

Rewriting the proteomics handbook

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A suite of Tecan's microarray products is ensuring that researchers at the Biodesign Institute in Arizona, USA, forge ahead with a range of functional proteomics projects looking at early biomarkers for several diseases.

The Virginia G. Piper Center for Personalized Diagnostics at the Biodesign Institute, Arizona State University, takes a multidisciplinary approach to looking at first line diagnostics, drawing on the expertise of engineers, physicists, molecular biologists and clinicians for a range of different diseases. Dr Joshua LaBaer, Director of the Center, explained: "We have a broad range of interests in our laboratory, and many of the biomarkers we are looking at are for cancers, for example, breast, ovarian and lung. Other projects, however, are targeted toward autoimmune diseases, like arthritis and diabetes, and, more recently, inflammatory bowel disease. Precision medicine underpins almost everything we do, and is changing the way that everyone views medical diagnostics."

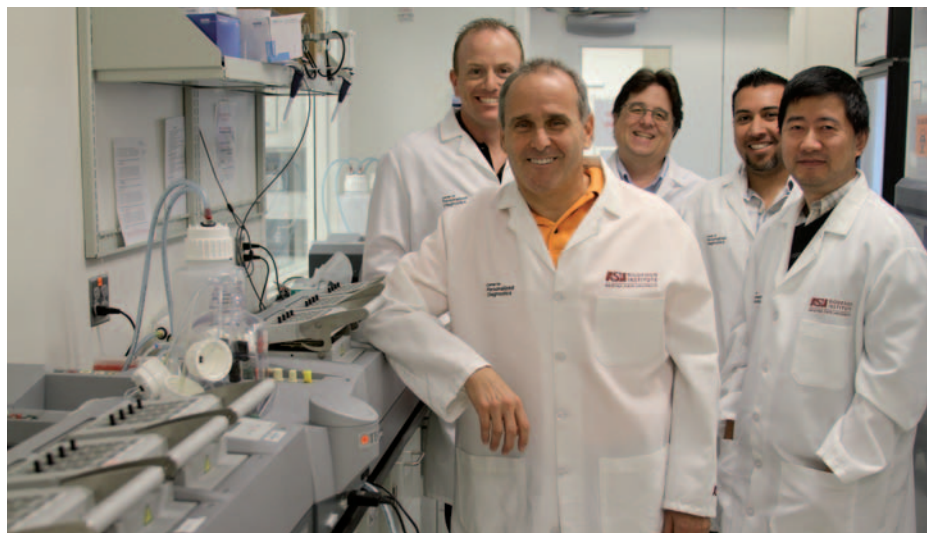
"A key element of our approach is functional proteomics and we have adopted a completely unique technology for protein

microarrays," Dr LaBaer continued. "Most groups who make protein arrays do so by developing high throughput platforms to purify proteins, and then spot the proteins onto the slides. However, this method doesn't work well for purifying proteins, particularly with regard to yield. We prefer to print the gene for the proteins on the slide, and then add a cell-free extract that synthesizes the proteins *in situ*. The proteins are made literally an hour before we test them. Then, for personalized diagnostic applications, we probe these arrays with serum from patients, looking for responses to certain proteins indicative of disease."

The technique is pivotal to many of the projects within Dr LaBaer's laboratory, and automation in the form of an HS 4800™ Pro automated hybridization station and two PowerScanner™ units has become essential to keep on top of the workload and produce

consistent and reliable results. "These are our newest pieces of Tecan equipment and they are proving to be real workhorses in the laboratory. The PowerScanners are essential because we need to repeatedly scan our slides on a regular basis, and the optics are very good, giving us nice strong signals. A huge consideration for our work is having statistically valid sample sizes; does each study have enough statistical power to get the answers we need, especially taking into account that there is a huge amount of biological variation from person to person? For this reason, we make sure that we always have adequate study sizes and, as a consequence, we're running many slides for many patients over and over again. This can be extremely tedious, and having reliable autoloaders on the PowerScanners has been extremely helpful. The accompanying software has also been very useful, enabling us to very quickly identify the features that have signals, measure those signals and then do all the different operations on them. We are now developing a full LIMS for the protein array platform, and the scanners will eventually be connected into that."

Historically, when the method was first developed, everything was done by hand, including all washing and incubation steps. "The problem in a high throughput setting is that human beings are simply not as precise. The HS 4800 Pro has been a really big advantage for us; it basically runs by itself overnight and has done wonders in terms of reproducibility from slide to slide. It allows us to produce these proteins *in situ* on the glass, wash them off, and even incubate them with samples, all in a single run, without any manual intervention at all."



Some key members of the Center's staff. Front row (left to right): Dr Josh LaBaer and Dr Ji Qiu. Back row (left to right): Mike Gaskin, Dr Mitch Magee and Alex Mendoza



Dr LaBaer has had Tecan instruments for more than ten years, including larger liquid handling workstations that were used to build a library of full length sequence clones for encoding human proteins. However, the team had a good look around at other microarray products on the market before making their choices. “In both cases, the devices were by far the best thing on the market. In the case of the PowerScanner, there was nothing out there with the same combination of good autoloading features, images and software. Other devices simply didn’t match the quality.”

The same was true for the automated hybridization station, as Michael Gaskin, Center Manager and Automation Scientist, explained: “We tried a number of different systems, but this was the only one that worked well for us. There really was nothing that competed with its capabilities. Like all new things, it took a little time to develop the right protocol and, when we had the instrument for demonstration, Peter Herzer from Tecan helped us to work out how best to apply it to our workflow. Having it here and being able to test and work with it was really critical; if it wasn’t going to improve our pipeline, there was no point in buying it. The data that we had from that time is really what convinced us that this was the right tool for our laboratory, and it now has long waiting lists because it is in such high demand.”

Dr LaBaer concluded: “When you’re trying to draw a conclusion about a clinical sample – about people – then the technology has to be spot on in terms of reproducibility. If not, your conclusions are going to be tainted by artefacts from the actual processing. With the HS 4800 Pro, we can do the same array



The Center’s PowerScanners provide reproducible, high throughput scanning

on two different days and still get the same answer. The reproducibility this instrument gives us has made all the difference.”

To find out more on Tecan’s microarray solutions, visit www.tecan.com/microarray

To find out more about Dr LaBaer’s work at ASU, visit labs.biodesign.asu.edu/labauer

To find out more about the plasmid collections created by the Center, visit dnasu.asu.edu



Dr Fernanda Festa loading slides onto the HS 4800 Pro