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Identify Protein Biomarkers for **Aging Research with the SomaScan® Assay**

Our genomes remain mostly unchanged throughout our lifetime; what changes are gene expression signatures[7] that determine which proteins are actively expressed and which ones are silenced.

Advanced age is the single greatest risk factor for disease; however, aging is a complex and multifactorial process, and its mechanisms are still poorly understood. It has been shown that aging activates common transcriptional patterns across most organs and tissues, such as inflammatory, stress response and transcriptional regulation pathways[1], suggesting the changes are systemic and interrelated. Exposing a young, healthy organism to plasma from old mice, for example, slows down tissues regeneration in a manner that resembles aging[2]. Conversely, exposure to plasma from young blood is capable of restoring youthful phenotypes[3,4]. Understanding the primary factors that affect tissue and organ function on a cellular level may lead to developing treatments that can help people stay healthy and live longer.

Studying the Mechanisms of Aging Using Big Data

Several different approaches have been undertaken in recent years to investigate the mechanisms of aging, including genomic, transcriptomic and proteomic analyses. Genome-wide association studies (GWAS) have been used to pinpoint the genetic signatures associated with longevity and lifespan[5,6]. However, genomics offers little insight into the causes of physiological shifts precipitated by time. Our genomes remain mostly unchanged throughout our lifetime; what changes are gene expression signatures[7], which determine which proteins are actively expressed and which ones are silenced.

New research has shown how large-scale proteomic studies can help reveal a comprehensive picture of health at a moment in time and can more accurately predict early signs of disease[8]. Popular methods for investigating the proteome are LC–MS/MS[9] and immune-based assays[10], but they both suffer from drawbacks such as high cost, difficult sample preparation, limited sensitivity and throughput. These limitations reduce the size of cohorts and restrict the amount of information that can be gathered through those studies.

Conversely, the SomaScan® Proteomic Platform can be used to analyze thousands of protetins across thousands of participants, enabling researchers to harness the power of big data to detect the underlying mechanisms of aging and disease progression[11,12]. The SomaScan Assay is a highly multiplexed, sensitive, and reproducible tool that can measure the expression of 7,000 proteins from a single blood sample. The large-scale proteomic studies enabled by the SomaScan Assay provide the opportunity to create predictive models for healthy or accelerated aging based on patterns in the proteome.

Research Utilizing the SomaScan Assay Discovers Links Between Aging and Disease

While aging is a risk factor for disease, aging-related diseases do not take hold at the same time across individuals. Some people live well into advanced age before developing hallmarks of aging, while others see the effects of aging much earlier. That is, our biological clocks and our chronological clocks do not always agree. Two recent studies used the SomaScan Assay to identify proteomic signatures of aging that can be used to identify risk factors independent of chronological age.

In a landmark study lead by Nir Barzilai (Albert Einstein College of Medicine) and Tony Wyss-Coray (Stanford University), the SomaScan Assay was used to identify distinct protein signatures associated with age that can serve as "proteomic clocks". By analyzing plasma proteomes of 4,263 adults ranging from 18 to 90+ years old, Lehallier et al. identified patterns of protein expression that could be tied to biological age and age-related disease[13]. The findings, which were reported in Nature Medicine, reveal three separate waves of changes in the plasma proteome, occuring in the 4th, 7th and 8th decades of life **(Figure 1)**. Importantly, these aging events were correlated with phenotypic outcomes measured by physiological and cognitive parameters.

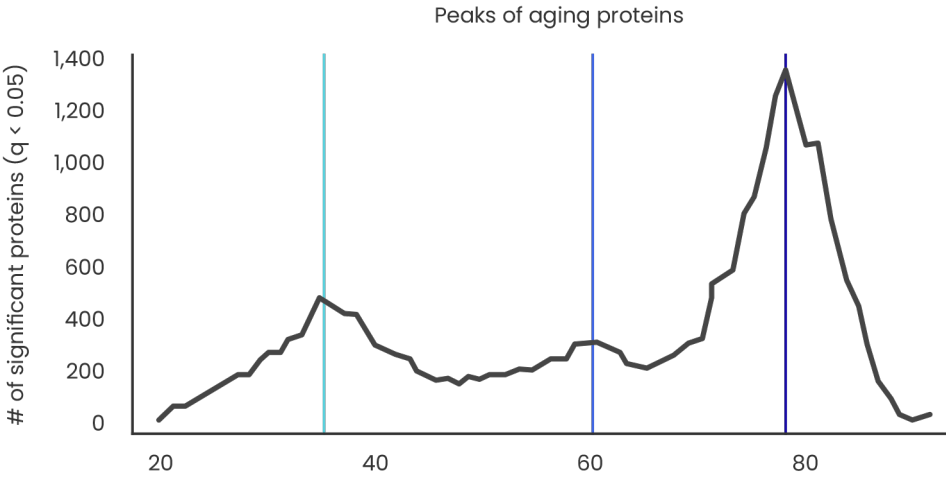

Figure 1. Adapted from Lehallier et al. The Y axis shows the number of differentially expressed proteins across age. Vertical lines mark local peaks.

In addition to identifying proteomic signatures that could serve to predict biological age, Lehallier et al. discovered a correlation between these biomarkers and age-related diseases. Protein clusters characteristic of middle and old age overlapped with proteins associated with cognitive and physical decline. Those signatures were enriched in patients with Alzheimer's, Down syndrome, and cardiovascular disease - conditions that are associated with accelerated aging.

A separate study out of the Institute for Aging Research at Albert Einstein College of Medicine focused on analyzing frailty in an elderly population[14]. Frailty was defined by decreased physiological reserves and increased susceptibility to poor outcomes in aging. Their analysis identified 143 frailty-associated proteins that were related to biological pathways associated with lipid metabolism, musculoskeletal development and cellular signaling. Identifying these pathways as markers of biological age that is advanced beyond chronological age serves as a clue to what systems need to be preserved in older age order to increase health span.

Potential Future Applications for the SomaScan Assay in Aging Research

By studying both the natural aging process and the signs of premature decline, scientists have been able to identify common proteomic signatures between aging and disease. This approach goes a step beyond the previous attempts to tie longevity and disease to genetic predisposition, providing a way to incorporate information on how our lifestyle and health events can influence life span by accelerating or slowing down the biological clock.

One of the most significant outcomes of this research is demonstrating that plasma protein biomarkers can indicate the health of different organs and tissues. These can serve as non-invasive diagnostic markers that monitor age-related molecular changes in blood. Aging-related protein biomarkers could also aid in identifying intervention strategies, including mitigating the effects of systemic tissue and organ deterioration through blood composition.

The SomaScan Assay enables researchers to mine the human proteome to build better predictive models for accelerated aging and disease progression across a variety of disorders, to understand sex differences in aging, and more. Protein biomarkers for many common aging-related diseases have already been elucidated with the SomaScan Assay, from cancer to cardiovascular disease[15,16]. These types of insights have led to diagnostic, prognostic and

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predictive tests that have bolstered aging research and set the stage for a new era in personalized medicine. In the future, such work could be expanded to include additional aging-related conditions, such as neurological and musculoskeletal diseases, providing a complete proteomic map for healthful aging.

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Founded in 2000, SomaLogic, a global leader in proteomics, pioneered the SomaScan Platform with unparalleled coverage. Unlike any other technology, the SomaScan Assay enables users to take up to 11,000 protein measurements from just 55 µL of various body fluids like plasma, serum, CSF, and urine.

The proprietary SomaScan Assay measures proteins with high specificity, high throughput, and high reproducibility, which enables the possibility of faster, more precise drug discovery. Our A.I. and machine learning-powered bioinformatics algorithms, operated in tandem with the company's database of more than 750,000 protein samples, helped to create a growing suite of SomaSignal® Tests. These tests provide additional insights into the current health status of patients and the future risk of conditions and diseases. Custom and disease-specific panels are also available for a more targeted approach.

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