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The SomaScan® Assay enables discovery of blood-based biomarkers in neurodegenerative diseases

Blood-based biomarkers show promise as a minimally invasive, cost-effective option for the detection, classification, and monitoring of neurologic diseases.[1-3]

Researchers currently have few validated pathophysiological biomarkers for [neurodegenerative diseases], covering mostly [Alzheimer's disease] and requiring expensive imaging tools or body fluid invasive sampling, totally inadequate for utilization in large populations.[15]

Overview

Alzheimer's disease (AD) and related dementias affect **more than 5 million Americans**, with roughly 13.9 million older Americans predicted to be diagnosed with dementia by the year 2060.[4] While genomics research has provided some understanding of disease risk,[5] translational research using a multiomics approach is needed to determine biomarkers and therapeutic targets.[6,7] Proteomics—the largescale study of protein expression and dynamics in healthy individuals and those in different stages of neurologic disease—can improve the understanding of disease pathology and guide the development of predictive models, diagnostics, and future treatments.[8,9] In recent years, blood plasma proteins have emerged as promising biomarkers of early disease and disease progression and may help identify pathways of therapeutic interest.[3,10,11]

Proteomics and the search for better biomarkers

The use of cerebrospinal fluid (CSF) as a source of potential biomarkers has emerged as an approach in neurologic research largely because the fluid is in close contact with both the brain and the spinal cord, where biochemical changes due to neurodegenerative disease are likely to be detectable.[12] CSF, however, requires invasive sampling. Blood plasma proteins may also serve as a source for disease biomarkers in neurologic research. However, brain-related proteins are often found in low amounts in peripheral blood and thus may be overshadowed by more common and abundant blood proteins, such as albumin and transferrin.[1,2,13] Other existing proteomic technologies, including mass spectrometry, can have difficulty in measuring a wide dynamic range of proteins as they require specialized sample preparation to enrich for the less abundant proteins.[2,13,14]

Use the SomaScan Assay for protein profiling to identify potential blood-based biomarkers associated with dementia

The SomaScan Assay offers a highly sensitive method of quantifying proteins in different biologic fluids such as serum, plasma, urine, and CSF. It is uniquely poised to help researchers measure 7,000 proteins (or a relevant customized subset) over a 10-log dynamic range in small volumes of different sample types.[16,17] Most multiplexed proteomics platforms measure a small number of proteins spanning a very narrow dynamic range (typically 2-4 log). The SomaScan Assay, however, uses a serial dilution approach to allow the quantification of up to 7,000 protein measurements over a 10-log dynamic range (femto- to micromolar), without sample pretreatment. This allows for broad protein measurements from small amounts of sample, with high reproducibility.[16]

The exceptional dynamic range afforded by the SomaScan Assay makes it an ideal highthroughput platform for identifying proteins that may be involved in disease pathology, leading to the discovery of potential biomarkers and therapeutic targets.[16]

Recent publications highlight the versatility of the SomaScan platform to generate new biological insights across a variety of neurodegenerative diseases. Here we summarize three studies in which the SomaScan Assay was used for large-scale protein profiling in dementia-related research.[3,10,11]

CASE STUDY #1

Understanding Alzheimer's disease pathology through blood plasma proteins[11]

Alzheimer's disease is characterized by the presence of amyloid beta plaques and neurofibrillary tangles composed of modified tau protein. However, these two occurrences alone do not seem to tell the whole story of disease progression.[11,18] The National Institute on Aging and the Alzheimer's Association have proposed a more extended diagnostic framework for classifying AD based on individual biomarkers for amyloid pathology (A), tau pathology (T), and neurodegeneration (N), in what is collectively called the ATN framework. Analysis of additional proteins and identification of protein signatures within the ATN framework may reveal more complex pathways than amyloid plaques and tau tangles alone and may provide a deeper understanding of AD pathogenesis.[11]

In the largest plasma proteomic study of different biomarkers of AD pathology to date, a multinational team of researchers used the SomaScan Assay to measure 4,001 plasma proteins

The increasing recognition that a broad spectrum of pathologies contribute to AD has highlighted the urgent need for biomarkers that more comprehensively reflect the complex mechanisms underlying this disease.[11]

in 972 individuals (191 with AD, 409 with mild cognitive impairment, and 372 cognitively normal controls). The SomaScan platform was used to perform both a proteomewide differential analysis as well as a protein coexpression network analysis within the ATN network.[11]

The data showed that the relation between proteins and the N factor in the ATN network varied across different common measures of neurodegeneration, such as brain atrophy or CSF markers. These findings offer new insights into changes in individual proteins and protein networks linked to AD pathology.[11]

CASE STUDY #2

Evaluating plasma proteins relating to neurodegeneration and vascular pathology in cognitively normal individuals[3]

Researchers looked to expand the ATN framework used with AD pathology to see if blood biomarkers that correlated with brain vascular damage could be used to detect, classify, or monitor disease pathology.[3]

In the largest study of its kind, researchers used the SomaScan Assay to measure the levels of 5,032 proteins in plasma from 1,061 cognitively healthy individuals (628 women and 433 men). Nearly 90% of the study participants had decreased hippocampal volume (a measure of neurodegeneration) and white matter hyperintensities (a measure of vascular damage), measured with magnetic resonance imaging (MRI).[3]

There is increasing evidence that the biological mechanisms that lead to AD are different in women compared with men, and proteomic analysis revealed four proteins that mediated sex-related differences in brain neurodegeneration and one protein that mediated sex-related differences in vascular damage.[3]

These results suggest that blood proteins could be used to predict brain changes in the very early stages of AD and point to sex-specific candidate protein targets for preventing AD in women and men.[3]

Compared to MRI measures, blood-based biomarkers show promise as a simple and potentially cost-effective option for the early detection, classification, and monitoring of AD pathology.[3]

CASE STUDY #3

Using plasma proteomics to assess proteins and pathways associated with dementia risk[10]

Research has shown that several blood molecules are associated with risk for dementia, and AD in particular. Data investigating the full plasma proteome, however, are still lacking, especially in terms of understanding protein profiles in the years preceding disease onset. To date, the largest challenge has been the lack of technology capable of looking at a broad range of plasma proteins in a large sample size.[10]

A multinational group of researchers used the SomaScan Assay to examine the relationship between 4,877 plasma proteins and the risk of dementia in a large biracial population of older adults in the United States from the Atherosclerosis Risk in Communities study. The results showed that 38 unique proteins were associated with incident dementia, 10 of which are currently targeted by known drugs. Notably, 16 of these proteins were associated with dementia risk in blood samples taken 2 decades earlier, during midlife. Protein quantitative trait loci of genome-wide significance further revealed that 2 dementia-related proteins were also implicated in AD.[10]

For more details

For more details on how the SomaScan Assay can help drive your neurologic research, contact us.

Until recently, the highthroughput technology needed to simultaneously quantify thousands of proteins in thousands of blood samples was unavailable and as such, an understanding of the spectrum of circulating protein changes associated with dementia risk remained incomplete.[10]

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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.

LEARN MORE - https://somalogic.com/somascan-assay-services/

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