Q&A SESSION WITH DAVID HENDERSON

DAVID HENDERSON, Principal Scientist, **Bayer HealthCare**

David has been employed in the pharmaceutical industry since October 1982, with positions of increasing seniority and responsibility in preclinical research and drug discovery at Schering AG in Berlin, Schering's US research division, Berlex Biosciences, in Richmond CA and at Bayer Pharma AG in Berlin.

His work has covered biochemical endocrinology, cancer drug discovery, cancer genomics and gene therapy and biomarker studies in early clinical development. Since returning to Berlin in 2000, he has worked primarily in the fields of genomics, diagnostics and personalized medicine as applied to early development of cancer therapeutics. His present position is in the department of Global External Innovation and Alliances at Bayer Pharma AG, where he is responsible for coordination of the IMI consortium OncoTrack. He also represents Bayer in the eTRIKS consortium.

B.Sc. with Honours in molecular biology (1970), University of Edinburgh, Scotland; Ph.D. in molecular biology (1974), Vanderbilt University, Nashville TN, USA. Post-doctoral studies as Research Fellow, California Institute of Technology, Pasadena, CA., in the laboratory of Dr. Jean-Paul Revel, December 1974 - June 1976, followed by a position as Staff Scientist until September 1982 in the laboratory of Prof. Klaus Weber, Max-Planck-Institute for Biophysical Chemistry, Göttingen, Germany.

Biomarkers are an integral and important part of pharmaceutical research and development. Their potential to transform the way we monitor and treat diseases is remarkable. What are the current challenges researchers are facing in the field?

In oncology, biomarkers are undoubtedly of significant importance. In the case of tumour diseases we are facing the situation that the tumours are very heterogeneous and that they differ among patients, sometimes considerably! Most patients have polyclonal tumours, so there is heterogeneity of disease and heterogeneity of response to treatment. The importance of biomarkers in this situation is simply to provide a basis for stratification of the patient population and to guide selection of the right treatment for the patient.

The biggest challenge we have here is, in fact, the tumour heterogeneity – finding biomarkers that are really specific for a particular phase of the disease or a particular clone of the tumour and then getting a clinical validation. Clinical validation is largely a question of patient numbers and statistical significance. We have to overcome two major challenges; one is the biological challenge of identifying the suitable marker and the second is achieving its clinical validation, allowing use of the biomarker(s) in a clinical setting for the benefit of the patient.

There is much debate as to whether personalised medicine will transform the industry. How do you see personalised medicine being implementing in the long term? How could this effect the industry?

Personalised medicine is already transforming the industry; the regulatory authorities are already very much behind the idea of personalised medicine, and they see this as a way of remarkably improving healthcare delivery. This means – and I am speaking once again for the area of oncology – that today if you reach out to the FDA or the EMA with a clinical trial protocol and you don't have biomarkers included, there will be some very pointed questions asked and you will have to produce a very good argument as to why it is not necessary to evaluate biomarkers and stratify or pre-select the patients in your proposed trial.

Implementation in the long term is a very complex and labour intensive procedure; at the technical level depending on the biomarker you are dealing with, you need access to a broad range of technical solutions in order to assess the biomarkers. This makes the development of companion diagnostic tests more complex. At Bayer HealthCare, we have a variety of different collaborations running with diagnostic companies in order to provide these services, because there is usually not a "one size fits all" solution. To be more specific - depending whether you need a protein marker or a genomic marker, you need a different partner and different technologies in order to perform the test.

In the field of registration of new therapeutic agents we have come a long way in the last 15 – 20 years in terms of harmonising globally, but there is much less harmonisation at the level of these technological assessments. One of the big challenges in drug registration at present and in the future is making sure that the discussion with the Health Technology Assessments (HTA) are being conducted in such a way that it is possible to market validated solutions.

The IMI is very active in the field of Personalized Medicine and Biomarkers, we are lucky to have a number of speakers joining us at the conference to share their work. Which challenges are initiatives like the IMI facing at the moment? Do you think that these public private partnerships are vital to move biomarker research forward?

I'll begin at the end – yes I think collaboration is vital to move research forward. As mentioned, one of the biggest challenges that researchers face is to identify robust biomarkers and to provide validation. One of the major reasons for companies like Bayer HealthCare to move into this space, and that probably goes for most of the companies involved in IMI projects, is the fact that in early research of biomarkers no company is large enough to do everything on their own. There is an enormous advantage in joining a consortium where you can draw upon the experience of other pharmaceutical companies and also selected academic partners or SME's, for example biotech companies that have interesting technologies; one can then make a concerted effort to approach some of these problems.

It is important to realise that most of the projects within the IMI are what we call pre-competitive projects – these are projects that are not necessarily aimed at detecting specific biomarkers for a specific drug. The projects are approaching the generic problems of the best way of conducting the search and to identify biomarkers. For example what biological information do you need? Is it sufficient to just look at genomic markers? Is it sufficient to just look at transcription? Are there very early signs pointing to a rare side effect? Or do we need to have a much broader picture in order to get a robust biomarker for a specific disease. That applies equally to cardiovascular, diabetes or other indications – not just to oncology.

I think that it is also worth noting that IMI has now launched the IMI 2 programme and are expanding activities in this area, since target validation and biomarker research have been identified as a focus for research in the new Strategic Research Agenda. Under the modified rule for participation in the new programme, it is now possible for non-pharma companies that work in healthcare (like imaging companies, diagnostics, etc) to join and contribute to IMI as 'associated partners' and have their contributions matched by funding from IMI. This means that, going forward, that we shall find it much easier to initiate collaborative projects in biomarker and diagnostics research for the benefit of our patients.

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