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PROTAGEN AND LUMINEX DEVELOPING BIOMARKERS FROM THE BENCH TO THE BEDSIDE

A conversation with **PETER SCHULZ-KNAPPE**, Chief Scientific Officer, Protagen AG

Luminex's technology combines advanced fluidics, optics, digital signal processing, and microsphere technology to create multiplexed assays for protein and nucleic acid applications. It has applications in drug and vaccine development and in clinical diagnostics for infectious diseases, molecular genetics, pharmacogenetics, HLA transplant typing, and autoimmune diseases. Biomarker specialist Protagen, based in Germany, is using Luminex's FLEXMAP 3D® multiplexing technology as part of its SeroTag® biomarker identification and development platform, to create assays to support the development of drugs and companion diagnostics.

When developing your protein arrays, what challenges did you face?
Protagen had developed its own protein arrays for biomarker discovery, which allowed us to look at up to several thousand proteins at any one time. However, we felt that the data quality and reproducibility just weren't high enough for the standard of research we wanted, so we had to look for other technologies.

How did Luminex attract your attention?
Luminex had developed a new multiplexing platform, the FLEXMAP 3D, which allows researchers to look at 500 different analytes simultaneously. We carried out experiments that compared our techniques to the Luminex technology, and we found it gave us data of much higher quality, higher throughput and speed, and improved the reproducibility of results. The dynamic range was also much better, and the results were quantitative as well as qualitative.

Also, at Protagen, we used typical planar microarrays in batches of 100, which meant that a study of a thousand patients needed ten different batches. As the FLEXMAP 3D system could process up to 2,000 patient samples per batch, with up to 500 data points per patient sample, we could eliminate batch-to-batch variability, meaning that we could be much more confident about our results.

Were there any challenges in the switch?
We decided to shift completely to the Luminex system. It was a nerve-racking move, as everyone had to adapt to the new techniques, and it left us wondering about all our existing data and patents, which were based on the old technology. But we took the step, and bravely decided to re-run all of our existing patient samples. The resulting data clearly mandated us to amend all of our patents, and we believe that they are much more convincing now.

Our research requires up to 8,000 data points per patient sample, so with the FLEXMAP 3D system, we still have to run a number of assays per patient, but because data quality and reproducibility are so high, we continue to see a huge benefit.

What difference did the shift to FLEXMAP 3D make?
Precision medicine demands biomarkers that can move from the bench to the bedside by transforming biomarkers into in vitro diagnostics. Luminex technologies are available worldwide and they are already used in a wide range of FDA-cleared, diagnostic tests. This means that developers of diagnostic assays can stay with the same platform for discovery, validation, clinical testing, and commercialisation, while maintaining their line of evidence. It also makes it easier for third-parties to be able to reproduce the results, for example during clinical trials.

How have you applied FLEXMAP 3D to your research?
Our SeroTag biomarker identification and development platform uses Luminex's xMAP® Technology for high-throughput discovery of biomarker candidates by measuring the levels of autoantibodies in serum samples from thousands of patients.

We screened samples from people with autoimmune disorders and used the outcomes to create NavigAID SLE, a multiplex assay that uses biomarkers to separate and define subgroups of patients with systemic lupus erythematosus (SLE). NavigAID SLE can help drug companies develop more effective therapeutics for patients with SLE through precise disease characterization, patient stratification, and response prediction.

Last year, we also launched our first in vitro diagnostics based on the SeroTag platform. Compared with the ten-plus years that it usually takes to move a biomarker assay from concept to the market, these projects have only taken around three and a half years to this point. Our Multilisa SLE multiplex assay will incorporate up to 10 standard markers and up to five autoantigens for SLE and will act as the proof-of-concept for our approach. We are also developing NavigAID SSc for Systemic Sclerosis, NavigAID SjS for Sjögren Syndrome, and Multilisa RA for rheumatoid arthritis. Many markers are in assay development, with consecutive launches expected this year. These products will validate both our approach and Luminex's technology.

We are also looking at other disease areas, including cancer. Patients who are treated with immuno-oncology drugs, such as checkpoint inhibitors and cancer vaccines, can develop immune-related problems, which moves them into our field of expertise. Here we have a substantial collaboration with the National Cancer Institute to identify biomarkers that can be used to predict therapy responsiveness, monitor patients receiving immunotherapies, and detect adverse events early. These will be useful both in drug development and as companion diagnostics.

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