PURDUE INSTITUTE
OF INFLAMMATION • IMMUNOLOGY • INFECTIOUS DISEASE

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"DEVELOPMENT AND MANUFACTURING OF NEXT GENERATION BIOPHARMACEUTICALS"

The development of recombinant antibodies and vaccines has allowed us to treat and prevent a number of life-threatening diseases. However, for highly variable viruses such as HIV and influenza, or even parasites such as plasmodium falciparum no vaccines exist and vaccine researchers want to elicit antibodies that protect against most or all viral strains - not just a few such as seasonal flu vaccines currently on the market. One of the latest strategies is the development of broadly neutralizing human antibodies from long-term pathogen-positive survivors, enriching antibody-producing B cells from blood samples and then to identify those that produce antibodies capable of neutralizing multiple strains of the relevant pathogen. Such broadly neutralizing antibodies typically work by blocking crucial functional sites on a pathogen that are conserved among different strains despite high mutation elsewhere. Technologies for identifying such B-cell clones to clone the relevant immunoglobulin genes and then to apply recombinant antibody technologies and protein engineering to improve the performance of such antibodies will be discussed here. Another key issue for biopharmaceuticals is the capacity and scalability of current production systems which is beginning to place limitations on this crucial technology. The large-scale production of antibodies, vaccines and other pharmaceutical recombinant proteins is restricted by the industry's current reliance on fermenter technology, particularly the culture of mammalian cells such as CHO cells. State of the art CHO technologies for accelerated development of highly productive cell lines will be presented. Unfortunately this expensive and time-consuming CHO production platform is often preventing the distribution of recombinant protein drugs to those most in need. One way in which the above limitations can be addressed is through the use of plants and plant-based expression systems for recombinant pharmaceutical protein production. The economic production of plant-based pharmaceuticals depends on satisfactory yields and product quality. This presentation will discuss the latest development in antibody and vaccine development and their production by mammalian cells versus molecular farming, focusing particularly on strategies to maximize protein yields during upstream production and optimize protein recovery in the downstream processing steps. Such strategies often involve careful consideration of how the protein is expressed and targeted within the plant cell, a factor which affects yield, stability, quality and ease of isolation. A long-term objective is to ensure that next generation of plant-based production systems for recombinant proteins will create the opportunity to deliver antibodies, vaccines and other biopharmaceuticals beyond the industrialized nations and into the developing world. Two case studies will be presented: HIV antibodies were chosen to undergo fast-track development, including risk assessment, expression in

tobacco and maize, scale-up, downstream processing and regulatory development, with the aim of implementing clinical trials. In addition use of engineered plant cells that produce animal and human vaccines will be discussed.

At the age of 59 I am currently the CSIO (Chief Science and Innovation Officer) at the IBRI (Indiana Biosciences Research Institute) since April 2017. Prior to this appointment I was for over 18 years Department Head of the Institute for Molecular Biotechnology (RWTH Aachen University, Germany, 70 employees) and Senior Executive Director of the Fraunhofer Institute for Molecular Biology and Applied Ecology (over 700 employees including the Fh-USA CMB and Fh-Chile Research).

My expertise covers many areas of Molecular Biotechnology including Genomics, Proteomics, Metabolomics, Cellomics, Protein Engineering, Molecular Medicine, Immunology, Virology, Plant and Industrial Biotechnology, Drug Discovery as well as the production and purification of recombinant proteins including biopolymers and biopharmaceuticals with a focus on GMP-manufacturing for clinical trials and regulatory approval.

Over the past sixteen years I have built the Fraunhofer IME in Aachen, Germany, its subsidiary the Fraunhofer CMB in Newark, DE, USA as well as the Institute for Molecular Biotechnology at the RWTH Aachen University. I've increased the number of employees more than sixteenfold over the last 15 years and have raised more than 800 million Euros from Europe and over 200 million USD from abroad for research funding. I have established international collaborations with more than 25 foreign nations both in academia and industry including many of the global key players in Biotechnology, Pharmaceutical, Agro, Food and the Chemical Industries. Furthermore I have made over 650 scientific presentations around the globe, more than 1.000 Fraunhofer concept presentations and published over 400 peer reviewed scientific publications including 53 book chapters and one book. Additionally, I hold over 80 pending patent applications and 47 granted patents. My current HF (Hirsch factor) is 66 and my peer reviewed publications have been cited over 16.400 times.

I personally created the University Department of Molecular Biotechnology at RWTH Aachen starting with my own funds. As Head of the Institute I have acquired 70 employees in less then 10 years, established a Bachelor and Masters programmes on Molecular Biotechnology and graduated over 200 MS in addition to more than 100 bachelors and 117 PhD students. Since 2008 I am also participating in the excellence cluster "tailormade biofuels from biomass" at the RWTH Aachen University. As Senior Executive Director at the Fraunhofer IME with centers in Schmallenberg, Newark (Delaware), a 60 million € R&D Center (including a cGMP pilot scale facility) in Aachen, Germany, I have shown that I can add new research dimensions to an applied Academic Research Organisation shaping it into a global operation that is highly respected in basic and applied R&D. This has more recently be reflected by securing funding for a new Fraunhofer Center for Systems Biotechnology in Chile, and four new german Centers for Plant Polymers in Münster, Insect Biotechnology & Bioresources in Giessen (where we secured a 78 million € grant for a new R&D center in 2013), Translational Medicine & Pharmacology in Frankfurt (where we secured a 84 million € grant for a new R&D center in 2014), High Throughput Drug Discovery in Hamburg and the Aachen-Maastricht Institute of Biobased Materials (AMIBM).
Based on my achievements I was awarded "Distinguished Professor" at the RWTH Aachen University in 2015 and full professor at Maastricht University, NL. From 2015 until 2017 I have been elected chair of the Fraunhofer Life Sciences Alliance with 7 Institutes and over 1.700 employees.

On the managerial level I have been exposed quite extensively in project acquisition and management; HR, operations, technology and information management, supervision of large groups, financial accounting, marketing, licensing, contract negotations, product development, strategic planning, business start-ups, due diligence, filing of IP and more recently in multiple clinical trials and regulatory approval. As a result of these activities I have contributed to establish five start-up companies and advise multiple international advisory boards.

Finally I also consult quite extensively for the german minister of science and education as well as health the german chancellor and several MP of the European Parliament as well as the European Commission and therefore serve on multiple scientific and programme advisory boards and working groups.

PI4D Seminar
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