Following the International Human Genome Sequencing Consortium announcement in 2000 of the first “working draft” of the human genome, the floodgates opened to what are now nearly 100,000 genetic tests of varying utility. And with the announcement of the Precision Medicine Initiative (2015), many (if not most) of these tests were soon marketed as a contribution to the advance of precision medicine. Yet the promised transformative effects of the Human Genome Project and the Precision Medicine Initiative have yet to be felt widely in medical practice.

Coincident with the HGP announcement, a small group of scientists in Boulder, CO, founded the company SomaLogic, with the stated purpose of developing a technology that would make measuring thousands of human proteins (proteomics) as straightforward as sequencing thousands of human genes (genomics). Their reasoning was that proteins were the “real-time stuff” of life, making up all the structures and functions of biology, and reflect more directly not only the influence of the transcribed and translated genome but also the influence of the environment (current and cumulative). Therefore, proteins would also be the best “sensors” to foretell the onset and trajectory of disease, especially compared to the relatively static genome. This kind of immediate, precise and highly personalized information could transform how individuals managed their personal health and wellness, and by extension, be more likely to transform medicine.

The technical challenge of reproducibly measuring protein concentrations at large scale across many years cannot be overstated. But for protein information to be clinically useful, it is absolutely necessary that the challenge be met. Today, 20 years after its founding, SomaLogic has brought to market the first of what are expected to be hundreds of new clinical products that translate the complex living language of proteins into a current snapshot of health information that matters – a readout not derivable from genomic analyses alone.

This new approach, so long in the making, finally gives SomaLogic the opportunity to demonstrate how it can move precision health from rhetoric to reality. We at JPM have been following SomaLogic almost from its beginning through contacts with its founders. Recently, Roy Smythe, MD, took up the position of CEO. We posed the following questions to him; his replies follow:

Q SomaLogic has been in business for some time and has continued to add to its novel proteomics platform. Recent developments have led to announcements of products for the clinical space with emphasis on health information offerings.

A Our business mission has evolved, but has evolved with the 2000 founding mission, in mind. It has just simply taken us this long
to realize that mission due to the scientific challenges associated with measuring proteins in the human body at a scale and sensitivity at which a truly informative signal could be discerned. Initially SomaLogic set out to develop a transformational way to measure proteins at this scale, and today we are working to use ability to do so to provide meaningful health information to individuals and health care providers.

Getting past the “who are you” question for an up and coming company is always hard. It starts with making sure people know you exist, and then differentiating yourself. In this case, we have the incredible advantage of offering something objectively disruptive, rather than a “me too” product, or even something that is just incrementally better.

What is SomaLogic’s message to convince the customer to engage you?

While we have one platform, we have various messages for a number of different customers. This is another advantage if we execute well – we can potentially serve different customer needs without running the risk of becoming unfocused as the entire process runs on one measurement platform technology.

The foundational message that we must communicate to all customer segments is that proteins are the best real-time “readout” or “sensors” of health and disease. The genome has captured both imaginations and market share in precision medicine, and there are also a lot of other “-omic”-type claims being made (with varying levels of veracity that will admittedly make getting our message out more difficult for us).

Next, I believe the “twenty-year-old startup” story is important. Our compelling message – namely, SomaLogic has kept at this incredibly difficult task over such a long period of time, resulting in the SomaScan Assay, our high-fidelity commercial measurement methodology – is a great differentiator for us.

As far as discrete customer segments using this one platform, we have already effectively messaged that this powerful tool can help biopharma companies and academic researchers resolve fundamental questions about fundamental biology and the effects of perturbations (e.g., drugs, genetic mutations, etc.) on that biology. We provide access to patients and providers what these health, wellness, and disease management tests can do. We have developed and will continue to develop tests over the next several years from the combination of clinical and proteomic information we have collected. We know our collaborations with biopharma and academic investigators still have incredible untapped potential. However, the potential impact of real-time current state and predictive information about the human body derived from protein signaling can only be described as disruptive – in an incredibly good way. More on this will come over the next 1-2 years as we grow the number and variety of tests available.

How does SomaLogic position itself vis-a-vis genomic, metabolomics, standard clinical assay tests? Is there a synergy when reviewing these data sets taken ensemble vs looking at each set individually?

As genomics are the predominant methodology in current use, it is important to make some distinctions between what genomics assay tests can do versus proteomics. The two most important points of discrimination are comprehensiveness and context.

Currently, genomic testing is somewhat limited to an important, but rather focused band of disease processes for which these data are clinically informative – mainly oncologic and pharmacogenomic applications. In addition, most genomic assay tests are not contextual – that is, they don’t give a result likely to change over time as the genome doesn’t change over time. Some recent, more dynamic uses of genomic approaches have been developed, such as T-cell recognition and cell free DNA, but these are, in turn, somewhat limited in disease scope.

Alternatively, the proteome is involved, by definition, in every aspect of human biology. We have borne out this claim in our success thus far in using proteins to model tests across a variety of current and future health and disease states. More important, however, the proteome is contextual. It “turns over” in the body about 40,000 times during an average lifetime, and these changes in protein expression mean you can retest individuals after treatments to see if progress is being made, discern changes in health and disease development over time, and even potentially model for changes in protein pattern expression in individuals to predict needed changes in therapy over time.

While omics approaches in general are aimed at getting a “deeper look” into a patient’s health status and trajectory, we (and others) believe that proteins are the most informative.
molecules for clinical purposes, at least for the common diseases (e.g., heart disease, metabolic disease, etc.). It may be that combinations of approaches (e.g., genomics data with selected protein biomarkers) can provide better results in some cases. However, preliminary efforts to evaluate these combination approaches have yet to show a significant contribution beyond what we measure on SomaScan (thousands of protein levels). Some of the work we are undertaking with Amgen/deCODE will examine this question more closely (at least for genomics and proteomics) at a larger scale.

**Q** How do you foresee the use of SomaLogic’s platforms for microbiomes – gut, skin, etc? Possible applications in metabolic diseases, obesity, diabetes? or skin conditions?

**A** The “end-effectors” of almost all biologic processes are proteins, and therefore virtually all health and disease is mediated in some way by proteins and protein interactions (e.g. host factors are as important as the microbes themselves in determining a microbiome composition). We believe our platform will have applications in all these areas and more. The platform itself is “agnostic” to the disease or condition being studied, which is what gives it such potentially transformative power for precision health. As obesity and metabolic diseases are an area of particular global concern, some of our very first tests have been directed at body composition predictors of metabolic diseases, and we have others in late stage development in this area, such as tests to better characterize and diagnose fatty liver disease, predict the onset of diabetes, and to predict the risk of developing secondary complications once diabetes has been diagnosed.

**Q** What informatics and analysis tools does SomaLogic offer? What other data types can be analyzed in combination with SomaLogic assay results?

**A** Our business consists of either providing the SomaScan Assay to pharma or academic customers from our reference lab in Boulder or delivering test results to clinical providers they request for patients. Currently, we do not offer any DIY type analytics, leaving the secondary analysis of proteomics results mostly to the pharma and academic customers in the former case, and actually delivering the results of our own analysis in the latter. In the future, we anticipate a direct-to-consumer offering as well. Obviously, from the standpoint of understanding protein drug targets, gene-protein interactions and networked biology, our pharma and academic customers are intensely interested in secondary analytics of SomaScan results, and we have done a large number of collaborative research projects with them in these areas. We have also published extensively with them as well, with more than 200 peer-reviewed publications in our bibliography related largely to this work.

**Q** How well do healthcare providers understand the data and what they can do with it?

**A** We are just now introducing the concept of “clinical proteomics” to health care providers. From the standpoint of how to use clinical diagnostics in general, these are the world’s experts, and we are working with our early clinical market users to ensure our technologic approach, suggested use cases, reports and messaging are understood and aligned with clinical expectations. However, there will be challenges, as in other areas in medicine where advanced pattern recognition and correlation is being used, such as the use of AI/ML in radiomics or computational pathology, rather than direct causal inference. Our predictive protein models consist of a subset of many (from tens to hundreds) of informative proteins that reproducibly stratify patients into risk or definition categories.

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Many of the predictive proteins in these models have no currently known relationship to the organ system that may be linked to the test in question—such as non-cardiac proteins in cardiac risk test results. It is the reproducible “pattern” of proteins that are predictive, so for us it is not important in the moment to understand all the network biology. While completely valid, this is a departure from the traditional diagnostic testing paradigm for most clinicians where the test variable being measured has a “known” causal relationship to pathology or health state.

While we are early in the process of communicating this to health care providers, we are very confident they will reach the right level of understanding for their needs and for their patients, and their own comfort with the validity of the approach.

SomaLogic’s strategy seems focused on clinical applications based on LDTs. Are there plans to offer an FDA-approved version? Otherwise, could you comment on SomaLogic’s view of the potential impact of the VALID act on clinical diagnostics?

Our initial offerings are, indeed, provided as LDTs performed in our CLIA/CAP-certified laboratory. However, we plan to seek FDA approval, and develop all our current applications with that goal in mind. Initial discussions with the FDA about our platform have been positive, and we look forward to working more closely with them as we continue to grow the number and variety of tests on our platform.

It’s hard to say what impact the VALID Act will have on clinical diagnostics, but I am hoping the effect is to allow those with high-quality LDT-validated platforms to continue to operate, and have a clearer and quicker path to FDA approvals as desired, with the elimination or improvement of LDT platforms that are not up to standards. If this is true, it could obviously be helpful to us, and others like us. We are in full support of the goal of more efficiently introducing high-quality, impactful diagnostic and therapeutic products into market, while more effectively protecting the general public.

Having noted the focus on clinical applications, SomaLogic has announced agreements with Novartis, Janssen, and Amgen/Decode for drug discovery and development. Presumably, biomarkers to assess lead candidates will come out of these arrangements.

How does SomaLogic view these agreements in terms of its long-term strategic goals? What are SomaLogic’s aspirations as it builds and adds assets for its core businesses?

As said above, our goal is to be the premier provider of precision health information, based on the ongoing measurement of each individual’s changing protein makeup. But we also see the power of our platform for pharmaceutical discovery and development; we look to be a critical technology underpinning the success of the biopharmas who choose to work with us collaboratively. We will continue to invest in growing the value of our discovery platform (number and specificity of proteins we can measure).

From a broader perspective, how does SomaLogic view its role in making precision medicine more affordable and accessible in the US as well as global markets?

While each of us has a unique genome, our ever-changing proteome contains a deeper and richer unique source of data. We are working hard to drive the price of our technology as low as possible to be most useful when it is employed multiple times over time—a kind of “health tracking” device that will be highly individualized for each person. By capturing changes in proteins early, even before symptoms are present, we may successfully drive the trajectory of a patient back towards health, with minimal, or more effective, targeted interventions.

We are also working to simplify the technology so it can be used in multiple settings throughout the world, especially in areas where there is access to care is limited, or non-existent. I imagine a future where a UN truck drives into a village somewhere in the medically developing world with personnel to line up all the people living there for a nurse to draw blood sample from each resident. The truck then turns around and goes back to a regional facility where SomaScan is run on all of the samples—testing everyone in the village for endemic infections, chronic disease risk, pregnancy complications, cancer risk, etc.

Later the same truck drives into the village and delivers all necessary care—based on the test results from one small tube of blood.

The alternatives? Either continue to deliver no care in half of the world (absolutely existentially unimaginable and unacceptable) or put a microbiology lab with a CT Scanner, an ultrasound machine and several medical and surgical diagnostic specialists on a truck that travels from site to site—which is absolutely economically unsustainable.