a given time—as an accurate gauge of how old a person is, not in years, but in terms of how their cells are functioning.

The findings provide insight into the biological pathways that lead to a person developing multiple age-related diseases, open doors to better understanding how genes and environment interact in aging, and could help researchers develop treatments for age-related diseases and assess their effectiveness.

Though the test is currently restricted to the research lab, the team is working on developing it into something anyone can order at a doctor's office.

Austin Argentieri, HMS research fellow in medicine in the Analytic and Translational Genetics Unit at Massachusetts General Hospital, is lead author of the study, published Aug. 8 in *Nature Medicine* and discusses his team's findings below.

## What question did you set out to answer with this study?

Can we develop a proteomic aging clock that can help predict the risk of common age-related diseases?

Age is the major determinant for most common chronic diseases but is an imperfect surrogate for aging, which is the driver of age-related

multimorbidity (having more than one chronic health condition) and mortality.

Aging can be estimated more precisely by using 'omics data to capture the biological functioning of an individual in comparison to an expected level of functioning for a given chronological age.

While the most common biological aging clocks use DNA methylation, protein levels may provide a more direct mechanistic and functional insight into aging biology. Moreover, the proteome is the most common target for drug development.

However, previous proteomic age clock studies have not been validated independently across populations with diverse genetic and geographic backgrounds.

So far, none have been developed in large or well-powered general population samples that allow for association testing across a wide spectrum of age-related disorders, multimorbidity, and mortality.

## What did you find?

We developed a machine learning model that uses blood proteomic information to estimate a proteomic age clock in a large sample of participants from the UK Biobank. Our sample included 45,441 participants ranging from 40 to 70 years old.

We further validated this model in two biobanks across the world: 3,977 participants aged 30-80 from the China Kadoorie Biobank and 1,990 participants aged 20-80 from the FinnGen biobank in Finland. These biobanks are geographically and genetically distinct populations that have distinct age ranges and morbidity profiles from the UK Biobank.

We identified 204 proteins that accurately predict chronological age, and we further identified a set of 20 aging-related proteins that capture 91% of the age prediction accuracy of the larger model.

We demonstrated that our proteomic age clock showed similar age prediction accuracy in the independent participants from China and Finland compared with its performance in the UK Biobank.

We found that proteomic aging was associated with the incidence of 18 major chronic diseases—including diseases of the heart, liver, kidney, and lung; diabetes; neurodegeneration, such as Alzheimer's disease; and cancer—as well as multimorbidity and all-cause mortality risk.

Proteomic aging was also associated with age-related measures of biological, physical, and cognitive function, including telomere length, frailty index, and several cognitive tests.

## What are the clinical implications of your work?

We provide some of the largest and most comprehensive evidence to date demonstrating that proteomic aging is a common biological signature related to numerous age-related functional traits, morbidities, and mortality.

We also provide some of the first evidence that a proteomic age clock can be highly generalizable across human populations of diverse genetic ancestries, age ranges, and morbidity profiles.

Multimorbidity is an important problem in clinical and population health that has a major impact on the cost of health care. Our proteomic clock gives us a first insight into the pathways that form the biological basis for multimorbidity.

In the near future, proteomic age clocks can be used to study the relationship between genetics and environment in aging, yielding novel insights into the drivers of aging and multimorbidity across the life span.

An important avenue will also be to use proteomic clocks as a biomarker for the effectiveness of preventive interventions targeting aging and multimorbidity.

Furthermore, proteomic clocks may be used to accelerate drug development and clinical trials through identification of high- and low-risk patients. For example, less than 1% of those in the bottom decile of proteomic aging developed Alzheimer's over the following 10–15 years.

**More information:** M. Austin Argentieri et al, Proteomic aging clock predicts mortality and risk of common age-related diseases in diverse populations, *Nature Medicine* (2024). DOI: 10.1038/s41591-024-03164-7

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