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Health & Physiology

Your biological age within a drop of your blood

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ABSTRACT

When is aging occurring? Why do I look younger/older than my age? What is my biological age? Here are just a few questions that can be answered using a single drop of your blood!

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If we took a blood sample from you and one from your elderly grandmother, could you tell which sample came from which person just by looking at the molecules in the blood? In our recent study published in Nature Medicine, we addressed this question and described - more generally - how we age throughout the entire lifespan.

We have known for a long time that measuring certain proteins in the blood can give detailed information about a person's health status. This is because proteins do virtually everything in the body and are required for the structure, function, and regulation of tissues and organs. In the blood, they also serve diverse biological functions. For instance, some assist the transport of hormones while others guide immune cells to sites of infection. Looking at thousands of proteins, therefore, gives a snapshot of what is happening throughout your body. In fact, the blood proteome (the entire repertoire of proteins found in the blood) includes dynamic markers of our health status, and several proteins actively inhibit or promote tissue aging. This is why a better understanding of how the blood proteome changes as we get older can help to build more robust diagnostic tests for age-related diseases like cancer, not to mention that we may discover new targets to prevent and treat these diseases.

In our study, we looked at the levels of 2,925 different proteins in the blood of 4,263 people, for a total of 12,469,275 measurements! We tracked how proteins changed across the entire adult lifespan, from 20-year-olds to 95-year-olds, and discovered that a third of the blood proteins significantly increased or decreased. Using machine learning

approaches, we shortlisted the number of proteins to 373 and built a clock predicting people's ages with great accuracy - the average error was only 2.6 years. However, several individuals strongly deviated from this clock; one person was predicted to be 35 years older than she really was! Could this clock provide some information regarding how well we age? Yes, indeed! We discovered that individuals who were predicted to be younger than their age performed better on cognitive and physical tests - and vice-versa. With further validation, this clock could be used to assess the efficiency of aging interventions but also could identify individuals who are aging faster biologically than others. These people might be at risk earlier in life for age-related diseases such as cardiovascular or Alzheimer's disease, and identifying this risk could save their lives.

We found remarkable patterns of proteins changing in an undulating manner when looking more closely at the aging trajectories of the 373 proteins constituting the plasma proteomic clock (and more globally at the 3000 proteins). This is particularly important because, for years, aging has been studied by comparing the extremes (young vs old) or using statistical models assuming linear changes throughout the lifespan. We now have evidence that aging is not one long and continuous process but seems to accelerate periodically. To quantify this phenomenon, we developed a new computational approach and discovered that the body shifts gears three times during our lives - at 34, 60, and 78 years old. These key ages reflect the starting, stopping, and changing of different biological processes. The proteins found in these 3 waves overlapped with proteins found in patients with age-related diseases and even age-related functional changes like impaired grip strength.

Altogether, our study is opening new avenues of research into exactly what's going on during the aging process. Understanding these waves of aging can help us to better comprehend why and how our bodies break down as we get older. Our results also have strong implications for the development of diagnostic and prognostic tests. Indeed, the undulating nature of the aging plasma proteome and its interactions with diseases must be considered when developing proteomic signatures for diagnostic purposes. Such reliable tests are urgently needed for several diseases. Of particular interest are studies of Alzheimer's disease, for which blood-based biomarkers are unavailable, and disease onset is believed to occur up to two decades before symptoms emerge.