Clinical Chemistry

Proteomic Aging Clock Predicts Mortality and Risk of Common Age-Related Diseases

Article:
Zoi E Sychev, Jesse C Seegmiller.
Proteomic Aging Clock Predicts Mortality and Risk of Common Age-Related Diseases.
Clin Chem 2025; 71(8): 920–1. https://doi.org/10.1093/clinchem/hvaf041

Guest: Dr. Jesse Seegmiller is an Associate Professor in the Department of Laboratory Medicine and Pathology at the University of Minnesota.

Bob Barrett: This is a podcast from *Clinical Chemistry*, a production of the Association for Diagnostics & Laboratory Medicine. I'm Bob Barrett. Chronological age, which is the number of years we've been alive, is a concept we're all very familiar with. From the first years of life, we're conditioned to think in terms of seasonal milestones that give each year its predictable rhythm. Another metric of aging, biological age, describes the physiological changes that occur over the course of the typical human lifespan.

In general, these two concepts of age align well. Individuals of a certain chronological age generally have physical features and cognitive functions that we associate with that age group. Still, we have all encountered individuals who seem much older or younger than their stated chronological age. The accumulated evidence suggests that this discrepancy can be attributed to genetics, lifestyle factors, and environmental exposure, on all of which impact the makeup of proteins within our body.

This then raises the essential question; can proteins in our blood reflect our biological age? And if so, how might this information be applied to guide healthcare decisions? A News & Views article, appearing in the August 2025 issue *of Clinical Chemistry,* describes a recent study that used proteomics and machine learning to calculate biological age from a large plasma biobank and found it to be associated with several age related diseases.

In this podcast, we welcome the author of that News & Views article. Dr. Jesse Seegmiller is an Associate Professor in the Department of Laboratory Medicine and Pathology at the University of Minnesota. He is a board certified clinical chemist and serves as a laboratory director and medical director for M Health Fairview where he oversees routine and esoteric mass spectrometry-based testing. So, Dr. Seegmiller, in your recent article you discuss differences in chronological age and biological age. And while chronological age is more straightforward, biological age is an emerging concept. What examples can you give our listeners to better discern the differences in biological and chronological age?

Jesse Seegmiller: That's a great question, Bob. When most people think of age, they think of time and date right now, and then they reference this back to your birthday. And this of course is the person's chronological age. In terms of biological age, this is a reference to an age that best reflects how your body presents itself, whether it be older, younger, or even matching your chronological age.

Some examples of where biological age are perceived to be different from chronological age can manifest itself in children, say in the 10 to 12-year-old range. There are many times that some kids develop faster than others and that the 12-year-old child may have the physique of a 17- or 18-year-old. In this case, their biological age would be perceived as older than their chronological age. Another example would be the 75-year-old adult who functions and looks like they are 50 years old. So these are examples that show how people can age either faster or slower with respect to their chronological age. The reasoning behind why this happens lies within the underlying genetic, environmental, and lifestyle factors specific to that person.

Bob Barrett: Your publication also mentions how a recent group of researchers defined some aging metrics using proteomic studies that may shed light on some of the differences we've seen in chronological and biological age. Could you expand a bit on just how they went about this?

Jesse Seegmiller: Yeah, absolutely. What the investigators did was surveyed patient plasma protein profiles using a proteomic platform. Now, this platform allows for the assessment and identification of thousands of proteins in each of the patients' plasma. These protein profiles were then cross-referenced to the patient's health profile, looking at phenotypical factors like physical and cognitive function, self-rated health, frailty index, along with many other features. They came up with these metrics and referred to them as the ProtAge, which is the biological measure, and the ProtAgeGap, which was suggested in part to define the difference between the chronological age and the biological age by pairing the phenotypical presentation with these biomarkers.

Now, the study was performed using over 45,000 patient profiles and incorporated machine learning techniques to distill these complex relationships into a model. There's quite a bit of power behind the model to come up with these metrics in a population that had well defined clinical characteristics. What they found, though, was striking, that those patients with a large ProtAgeGap, so the gap metric, were strongly associated to things like type 2 diabetes, cancer, pulmonary disease, and even facial aging.

Bob Barrett: How do you see metrics such as the ProtAge and ProtAgeGap being used in clinical practice?

Jesse Seegmiller: Yeah, I think if clinicians had a diagnostic crystal ball providing insight into a patient's biological age, it could have profound implications on how they treat that patient. Many times, you'll hear in situations of cardiovascular disease or in cancer cases that the patient is just too weak for a specific treatment, or that the patient tolerated the treatment better than expected. By incorporating these relatively hard to quantify metrics, it really starts moving into the realm of personalized medicine and allowing for the application of treatment approaches specific to that patient. Metrics like this could potentially assist in how aggressive the clinician's approach to treatment will be in a specific patient.

Bob Barrett: Well, finally, Dr. Seegmiller, what barriers, if any, do you foresee in moving metrics like the ProtAge and ProtAgeGap into everyday clinical use?

Jesse Seegmiller: Yeah. Presently, these proteomic profiling studies were performed on testing platforms that were designed for research studies. Another thing to consider, while there were thousands of proteins analyzed in these studies and there are likely protein subsets that are driving the biological process with respect to the biological aging, I think that now that they discovered these protein patterns, they could potentially be translated into much smaller protein panels that could then be validated and translated on routine clinical analyzer systems. Once this happens, then the diagnostic utility could be assessed along with the various protein panels' analytical performance. Let's say this approach should provide adequate diagnostic information regarding a patient's biological age or some metric like the ProtAgeGap, then I believe there'd be a path forward in this personalized medicine approach of aging.

Bob Barrett: That was Dr. Jesse Seegmiller from the University of Minnesota in Minneapolis. He wrote a News & Views article, appearing in the August 2025 issue of *Clinical Chemistry,* about a new proteomic tool to identify biological age, and he's been our guest in this podcast on that topic. I'm Bob Barrett. Thanks for listening.