4th Annual Therapeutic Protein Production Event

Wednesday, 15 May 2013
The Stevenage Bioscience Catalyst , UK

The purpose of this annual event is to look at the challenges facing therapeutic protein production and demystify some of the novel approaches and new technologies currently being developed. This event will appeal to both academics and industrialists who are interested in the future of therapeutic protein production.

This event is part of the 2013 ***Euroscicon BioTherapeutics Week***,
to find out more see www.biotherapeutics2013.com

This event has CPD accreditation

Meeting chair: *Laura Bailey*, Eden Biodesign

9:00 – 9:45 **Registration**

9:45 – 10:00 **Introduction by the Chair**: *Laura Bailey*, Eden Biodesign

10:00 – 10:30 **Production of therapeutic proteins from bacterial systems**
Dr Tim Overton, University of Birmingham, UK

10:30 – 11:00 **A novel technology for visualising, sizing and counting sub-visible protein aggregates**
Ben Owen, Product Specialist, *NanoSight Ltd*

11:00 – 11:30 **Downstream Processing of Monoclonal Antibodies**
Dr Graziella El Khoury, University of Cambridge, UK
Therapeutic monoclonal antibodies (mAbs) now constitute one of the most important and rapidly growing segments of the biopharmaceutical industry with 24 products approved by the FDA and 240 currently in clinical trials. This interest in monoclonal antibodies requires improved downstream bioprocessing protocols which are cost effective and allow the resolution of complex protein mixtures and the isolation of individual target proteins in high yield, in a relatively short period of time. This talk will focus on the advances in the affinity purification strategies for the purification of antibodies and their fragments.

11:30 – 12:00 **Speakers' photo then mid-morning break/networking and trade show**
Please try to visit all the exhibition stands during your day at this event. Not only do our sponsors enable Euroscicon to keep the registration fees competitive, but they are also here specifically to talk to you

12:00 – 12:30 **Developing long-acting growth hormone agonists and antagonists**
Professor Richard J Ross, University of Sheffield
Growth hormone (GH) is a potent anabolic hormone; deficiency results in extreme short stature and excess in gigantism and acromegaly. It is just over 50 years since Raben first demonstrated the dramatic impact of GH replacement on linear growth in a young boy with pituitary infantilism. Since then milestones in GH research have included identification of the GH binding protein (1986), the crystal structure of GH (1987), cloning of the GH receptor (1987) and the discovery of a GH antagonist (1990). Studies in patients with GH insensitivity, secondary to mutations in the GH receptor, have allowed the elucidation of the molecular interaction of GH with its receptor and the mechanism underlying activation of GH receptor signalling. Based on this understanding of the structure and physiology of GH we have been investigating the rational design of novel GH agonists and antagonists. We have examined tandem fusions of GH with flexible, rigid, and glycosylated linkers, addition of lipid anchors to both GH and its binding protein and the generation of ligand-receptor fusions through flexible peptide linkers. Despite apparent rational design, tests of bioactivity often produce surprising and unexpected results with the addition of a lipid anchor to GH creating an antagonist and a GH ligand-receptor fusion a potent agonist. Ligand-receptor fusions have unique properties forming a partially inactive complex in solution, with delayed clearance, whilst providing a constant supply of active GH that promotes growth. These novel GH constructs generate long-acting GH therapies with the potential for monthly dosing which would be a major advance over current daily treatment regimens.

12:30 – 13:00 **The Innovative World of DSM Biologics Biopharmaceutical Manufacturing: Smaller, Better, Faster**
Mr John Mcguire, DSM, UK

13:00 – 14:00 **Lunch/networking and trade show**
This is also a good time to fill out your feedback forms and any questionnaires

14:00 - 14:30 **New stapling technology for production of therapeutic proteins**

Professor Bazbek Davletov, Chair of Biomedical Sciences, University of Sheffield, UK

Combining proteins or their defined domains could bring new enhanced functions. Conventionally, two proteins are either fused into a single polypeptide by recombinant means or chemically cross-linked. However, these strategies have drawbacks such as poor expression (recombinant fusions) or aggregation and inactivation (chemical cross-linking). We developed a new protein linking method which allows site-oriented, non-covalent, yet irreversible stapling of modified proteins at neutral pH and ambient temperature. This method is based on two distinct polypeptide linkers which self-assemble within minutes, in the presence of a short peptide staple. On-demand and irreversible combination of botulinum domains allowed us to design new neuronal blocking agents with enhanced medicinal features. Furthermore, we demonstrate the general versatility of this modular approach by stapling a variety of proteins to required surfaces.

14:30 – 15:00 **ADCC Reporter Bioassay: A Novel, Bioluminescent Cell-Based Assay for Quantifying Fc Effector Function of Therapeutic Antibodies**

Mr Craig Malcolm, Promega UK, UK

Therapeutic antibody dependent cell-mediated cytotoxicity (ADCC) assays are typically performed using PBMCs or NK cells and suffer from high variability and poor reproducibility. To circumvent these issues, Promega has developed a reporter-based ADCC bioassay using an effector cell line that stably expresses an NFAT luciferase response element and human FcgIIIa high affinity (V158) receptor. When the effector cells are exposed to antibodies bound to target cells, activation of the FcgIIIa receptor signaling pathway occurs resulting in increased luciferase activity, which correlates to cytotoxic ADCC assays. By eliminating PBMCs or NK cells, the assay reproducibility is greatly increased and the variability is significantly reduced, while retaining the ability to discriminate antibodies with varying degrees of Fc effector function. The novel ADCC Reporter Bioassay contains effector cells in frozen, thaw-and-use format, which greatly reduces hands-on preparation typically required for an ADCC assay. Following DOE studies, the ADCC Reporter Bioassay was tested with FDA-approved antibodies (i.e., rituximab and trastuzumab) in qualification studies and the assay showed excellent linearity, accuracy, and precision. Studies using treated samples demonstrated the assay to be stability-indicating. Furthermore, the assay shows good linear correlation between levels of glycosylation and afucosylation with ADCC activity. Overall, the ADCC Reporter Bioassay is able to quantify Fc effector functionality and is a suitable replacement for classic cytotoxic ADCC assays, when low variability and high reproducibility are required.

15:00 – 15:30 **Analysis of host cell residuals for novel and biosimilar protein production: Requirements, regulations and the application of new technologies**

Matthew Hankinson, Eden Biodesign, Liverpool, UK

Host cell residuals are a key quality attribute for any protein product and the importance of determining and characterising these contaminants are often overlooked and the methods misunderstood, especially in the early stages of a project. In addition, the methods for the analysis of host cell residuals are usually extremely time consuming and typically have a low throughput. This presentation will look at the requirements and regulations concerning the analysis of host cell residuals and will discuss several examples of new technologies and equipment that can significantly increase the throughput and accuracy of these methods.

15:30 – 16:00 **Afternoon Tea/Coffee, networking and trade show**

16:00 – 16:30 **Polishing Technologies - how to get rid of process impurities and potential contaminants effectively**

Dr. Juan Pablo Acosta Martinez, Sartorius Stedim, UK

Cost and time are very valuable elements during the development and production of any biopharmaceutical product. By implementing more efficient methods and adopting innovative techniques it is possible to reduce the processing cost and time. Several innovative products and case studies are presented.

16:30 – 17:00 **Question and Answer Session**

Delegates will be asked to submit questions to a panel of experts. Questions can be submitted before the event or on the day

17:00 **Chairman's summing up**

About the chair

Laura Bailey is a member of the Process Development Team at Eden Biodesign, working as a Senior Fermentation Scientist. Laura's role involves biosimilar protein production, from mammalian cultures at different bioreactor scales. Before working at Eden Biodesign Laura completed both her undergraduate and postgraduate degrees at the University of Manchester. Laura's PhD project, a collaboration with MedImmune, involved the investigation of protein production stability from CHO cells after prolonged culture. Laura is also a dedicated member of the ESACT-UK committee, and has had a role of Treasurer for the last 3 years.

About the Speakers

Richard Ross trained in medicine at The Royal London Hospital (1974-1979) and in Endocrinology at St Bartholomew's Hospital, London (1983-1988). He was appointed to Sheffield University in 1995 and is Professor of Endocrinology and Head of the Unit of Diabetes, Endocrinology and Metabolism. Richard's research and clinical interests are in pituitary disease, transition endocrinology and the late effects of cancer. His research has yielded some 120 papers, 50 chapters, 2 books, and over 20 granted patents. Richard has a particular interest in commercial research and is the Faculty Academic Lead for Innovation. He is a founding Director of two university spin-out companies; Asterion Ltd developing long-acting growth hormone analogues and Diurnal Ltd developing circadian endocrine therapies. He personally obtained Orphan Drug Designation for Chronocort; a new therapy for Adrenal Insufficiency. He has served on the editorial boards of: Clinical Endocrinology (1996-2000), Growth & Growth Factors (1986-2006), Hormones (2004-), and J Clin Endocrinol Metab (2010-). He was a council member for the Society of Endocrinology (1999-2002), Editor Endocrinologist (2001-2004), Chair of CaHASE (2002-), member of the Bioscientifica Board (2006-2010) and serves on the Executive Committee of the European Society of Endocrinology (2011-), The Growth Hormone Research Society Council (2011-), Society for Endocrinology Public Engagement Committee (2008-2011) and Nominations Committee (2010-).

Matthew Hankinson joined Eden Biodesign in 2008 and currently the team leader for analytical molecular biology specialising in qPCR based technologies, host cell residual analysis and *In vitro* bioassays. He has almost ten years experience in biopharma and previously worked at Cobra Biologics in Keele. He received my undergraduate degree from The University of Sheffield in 2003.

Bazbek Davletov is a protein biochemist by education (Moscow State University, 1985). He obtained his PhD from the University of Texas Southwestern Medical Center at Dallas in 1994, where he helped to decipher molecular mechanisms underlying neuronal communication. Following postdoctoral training at the Imperial College, London, he moved to Cambridge in 1997 to become a Principal Investigator at the Medical Research Council Laboratory of Molecular Biology. Prof. Davletov made seminal contribution to uncovering mechanisms of action of several neurotoxins, molecular mechanisms of neurotransmission and recently invented 'protein stapling' technology utilizing his knowledge of neuronal proteins. In 2012, Bazbek Davletov took up the Chair of Biomedical Science at Sheffield University, UK.

Graziella El Khoury received her MSc degree in Physiology and her PhD in Biotechnology from the University of Lyon, France. Her PhD thesis focused on the implementation of miniaturised immunoassays for peptide and protein microarrays. She is a Postdoctoral Research Associate in the Department of Chemical Engineering and Biotechnology working on the development of synthetic ligands for affinity chromatography and the downstream processing of biopharmaceuticals. She has been awarded the "Journal of Molecular Recognition Year Travel Award for a Young Scientist" at the 19th Biennial Meeting of the International Society for Molecular Recognition - Affinity 2011.

Juan Pablo Acosta-Martinez is a Chemical Engineering graduate from University of Guadalajara, Mexico and was awarded a PhD in Biochemical Engineering from University College London in 2010. He started his career working in areas such as process engineering and consultancy. He later became the lead bioprocess development engineer in Probiomed, one of the leading biopharmaceutical companies in Mexico. In 2011 he joined Sartorius Stedim Biotech as Project Manager for all activities in the field of Virus and Contaminant Clearance covering all Europe. He has been working on developing clients purification and polishing platforms.

Craig Malcolm, PhD is currently Product Manager for Cell Analysis and Proteomics at Promega UK, based in Southampton. After receiving his PhD in Neurochemistry from St Andrews University he was in the pharmaceutical industry for seven years as a Team Leader in Molecular Pharmacology (Vernalis Ltd.), developing cell-based assays and supporting drug discovery screening projects. After several more years in product development as a Senior Cell Biologist (PerkinElmer), and various other roles in several other UK-based Life Sciences companies (Scientifica, Roche Applied Science), Dr Malcolm joined Promega UK last year and is responsible for cell-based assay reagents, proteomics products and related instrumentation in these areas.

Keywords: Gene correction/modification, AAV vectors, Cell line engineering, biopharmaceutical manufacturing processes, antibody purification, process economics, genetic algorithms, multi-product facility design, homologous recombination, cell line engineering, CHO cell lines, gene targeting, endogenous genome, Cell line development, cell line selection, screening, CHO, mammalian expression systems, glycosylation, protein therapeutics, E.coli, microbial, antibody, NTA, Protein Aggregation, Nanoscale, Analysis,Growth Hormone, Long Acting Biological, Fusion, Protein,protein linking, stapling, botulinum, domain, therapeutic, Affinity chromatography, Antibody purification, Therapeutic antibodies, Downtream processing,mAbs, therapeutic protein production, downstream processing, monoclonal antibodies, hormones, new technologies, Polishing, Virus, Contaminant, Cost, Time, Immunogenicity, deimmunizaion, tolerization, validtaion, immunomodulation, ADCC, therapeutic antibody, screening, quality control, stability testing

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For your convenience we would like to bring your attention to the following

- You will be issued with a FULL delegate list within 14 days of the event, which will include the email addresses of the delegates (we are sorry that there is this delay in emailing the list, but we need to make sure that it takes into account any late arrivals). You will not be included in this list if you have opted out and you can do this by logging into your registration details. This list will not be sold or ever give out to third parties. Only people attending or sponsoring the event have access to the list
- There may be an independent meeting report published within a few months of this event. If this is published we will send you an email to let you know the reference details
- Notepads and pens are available from the Euroscicon reception desk
- We cannot give out the slides from our speaker's presentations as they are deleted immediately after each event. If you require a particular set of slides please approach the speaker
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- To keep updated on our events and other Life Science News, please sign up for our newsletter at www.eurosciconnews.com
- We may take pictures during the meeting. These pictures will be used to promote our events and placed on our various websites and the closed Euroscicon group on Facebook. If you do not want your photograph distributed please let one of the Euroscicon staff know.