

Bob Barrett: This is the podcast from '*Clinical Chemistry*'. I am Bob Barrett. Over the past ten years DNA microarrays have achieved a robust analytical performance. They are used to enable scientists to analyze whole transcriptome or to screen thousands of single nucleotide polymorphisms at a single time. However, the real key molecules in a cell or tissue are proteins and their manifold functions.

Protein concentrations have been shown to reflect the physiological and pathological state of an organ, tissue, or cells far more directly than DNA. And proteins can be profiled effectively with protein microarrays, which require only a small amount of sample material.

A review in the March issue of '*Clinical Chemistry*' focused on protein microarray applications for biomarker discovery and validation, disease diagnosis, and used within the area of personalized medicine.

Dr. Thomas Joos, Head of Biochemistry at the Natural and Medical Sciences Institute at the University of Tuebingen in Germany is a coauthor of the article and he is our guest in this podcast.

Tell us Dr. Joos, what is the current status of protein microarrays?

Dr. Thomas Joos: Protein microarrays have been developed more than 20 years ago, and it was a very, very slow development. There were only a few people in the beginning of 1990s who were looking at multiplexed immunoassays. But with the development in the field of genomics, DNA chips, a lot of activities have been started to transfer the power of DNA chip technology into the world of protein. And nowadays protein microarrays have really reached a mature level. The technology is mature and they deliver datasets.

Bob Barrett: Now, could you give us an overview of the applications for micro protein arrays and the time frame for the technical developments?

Dr. Thomas Joos: Yeah. As already mentioned, technical development has reached a level that you now can really look into applications. One of the leading multiplexed immunoassay technology is the bead-based Luminex technology.

The company was found in 1995, the first instrument was delivered in 1998, and then it took them another three, four years to have it really robust and in a reliable fashion that it can be used for biological research or even clinical applications.

We have seen similar approaches in the planar array world. We have excellent array of scanners, and we have partly

automation, and the technology has reached after five to ten years of technology development now at the level that applications are much more demanding and even a good application takes three to five years to deliver the results the community wants to see.

Bob Barrett: Okay. With that in mind, what about the industrial failures we have heard about in the past, for instance, the big hype in 2002 concerning biochips?

Dr. Thomas Joos: If you go back to this hype, lots of activity was going on to mimic the success of the DNA chip world. With the high density DNA microarray you are able to look at the whole transcriptome with a single experiment, and there was huge expectation, let's do the same with the world of proteins.

We wanted to array-based proteomics. We want to look at the content of the whole proteome with a single experiment. And we have seen big investments into this hype in biochip technologies; Motorola was developing the eSensor. Dyomics wanted to revolutionize the protein chip world. Nanogen was propagating, we want to dominate the molecular diagnostic market. CIPHERGEN with protein chip approach, they had lots of papers which state discovery of biomarkers.

But more or less at the end of the day, none of these technologies really matured and delivered the promising features which was propagated by the companies, and I think hundreds of millions of dollars were more or less burned, not really burned, we learned a lot during this time. But some of these big approaches definitely failed, partly due to the technology, partly due to the application.

Bob Barrett: How exactly have genomic and proteomic technologies revolutionized the improvement of healthcare?

Dr. Thomas Joos: That's still at the beginning; these technical driven developments that are initiated by propagating improved technology will improve health and the healthcare system. But it's not the technology which really delivers the improvement, it's the right application.

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If you have a good technology, it takes you five to ten years to develop good technology, but then you have to invest more or less the same amount of money to get it into an excellent application. So the application independent of the type of the technology will finally improve the healthcare system.

Bob Barrett: So why do we need protein information?

Dr. Thomas Joos: Protein information is important because the proteins within a cell are the key molecules. They regulate the decisions in the cell, whether to proliferate that the uncontrolled growth will take place or whether differentiation into different tissue types will occur.

It's of course everything relies on the genomic information, but the genome, the DNA is more or less very static information, and if you just know the genome, it's very useful, you can do lots of analysis, but it will be very difficult to have a close link why this genome will develop cancer and the other one not.

It's a static information we collect, whereas the proteome and the living cells and tissue are very dynamic, therefore we need to look at the proteins. We have to look at the post-translational modifications, because if they are switched on and off in the activity, there is a network of interaction and of course this makes it much more complicated to analyze complex proteins.

Bob Barrett: Well, finally Dr., in your opinion, why hasn't genomics fully delivered on the anticipated potentials?

Dr. Thomas Joos: Because there was a huge expectation. When we look back at the beginning of the Human Genome Sequencing Project, it was propagated, if we have the sequence, we understand human beings, we understand disease development, and we can cure disease.

At the end, the genome was sequenced and we realized we are still at the beginning of our learning curve. We have lots of knowledge, and it's amazing what has been accumulated over the last decade.

And to draw the right conclusion out of it, we have now the International Genome Sequencing Consortium. They want to look at the DNA at the genome of diseased and healthy tissue of a variety of tumors coming from the same patient that has in diseased, and again, we will learn a lot, but it may give us also a lot more questions and not an immediate therapeutic approach to cure the cancer.

So in summary, life is much more complex, it's not sufficient just to know the sequence information, we have to understand the complex regulatory mechanism and therefore we need to look more carefully into the proteome.

Bob Barrett: Dr. Thomas Joos is Head of Biochemistry at the Natural and Medical Sciences Institute at the University of Tuebingen in Germany, and he has been our guest in this podcast from '*Clinical Chemistry*'.

I am Bob Barrett. Thanks for listening.

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