SomaLogic
www.somalogic.com

somalogic™

Precision proteomics for diagnostics, drug discovery, and health management

Using an aptamer-based approach, SomaLogic can identify up to 7,000 proteins at high levels of specificity, providing real-time precision proteomics for use in the lab and the clinic.

Genomics has revolutionized how we study inherited and genetically-mediated disease. In 2000, University of Colorado, Boulder, USA, molecular biologist Larry Gold set up SomaLogic to take on a challenge—to study disease by analyzing changes in the body's proteome. It took almost two decades of innovative research and investment to reach that goal, but today SomaLogic's SomaScan Platform makes protein measurement as straightforward as DNA measurement.

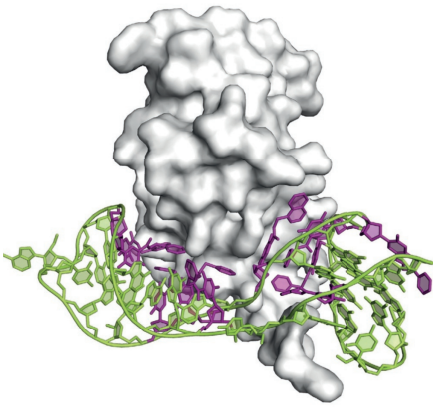
"Wide and deep protein measurement can move the precision healthcare from niche offerings and rare diseases to everyday prevention and management of common morbidities," said Steve Williams, Chief Medical Officer at SomaLogic. The company, headquartered in Boulder, Colorado, has more than 300 employees worldwide, working to meet this challenge. "In the past, the scientific community has looked to the genome for information on current health, despite its limitations, because measuring proteins was too technically challenging. But our pioneering platform allows us to measure 7,000 proteins across a 10-log fold range of concentrations from a single 55 µl blood sample," said Williams.

Aptamer-based approach

The approach the company takes is based on aptamers—single-stranded oligonucleotides each of which recognizes a single individual proteoform. These unique Slow Off-rate Modified Aptamer (SOMAmer) protein affinity reagents incorporate chemically modified nucleotides that enhance the specificity and affinity of protein–nucleic acid interactions compared to standard aptamers and antibodies, enabling thousands of reagents to coexist in the same assay. "This addresses the weaknesses of other aptamer-based technologies and the scale limitations of antibody pairs," said Williams.

Because they are made out of nucleic acids, SOMAmer reagents are stable, have consistent synthesis over decades, and are quantifiable, using existing sensitive and advanced DNA detection methods. The SomaScan Platform converts protein concentrations into measurable nucleic acid signals using common DNA quantification methods. SOMAmer reagents are designed for slow off-rates to ensure that the intended protein complexes for each aptamer remain bound during rigorous washing, whereas non-specifically bound proteins disassociate more rapidly and are prevented from rebinding using a 'universal' poly-anionic competitor.

> **"Our pioneering platform allows us to measure 7,000 proteins across a 10-log fold range of concentrations from a single 55 µl blood sample**
>
> Steve Williams, Chief Medical Officer, SomaLogic



2 X-ray crystal structure of a SOMAmer reagent bound to IL-6. Modified nucleotides are shown in purple, and the DNA backbone and unmodified bases are in green.

The platform can currently identify 7,000 proteins; "that's a third of the proteome," said Williams and almost three-fold more than any other method. Added to this is a large dynamic range, from femtomolar to micromolar protein concentrations, enabled through partitioning the aptamers into three different sample dilutions.

Another feature of the method is its high levels of specificity, based on proteoform recognition. The high degree of 3D shape matching of the company's SOMAmer reagents allows discrimination between nearly identical proteins. An example of this is their ability to differentiate growth differentiation factor 8 (GDF8) and GDF11, both members of the transforming growth factor (TGF) protein family sharing 90% of the same protein sequence. "Uniquely, our process can develop ultra-specific aptamer reagents to recognize these subtly different proteins, even if they are not recognized as different by antibodies," explained Williams.

He adds that the specificity SOMAmers offer, based on shape, can often be a better measure of protein function in biology. For example, SomaScan Assay results for the protein GDF-15, which is prognostic for obesity and cardiovascular events, showed that it was not the abundance but the form of the protein that correlated to relevant disease phenotypes. "By measuring the presence, availability and relative 'attractiveness' of the 3-D binding site on the protein itself, the aptamer signal can detect errors in protein-folding, the presence of protein-protein interactions and impact of genetic variants in protein structure."

Targeting a wide spectrum of diseases

The SomaScan Platform is being applied to a wide range of diseases and conditions to deliver insights that enable diagnostics development, pharmaceutical discovery, and health management. "Because our assays are controlled and maintained over long periods, it means that individual patient samples can be tracked over time and provide reliable and medically useful health information transmitted back to the patient, without the need of any control group," said Williams.

A 2016 cardiovascular study from cardiologist Nelson Trujillo in Boulder, Colorado, illustrates the power of the SomaScan Platform to understanding the molecular bases of disease in a clinical setting. Trujillo's pilot study aimed to identify residual risks of a major adverse event in patients with known cardiovascular disease. The SomaLogic test was derived by measuring thousands of proteins in tens of thousands of blood samples and used machine learning to identify protein patterns that reflect disease presence and risk. The resulting prediction of individualized and near-term risk enabled Trujillo to advise 45% of his evaluated patients to change therapy.

Another area in which SomaLogic expects to have an impact is in biomarker discovery and validation. "Looking for biomarkers when measurements are limited is restricted to a literature popularity contest. But finding the best combination requires a highly multiplexed, high-throughput approach, which allows us to turn the dial up on all of the things needed to optimize the search," said Williams.

SomaLogic believes its technology can make precision healthcare a reality and is eager to work with companies and researchers to help them accelerate their contributions to a healthier world.

CONTACT
Emilia Costales
SomaLogic
Boulder, CO, USA
Tel: +1-720-798-5054
Email: ecostales@somalogic.com