



Keynote Lecture XIV

Antibody Engineering Technology may provide a Route to a New Generation of Anti-bacterial Therapies

Gillian Strachan, Ian D Broadbent, Lorna Thornthwaite, Keith A Charlton, and

Andrew JR Porter

Institute of Medical Sciences, Foresterhill, Aberdeen AB25 2ZD UK
a.porter@abdn.ac.uk

Andy is, Professor of Biotechnology and Deputy Director of the Institute of Medical Sciences, University of Aberdeen, Scotland and also CSO of Haptogen Ltd. He did his post-doctoral training at the Institute of Arable Crops Research, Rothamsted, UK and the Department of Molecular and Cell Biology, University of Aberdeen where he was awarded in 1993 the Senior Fellowship in Antibody Engineering. Andy received a PhD in Biochemistry from the University of Reading, UK and a BSc degree from the University of St Andrews, Scotland in 1984. In 2002 he received an MSc in Technology Business from the Caledonian University Business School, Glasgow, UK.

Andy has expertise in the development of both antibody and whole cell based biosensors and in particular the isolation of genetically modified antibodies specific for small molecules such as drugs, bio-toxins, cell signalling molecules and pollutants.

Andy was one of the founding academics and Research Director of Remedios Ltd, Aberdeen, Scotland, UK. Remedios is a biosensor company with proprietary technologies in the areas of toxicity determination and was Scottish biotechnology company of the year in 2000. Also in 2000 he was awarded a Royal Society of Edinburgh commercialisation fellowship in Biotechnology. In April 2002 Prof Porter was the founding academic of a new antibody engineering company, Haptogen Ltd, which specialises in the isolation of antibodies to novel therapeutic targets. Haptogen is currently developing a new class of antibiotics and has other interests in liver disease, obesity and bioterrorism/biowarfare. In 2005 Andy was made the Ernst and Young Plc, Science and Technology Entrepreneur of the Year.

Many bacterial pathogens use small diffusible molecules (haptens) as extracellular signals to co-ordinate gene expression in response to changes in cell population densities ("quorum sensing"). Quorum sensing is an attractive target for the development of antimicrobial drugs, particularly as many bacterial virulence factors are regulated in a quorum sensing-dependent manner. Our approach has been to block the signaling activity of these molecules with highly specific human antibodies. By targeting these extracellular signals, rather than the bacteria themselves, we believe that drug resistance is unlikely to develop to this novel antibody-based approach. However, haptens are traditionally regarded as difficult targets for antibodies, due to their low molecular weight, which renders them invisible to host immune responses. We have developed a range of approaches (Haptomics®) that circumvent these problems, and have used our patented DBDX™ platform to isolate a panel of human antibody fragments that specifically bind bacterial signaling molecules. We have evaluated the effects of these antibodies on quorum sensing in Gram-negative bacteria using a variety of *in vitro* and *in vivo* assays, and present evidence that they significantly attenuate virulence of *Pseudomonas aeruginosa* in a pulmonary infection model, demonstrating their potential as safe, deliverable and efficacious antimicrobial agents.