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Sixth Annual

Final Agenda

PEGS EUROPE

Protein & Antibody Engineering Summit

3-7 NOVEMBER 2014 | MARRIOTT HOTEL | LISBON, PORTUGAL

Two Consecutive Years of **40% Growth in Attendance!**

PLENARY KEYNOTES

The Impact of the New Regulatory Guidance Landscape on the Validation of the Manufacturing Process and the Characterisation of Starting Materials, Drug Substance and Drug Product
Steffen Gross, *Ph.D., Paul-Ehrlich-Institut*

Current Progress with Armed Antibody Products
Dario Neri, *Ph.D., ETH Zurich*

KEYNOTE PRESENTERS

Roslyn Bill, Aston University Birmingham
H. Kaspar Binz, Molecular Partners AG
Klaus Bosslet, Roche Pharmaceuticals, Penzberg
Rakesh Dixit, MedImmune LLC
Stefan Dübel, Technische Universität Braunschweig
Jacques Dumas, sanofi
David James, University of Sheffield
Ewa Marszal, U.S. Food & Drug Administration
John McCafferty, IONTAS Ltd.
Jonas Schaefer, University of Zurich
Ralf Schumacher, Roche Penzberg & pRED
Janine Schuurman, Genmab
Florian Wurm, Swiss Federal Institute of Technology Lausanne (EPFL)

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Short Courses* Maximize Your Productivity

Maximize your educational and networking opportunities while in Lisbon by adding a short course. Continued training and education are essential for staying competitive. These interactive short courses are a great introduction for those new to a particular discipline or as a refresher for those who want to brush up on their knowledge or expand their horizons. Attendance is limited to ensure an interactive environment. Group discussions are a key component in which participants will have the opportunity to ask questions of the expert instructors and other participants. Course materials are included.

MONDAY, 3 NOVEMBER 09:00 – 12:30

SC1: Engineering of Bispecific Antibodies

Instructors: Nicolas Fischer, Ph.D., Head, Research, Novimmune SA
Julian Bertschinger, Ph.D., CEO, Covagen

By attending this interactive workshop, you will learn about the various approaches used for the engineering of bispecific antibodies and bispecific scaffold-based binding proteins. Different technologies will be compared, and examples for applications of bispecific antibodies in drug development will be presented with a focus on candidates that are currently being evaluated in clinical trials. Opportunities and challenges in the field of bispecific antibodies will be discussed.

SC2: Mutation and Selection Strategies for Multi-Parameter Antibody Optimisation

Instructors: William Finlay, Ph.D., Director, Global Biotherapeutic Technologies, Pfizer, Inc.
Matthew Lambert, Ph.D., Principal Scientist, Global Biotherapeutic Technologies, Pfizer, Inc.

In therapeutic antibody discovery, few primary lead antibodies meet all of the desired product characteristics of ideal potency, expression, stability, formulation and immunogenicity. As a result, *in vitro* engineering is often necessary ranging from basic humanization all the way up to affinity, stability and solubility improvement. In recent times, a bewildering array of potentially useful mutagenesis, selection and screening technologies have become readily available to perform these tasks. In this course we will help attendees to critically assess their options and navigate through this complex field.

THURSDAY, 6 NOVEMBER 17:30 – 20:30 TO INCLUDE DINNER

SC5: Aggregation and Immunogenicity: How Do Formulation, Process and Delivery Influence Immunogenicity of Therapeutic Proteins?

Instructors: Melody Sauerborn, Ph.D., Senior Expert Immunogenicity/Bioanalysis, TNO Triskelion
Joel Richard, Ph.D., Senior Vice President, Peptides, Head, CMC & Engineering Dreux Site, IPSEN

Formation of anti-drug antibodies (ADA) represents a risk for the patient as it possibly alters pharmaco-kinetics and compromises safety and efficacy. The course will review the immunogenicity aspects related to formulation composition, excipients, storage and in-process stability issues. The focus will be on the influence of degradation products (oxidized forms, aggregates, particulates, etc.) and process-related impurities (contaminants, particulates) on the immune system. In addition, key analytical methods for identification, characterisation and composition determination of aggregates/particulates in the formulation will be reviewed, particularly the characterisation of aggregates/particulates in the lower sub-visible size range. We will also discuss how in-depth formulation analysis can be connected to biological consequences of aggregates and particulates.

SC6: Troubleshooting and Engineering of Antibody Constructs

Instructors: Jonas V. Schaefer, Ph.D., Head, High-Throughput Laboratory, Biochemistry, University of Zurich
Christian Kunz, Ph.D., Associate Director, Discovery Alliances & Technologies, MorphoSys AG

Recombinant antibodies vary widely in their biophysical characteristics, from stable monomers to metastable aggregation-prone oligomers. In particular, antibody variable domains differ in their intrinsic thermodynamic stability and often require labor-intensive engineering. While most antibody engineering is performed with small antibody fragments, the majority of molecules in the clinics still are of the full-length IgG format. Thus it is critical to understand how the poor stability of individual variable domains not only limits the biophysical properties of small fragments, but also affects the production yield, stability and homogeneity of full-length IgGs containing these domains.

SC7: Immunotherapy Approaches

Instructors: Andrea van Elsas, CSO, BioNovion B.V.
Sergio A. Quezada, Ph.D., Professorial Research Fellow, Research Haematology, University College London Cancer Institute

Cancer immunotherapy is distinct from other paradigms in that treatment is directed towards a patient's immune system and not their malignant cells. During the past few years, novel approaches to immunotherapy of cancer using antibodies targeting T cell regulatory proteins produced highly encouraging clinical data. Patients responding to T cell check-point inhibitors have shown long-term benefit suggesting that, in addition to surgery, radiotherapy and (targeted) chemotherapy, immunotherapy will become a novel treatment paradigm in oncology. Besides targeting T cell checkpoint proteins other pathways and novel agents are being investigated to induce or enhance anti-tumour immunity.

SC8: Recent Advances in Antibody-Drug Conjugates

Instructor: Edmund I. Graziani, Ph.D., Associate Research Fellow, Oncology Medicinal Chemistry, Pfizer, Inc.

Antibody-drug conjugates (ADCs) consist of a monoclonal antibody (mAb) conjugated to a small molecule via a tether or linker. ADCs are an attractive therapy for cancer since the ADC provides a means to target highly potent cytotoxic small molecules to specific tumour cells that bear an antigen recognized by the mAb portion of the ADC. This short course will focus on advances in linker technology, new methods for evaluating the potential benefits of site-specific ADCs, and advances in our understanding of the fate of the ADC after *in vivo* exposure, with an emphasis on strategies for improving ADC pharmacokinetic (PK) exposure.

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Conference **At-A-Glance**

A three-stream, nine-conference, five-day event

	Antibody Engineering Stream	Biologics Development Stream	Protein Expression Stream
3 NOVEMBER - Monday (09:00-12:30)	Pre-conference Short Courses		
3 NOVEMBER - Monday (13:45-15:30)	Plenary Keynote Speakers: Steffen Gross and Dario Neri		
3-4 NOVEMBER - Monday Afternoon - Tuesday	Phage & Yeast Display	Optimisation & Development	Difficult to Express Proteins
5-6 NOVEMBER - Wed. - Thurs. Morning	Constructs and Scaffolds	Aggregates & Particles	Optimising Protein Expression
6 NOVEMBER - Thursday (17:30-20:30)	Dinner Short Courses		
6-7 NOVEMBER - Thursday Afternoon - Friday	Cancer Biotherapeutics	Characterising Biotherapeutics	Antibody Expression

Colleague **Testimonials**

"One of the best antibody conferences I've been to. The presentations were of superb quality and captured the excitement of recent developments in this field. For anyone interested in antibodies and antibody mimetics, I would unhesitatingly recommend the PEGS conference in Lisbon next year."

- Mike W., Ph.D., Research Scientist, Wellcome Trust Sanger Institute

"I have enjoyed this meeting very much and the quality of the talks has been very good. I also enjoyed our roundtable. It was a very engaged group and I thought the discussion went very well."

- Luis B., Ph.D., Scientific Director, Amgen, Inc.

"I was pleased to find so many scientists in the European industrial sector who were willing to talk about their research in great detail. It is a refreshing viewpoint when compared to similar conferences held in the US."

- Kathleen H., Ph.D., Scientist, Cell and Systems Biology, University of Toronto

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MONDAY, 3 NOVEMBER

12:00 Conference Registration

PLENARY SESSION

13:45 PEGS Europe Team Welcome

13:50 Chairperson's Opening Remarks
William Finlay, Ph.D., Director, Global Biotherapeutic Technologies, Pfizer, Inc.

14:00 The Impact of the New Regulatory Guidance Landscape on the Validation of the Manufacturing Process and the Characterisation of Starting Materials, Drug Substance and Drug Product
Steffen Gross, Ph.D., Head, Monoclonal and Polyclonal Antibodies, Paul-Ehrlich-Institut
The regulatory guidance landscape regarding biological products changes rapidly. Documents overseeing process validation is currently facing major overhauls. New guidelines are published defining the requirements for starting materials and excipients. This might have a deep impact not only on the process development of traditional monoclonal antibody type products but also on new antibody formats such as conjugates as well as on new developed formulations.

14:45 Current Progress with Armed Antibody Products
Dario Neri, Ph.D., Professor, Chemistry and Applied Biosciences, ETH Zurich
There is an emerging trend in Pharmaceutical Biotechnology to "arm" antibodies, capable of selective localization at the site of disease, with suitable therapeutic payloads (e.g., drugs, cytokines, radionuclides, a second antibody moiety, hence producing a bispecific product). This strategy aims at concentrating therapeutic agents in diseased part of the body, while sparing normal tissues. In this lecture, I will present a comparative evaluation of different classes of armed antibody products, developed in my laboratory in collaboration with Philogen. In particular, I will present preclinical and clinical data of armed antibodies in the field of cancer, of chronic inflammation and of endometriosis.

15:30 Refreshment Break

OPENING SESSION

16:00 Chairperson's Opening Remarks
John McCafferty, Ph.D., Co-Founder, Director and CEO, IONTAS Ltd.

» 16:05 KEYNOTE PRESENTATION:

Construction and Use of Large Antibody Libraries in Mammalian Cells
John McCafferty, Ph.D., Co-Founder, Director and CEO, IONTAS Ltd.
Construction of libraries of binders displayed on the surface of mammalian cells will allow the screening of millions of clones by flow sorting while providing information on both the level of expression and the extent of binding within individual clones. The main limitation to achieving this has been the inability to construct large libraries containing 1-2 antibody genes/cell. We have solved this problem by directing the integration of antibody genes into a single genomic locus through the use of site-specific nucleases. The presentation will describe construction of libraries of millions of clones and selection of binders including antibodies formatted as IgGs.

16:35 Bench to Bedside: Taking Antibodies Derived from Phage Display to the Clinic
Kerry Chester, Ph.D., Professor, Molecular Medicine, University College London Cancer Institute
The application of phage display technology to create and mine vast libraries of antibody fragments can provide a diversity of new binders from naive, immunised or synthetic repertoires. We have taken the approach of using PCR-mediated amplification of antibody V genes from immunised rodents as a source of V-regions; exploiting the single chain Fv (scFv) format, for display and as a building block for potential therapeutics. Selected scFv are readily converted into a variety of potential biotherapeutics, including antibody-enzyme fusion proteins, dual-specific binders, scFv-Fcs and Chimeric Antigen Receptors (CARs). Bench-to-bedside case studies will be presented.

17:05 Full-Length IgG Antibody Surface Display in Mammalian Cells
Josef Platzer, Ph.D., Senior Principal Scientist, Large Molecule Research, Roche Diagnostics GmbH
Therapeutic proteins are currently evolving from standard monoclonal antibodies to more complex formats and fusion proteins. The display of antibody libraries is an important tool to identify the most potent hits. For complex formats a display in the final format is desirable. Here we report on a mammalian cell surface display for full length IgGs and bispecific antibodies.

17:35 Breakthrough Therapy: Targeting Therapeutic Specifically to Inflamed Arthritic Joints
Ahuva Nissim, Ph.D., Reader, Antibody and Therapeutic Engineering, Biochemical Pharmacology, William Harvey Research Institute, Queen Mary University of London

18:20 Welcome Reception in the Exhibit Hall with Poster Viewing

19:20 End of Day One

TUESDAY, 4 NOVEMBER

07:30 Registration

07:45 Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

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TACKLING COMPLEX MEMBRANE TARGETS WITH DISPLAY TECHNOLOGIES

08:30 Chairperson's Remarks

Claire Dobson, Ph.D., Associate Director, Antibody Discovery & Protein Engineering, MedImmune

08:40 Isolating and Optimising Antibodies to Complex Membrane Targets

Claire Dobson, Ph.D., Associate Director, Antibody Discovery & Protein Engineering, MedImmune

Isolating antibodies to G protein coupled receptors (GPCRs) is challenging due to their complex nature. This presentation will provide an overview of strategies adopted by MedImmune to successfully identify potent functional antibodies directed to these complex membrane targets.

09:10 Development of Conformation-Selective Antibodies by Yeast Display

Bradley Pearse, Ph.D., Scientist II, Antibody Discovery, Biogen Idec

Generating antibodies that are able to distinguish between active and inactive conformations of integrins is of great therapeutic interest. In this presentation, the discovery of conformation-selective human antibodies using yeast surface display will be discussed. The focus will be on the design of selection strategies to enrich antibodies of interest by yeast display and characterisation of conformer selectivity. Examples of conformationally-selective non-ligand mimetic antibodies will be highlighted in greater detail.

09:40 Development of Potent and Selective Nanobodies against Difficult Targets: Tackling GPCRs and Ion Channels

Gerald Beste, Ph.D., Associate Director, Discovery, Ablynx

Nanobodies® are therapeutic proteins based on single-domain antibody fragments derived from naturally occurring heavy-chain only antibodies from camelids. They can be easily engineered via genetic fusion into multi-valent and multi-specific molecules. Case studies on how this formatting flexibility can be exploited for the generation of potent and selective biologicals against GPCRs and ion channels will be presented.

10:10 Coffee Break in the Exhibit Hall with Poster Viewing

10:50 Discovery of Rare Antibody Specificities to Difficult Targets Using High Content Screening of Avian Repertoires

William D. Harriman, Ph.D., CSO & Founder, Crystal Bioscience

Chickens are known to generate antibodies to epitopes on therapeutic targets that are highly conserved amongst mammals. These antibodies often demonstrate reactivity across multiple species, and are preferred when rodent or primate models of disease are anticipated. Using alternative immunization strategies we can enhance the prevalence of such clones, and by evaluating antibody profiles through a multi-parameter GEM screen of primary B cells, we can efficiently recover antibodies with desired biological activity and/or multispecies cross-reactivity.

11:20 High-Throughput Design, Production, and Evaluation of Bispecific Antibodies

Maria Wendt, Ph.D., Senior Scientific Consultant, Biologics, Genedata

Work on multispecific antibodies has exploded and more sophisticated engineering approaches are now used. Concurrently, increasing numbers of bispecific platforms (e.g. tandem-scFv-Fc, DVD-Ig, diabodies) and parametric variants (e.g. linkers, V-domain orientation, Fc) must be tested. We present latest advances in our workflow platform for fully automated molecule design, DNA synthesis, and verification. Integrated into a comprehensive data management system for samples, assays, and analytics results, it enables systematic evaluation of large panels of next-generation antibodies.

11:50 Problem Solving Roundtable Discussions

The Selection, Screening and Characterisation of Bispecifics

Moderator: Christopher J. Plummer, Ph.D., Scientific Investigator, Biopharm Innovation, GlaxoSmithKline

Complex Membrane Targets

Moderator: Claire Dobson, Ph.D., Associate Director, Antibody Discovery & Protein Engineering, MedImmune

How to Get What You Want from Antibody Phage Display

Moderator: Stefan Dübel, Ph.D., Professor, Biotechnology, Technical University of Braunschweig

12:50 Luncheon Presentation: Antibody Library Display on a Mammalian Virus: Combining the Advantages of Panning and Cell Sorting in One Technology

Sponsored by VACCINEX

Ernest S. Smith, Ph.D., Senior Vice President, Research & CSO, Vaccinex, Inc.

We have developed an antibody discovery platform that enables efficient mammalian cell based expression of a library of human antibodies in full length IgG format on the surface of vaccinia virus. Upon infection of mammalian cells the antibody is not only incorporated into newly produced virus, it is also displayed on the surface of the host cell. This technology enables a selection method that combines the advantages of virus panning and cell sorting into one technology.

14:00 Dessert Break in the Exhibit Hall with Poster Viewing

GENERATING ADCs, BISPECIFIC ANTIBODIES AND NOVEL SCAFFOLDS

14:30 Chairperson's Remarks

Kerry Chester, Ph.D., Professor, Molecular Medicine, University College London Cancer Institute

14:35 Selection, Screening and Characterisation of Bispecific "mAb-dAbs"

Christopher J. Plummer, Ph.D., Scientific Investigator, Biopharm Innovation, GlaxoSmithKline

This talk will provide an overview of the process involved for the lead discovery of bispecific mAb-dAbs, detailing the methods of selection, screening and characterisation to identify bispecific molecules with suitable biological, biophysical and pharmacokinetic properties for therapeutic use.

15:05 The Cyclotide Microprotein Family as a Scaffold for Drug Discovery and Delivery

Bill Eldridge, Ph.D., CSO, Cyclogenix Ltd.

Cyclotides, or knottins, are plant-derived cystine knot microproteins (CKMs). Despite their very high structural rigidity there is great sequence diversity within this family. We have therefore substantially modified the wild type primary sequence and used to phage display to select mutated CKMs which demonstrate a range of modalities, including oral availability, traditional protein target-specific binding and the possibility of blood-brain barrier delivery of therapeutic peptides. Specific examples will be discussed.

15:35 Advancing Novel Bispecific Antibody Biologics

Jose M. Munoz-Olaya, Ph.D., Scientist, Discovery, F-star Biotechnology Ltd.

F-star has developed a novel modular bispecific antibody technology. First, Fcab™ or antigen-binding Fc heavy chain (CH3) domains are selected using proprietary phage or yeast display technology. Next, bispecific mAb^{2}™ antibodies can quickly and easily be expressed by replacing the wild-type Fc domain of existing monoclonal antibodies. F-star is now developing a preclinical oncology pipeline based on this next generation biologics technology platform.

16:05 Sponsored Presentation *(Opportunity Available)*

16:35 Refreshment Break in the Exhibit Hall with Poster Viewing

CHIMERIC ANTIGEN RECEPTORS (CARS)

17:15 Novel Targeting Concepts in CAR Technology

Martin Pule, Ph.D., Clinical Senior Lecturer Honorary Consultant, Haematology, University College

In order to resolve the "on target off tumour" toxicity in CAR therapy we developed logic gate platforms that can engineer T cells to either broaden their specificity to more than one phenotype of cancer (OR gate platform) or to specifically recognise cancerous cells in the absence of cancer specific antigens (AND and ANDNOT gate platform). This was achieved by transducing T cells with two modified CARs which, depending on the target cell phenotype and platform, resulted in the co-operative or destructive integration of ligated signals.

17:45 Preclinical Engineering and Clinical Evaluation of First Generation CAR T-Cells Employing a Phage Display-Derived scFv against Carcinoembryonic Antigen (CEA)

David Gilham, Ph.D., Senior Research Fellow, Clinical and Experimental Immunotherapy Group, Institute of Cancer Sciences, University of Manchester

A key limitation of Chimeric Antigen Receptor (CAR) T-cell technology is the availability of a suitable antibody scFv fragment that functions in the CAR format. This talk will explore the engineering issues and clinical grade cell production issues relevant to using a phage display generated scFv specific for CEA in a first generation CAR format and the testing of these gene-modified T-cells in a phase I clinical trial setting.

IMPROVING BIOPHYSICAL PROPERTIES

18:15 Expression of IgG in Mammalian Cells Directly from Phage Display Vectors without Subcloning

Isidro Hötzel, Ph.D., Senior Scientist, Antibody Engineering, Genentech

Phage display is widely used in discovery of therapeutic antibodies. A bottleneck in the screening of clones from phage display libraries is the subcloning of variable regions to mammalian vectors for expression of IgG. We developed a vector for phage display that expresses IgG in mammalian cells without reformatting, expediting the screening of clones derived by phage display.

18:45 End of Phage & Yeast Display of Antibodies

> "Round table directly helped with real experimental problems",
>
> ***Andrew W., Scientist, Protein Expression, Abcam Ltd.***

Recommended Short Courses*

SC1: Engineering of Bispecific Antibodies

SC2: Mutation and Selection Strategies for Multi-Parameter Antibody Optimisation

SC6: Troubleshooting and Engineering of Antibody Constructs

*(*Separate Registration Required. Please see page 2 for more details.)*

WEDNESDAY, 5 NOVEMBER

07:45 Registration and Morning Coffee

NOVEL APPLICATIONS OF BISPECIFIC TECHNOLOGY

08:30 Chairperson's Opening Remarks
Katherine Vousden, Ph.D., Senior Scientist, Antibody Discovery and Protein Engineering, MedImmune

08:35 Seamless Transition from Mono- to Multi-Specific Antibodies Based on Light Chain Diversity
Nicolas Fischer, Ph.D., Head, Research, Novimmune SA
We have developed an antibody generation platform based on light chain diversity. Having at disposal antibodies sharing the same heavy chain enables the evaluation of antibody specificity in multiple formats and the scalable generation of bispecific antibodies as well as antibody mixtures. Due to their unmodified human IgG structure, the final products have characteristics that are identical to standard mAbs and are therefore ideally suited for development.

09:05 Engineering of Fully Human Bispecific Antibodies with Two Binding Sites in Each Fv Region
Roland Beckmann, Ph.D., Co-Founder and CSO, Dutalys
DutaMabs are fully human bispecific antibodies, comprising one normal heavy chain and one normal light chain, with two non-overlapping binding sites within the natural CDRs of each Fv. These two paratopes within the DutaMab CDRs are fully independent, due to an unprecedented stability, which exceeds that of all previously described antibodies. This allows the combination of any two specificities within one Fv, and their independent maturation to very high affinities.

09:35 A Novel Monovalent-Bispecific IgG Design
Partha S. Chowdhury, Ph.D., Principal Scientist, Antibody Discovery and Protein Engineering, MedImmune LLC
Most bispecific antibodies are multivalent in nature. For certain specific applications monovalent bispecific designs are better suited. A new design to generate monovalent bispecific IgGs will be described with a focus on biological and physic-chemical properties.

10:05 Biological Recognition: Beyond the Antibody
Matt Johnson, CTO, Avacta Life Sciences
Sponsored by Avacta Life Sciences
Antibodies are ubiquitous in life science research; their high affinity and specificity have enabled biological detection in a range of settings, from basic research to clinical diagnostics. Antibodies, however, are not suitable for all applications, and have limitations around targets and applications. Engineered non-antibody protein binders, largely focused on therapeutics, have been developed more recently. Here, I will review existing alternatives to antibodies and present Affimers as next generation reagents for biological recognition.

10:35 Coffee Break in the Exhibit Hall with Poster Viewing

Fc ENGINEERING APPROACHES

11:15 Antibody Engineering for Fc Silencing
Tilman Schlothauer, Ph.D., Senior Scientist, Large Molecule Research, Pharma Research and Early Development, Roche Diagnostics GmbH
The constant part (Fc) of the human IgG interacts with various receptors of immune effector cells. The goal of our attempts was to establish the most silent antibody format without exerting any receptor-mediated effector functions e.g. for therapeutic use in inflammatory diseases. Several combinations of mutations have been tested in a comprehensive set of cell free and cell based *in vitro* functional tests, part of our Fc receptor platform.

11:45 Structural and Functional Insights into Neonatal Fc Receptor-Based Recycling Mechanisms
William Dall'Acqua, Ph.D., Senior Director, Research and Development, Antibody Discovery and Protein Engineering-ADPE, MedImmune
We report the structure of the complex between human FcRn, human serum albumin (HSA) and a human Fc engineered for improved pharmacokinetic properties (Fc-YTE). A molecular explanation for HSA and IgG pH-dependent binding to FcRn is provided. We also explain structural mechanisms by which Fc mutations (including YTE) result in increased IgG binding to FcRn. Our study provides an unprecedented understanding of IgG and HSA interaction with FcRn.

12:15 ProxiMAX Randomisation: Non-Degenerate, Controllable Saturation Mutagenesis for Use in Antibody Engineering
Anna V. Hine, Ph.D., FSB, Reader, School of Life and Health Sciences, Aston University
'ProxiMAX' randomisation is a saturation mutagenesis process that encodes required chemical function without degeneracy. Either unbiased or pre-defined ratios of amino acids may be encoded and each saturated position can be defined independently. With achieved diversities of >99% (6 & 11 saturated codons) and the potential to generate libraries of up to 10^14 components, we contest that ProxiMAX randomization is key for engineering antibody libraries of the highest quality.

12:45 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

UNIQUE APPROACHES FOR CREATIVE ENGINEERING

14:00 Chairperson's Remarks
Nicolas Fischer, Ph.D., Head, Research, Novimmune SA

KEYNOTE PRESENTATION

14:05 Protein Inactivation *in vivo* in Intrabody-Expressing Mice

Stefan Dübel, Ph.D., Director, Biotechnology, Technische Universität Braunschweig

We demonstrate for the first time that endoplasmatic reticulum retained antibodies ("intrabodies") can induce a knock down phenotype in transgenic mice. The phenotype found in adult mice expressing VCAM1 intrabodies included aberrant distribution of immature B-cells in blood and bone marrow. The availability of our technology and the rapidly growing number of available antibody genes will spark a new level for the functional study of membrane and plasma proteins *in vivo*.

14:35 Natural and Engineered Sortases for the Masses: A New Enabling Technology for Protein Engineers

Christian Freund, Ph.D., Professor, Biochemistry, Freie Universitaet Berlin

Sortases, originating from the cell wall of gram-positive bacteria, can be used to ligate (poly) peptide-based scaffolds of various kinds. Their further development as ubiquitous tools hinges on the ability to modify their specificity and catalytic efficiency. We have recently created sortases with altered sorting motif specificity that indicate the potential of a newly developed sortase portfolio for traceless protein ligation.

15:05 Rationalising the Pharmacological Effect of a High Affinity Neutralizing Serpin Antibody through Co-Crystallography

Katherine Vousden, Ph.D., Senior Scientist, Antibody Discovery and Protein Engineering, MedImmune

Plasminogen activator inhibitor 1 (PAI-1) is an important mediator of fibrotic disease; understanding how antibodies neutralize this molecule is key for the development of therapeutics. We describe here the first co-crystal of PAI-1 with a high affinity neutralizing antibody. This has enabled the rationalization of *in vivo* and *in vitro* observations in the context of the resolved antibody epitope. How the isolation and affinity maturation strategy lead to the identification of this novel therapeutic will also be discussed.

15:35 Refreshment Break in the Exhibit Hall with Poster Viewing

INNOVATIVE ENGINEERING FOR DIFFICULT TO REACH TARGETS

16:15 Receptor-Mediated Delivery of a Bispecific Antibody into the Primate Brain: Challenges and Safety Findings

Mark S. Dennis, Ph.D., Principal Scientist, Antibody Engineering, Genentech, Inc.

We have previously demonstrated that the transferrin receptor transcytosis pathway at the blood brain barrier (BBB) can deliver a therapeutically relevant dose of a bispecific antibody into the rodent brain. The therapeutic arm of the bispecific, directed against β-secretase (BACE1), significantly lowered brain A-beta production. This approach has now been extended to non-human primates. The challenges and safety findings encountered will be discussed.

16:45 Engineering Brain Shuttle Antibodies

Jens Niewöhner, Ph.D., Principal Scientist, Large Molecule Research, Pharma Research and Early Development, Roche Diagnostics GmbH

By manipulating the binding mode of an antibody fragment to the transferrin receptor (TfR), we have developed a Brain Shuttle module, which can be engineered onto a standard therapeutic antibody for successful BBB transcytosis. The Brain Shuttle version of an anti-Abeta antibody, which uses a monovalent binding mode to the TfR, increases beta-Amyloid target engagement in a mouse model of Alzheimer's disease, translating into a significant improvement in amyloid reduction.

17:15 Problem Solving Roundtable Discussions

Bispecific Protein Therapeutics
Moderator: Partha S. Chowdhury, Ph.D., Principal Scientist, Antibody Discovery and Protein Engineering, MedImmune LLC

Antibody Engineering - Chances and Challenges
Moderator: Ralf Schumacher, Ph.D., Site Head, Large Molecule Research, Roche Penzberg & pRED

Targeting the Immune System
Moderator: David Urech, Ph.D., CSO and Co-CEO, Numab AG

Engineering for Affinity and Specificity
Moderator: Katherine Vousden, Ph.D., Senior Scientist, Antibody Discovery and Protein Engineering, MedImmune

18:15 Networking Reception in the Exhibit Hall with Poster Viewing

19:15 End of Day One

THURSDAY, 6 NOVEMBER

08:00 Breakfast Presentation *(Sponsorship Opportunity Available)* or Morning Coffee

UNIQUE MODES OF ACTION

08:30 Chairperson's Remarks

Stefan Dübel, Ph.D., Director, Biotechnology, Technische Universität, Braunschweig

KEYNOTE PRESENTATION

08:35 Philosophy and Principal Dogma behind Modern Discovery and Development of Biologics

Ralf Schumacher, Ph.D., Site Head, Large Molecule Research, Roche Penzberg & pRED

This talk will examine challenges facing the industry today, e.g. recognition of redundancy of pathways; the understanding of the signalling and interaction between cells and organs, e.g. what is responsible for suppression of the immune response to a cancer and how it can be overcome; the importance of linking together deep biological understanding, disease understanding, and MOA for targeted therapies, companion diagnostics for stratification of patients, and clinical study design. Examples will be provided.

09:05 Engineering of Probodies: Antibodies that Become Activated at the Target Site and Target Widely-Expressed Tumour-Specific Antigens

James West, Ph.D., Research Fellow, Protein Engineering, CytomX Therapeutics, Inc.

Antibodies have demonstrated therapeutic benefit through binding to targets in tumour tissues, however, engagement of targets also present in normal tissues can result in dose limiting toxicities. We have developed a novel antibody scaffold, the Probody, engineered to restrict antibody activity to the tumour. Probodies targeting EGFR or Jagged retain potent anti-tumour activity with substantially reduced on-target toxicities, demonstrating the power of the Probody platform to expand the target landscape to include widely expressed antigens for which conventional antibodies are not viable.

09:35 Novel Affitin Designs: Structural Basis for Two Modes of Action for Potent and Specific Inhibition of Glycosidases

Frédéric Pecorari, Ph.D., Researcher, Cancer Research Center of Nantes-Angers, University of Nantes

Achieving specific and efficient inhibition of glycosidase enzymes is challenging as they can have similar mechanisms and active sites. We report two designs of artificial affinity proteins, Affitins, which specifically and potently inhibit two glycosidases. The crystal structures of glycosidase-Affitin complexes showed two binding modes, involving or not a loop, preventing substrate access to catalytic sites. The potential of Affitins to become general tailored enzymatic inhibitors will be discussed.

10:05 MISCs: Multimeric Interaction Scaffolds for High Avidity Cell Targeting

Harald Kolmar, Ph.D., Professor and Department Head, Biochemistry, Technical University of Darmstadt

In recent years, several concepts evolved that rely on improvement of affinity and specificity via presenting multiple independent binding domains on an oligomeric scaffold. In many cases, recombinant expression of such fusion constructs is a bottleneck for their application. We investigated the avidity effects of peptides, miniproteins, and DNA aptamers when fused by sortase-mediated ligation to several structural and functional different scaffolds that allow for bi- to heptavalent display. I will review strategies for bioconjugation and scaffold functionalization with binders, fluorophores, and toxins.

10:35 Coffee Break in the Exhibit Hall with Poster Viewing

T CELL REDIRECTION AND IMMUNE MODULATION

11:15 Towards Predictability in Discovery and Engineering of Bispecific Therapeutics

David Urech, Ph.D., CSO and Co-CEO, Numab AG

The use of a single human variable domain scaffold allows for the reproducible engineering of highly stable and potent humanized rabbit antibody variable domains. Such variable domains are used as building blocks for the engineering of bispecific single-chain diabodies (scDb) with excellent CMC properties. Numab is exploiting bispecific scDbs with T killer cell redirecting activity for the therapy of chronic inflammatory diseases.

11:45 SM201/SM211: Two Anti-FcγRIIB mAbs Differing by a Single Amino Acid with Distinct Immunomodulatory Properties for the Treatment of Autoimmune Diseases

Peter Sondermann, Ph.D., CSO, SuppreMol GmbH

FcγRIIB plays a central role in the negative regulation of the immune system. We describe two unique anti-FcγRIIB antibodies that recognize FcγRIIB but that do not interfere with the natural binding of the IgG-Fc part to the same receptor. The antibodies that differ just by a single amino acid recruit FcγRIIB to a different extent which renders them to be attractive drug candidates for the treatment of various autoimmune diseases.

12:15 End of Constructs and Scaffolds

THURSDAY, 6 NOVEMBER

12:30 Conference Registration

13:00 Dessert Break in the Exhibit Hall with Poster Viewing

TARGETING THE IMMUNE RESPONSE

13:30 Chairperson's Opening Remarks
Janine Schuurman, Ph.D., Vice President, Research, Genmab

» KEYNOTE PRESENTATION

13:35 Safety Challenges and Risk Mitigation Strategies to Develop Immune Activating Biologics
Rakesh Dixit, Ph.D., Vice President, Research and Development, Safety Assessment, MedImmune LLC
This presentation will cover: how immunotherapy may result in autoimmune and off-target toxicities to self versus tumours; combining immunotherapy with other agents; how to maximize the efficacy and balance safety vs. efficacy; measures to streamline the combined approach and reducing toxicity to self; and strategies to risk mitigate safety concerns with the immune activating biologics and their combination.

14:05 ImmTACs: TCR-Based Bispecific Reagents for Targeted Cancer Therapy
Annelise Vuidepot, Ph.D., Head, Protein Science, Immunocore Ltd.
ImmTACs are soluble bispecific-TCR-anti CD3 fusions suitable for the treatment of several tumour types. Unlike antibodies, TCRs target MHC-bound peptide antigens derived from endogenously processed proteins, providing a large pool of intracellular antigens from which to select appropriate target molecules. Our most advanced program is in the treatment of malignant melanoma and is currently in a phase IIa clinical trial.

14:35 Camelid Single Domain Antibody Fragments to Cardiac Troponin I: A Case Study
Sponsored by RANDOX
Shirley Schön, Ph.D., Team Leader Recombinant Antibodies, Molecular Biology, Randox Laboratories Ltd.
Camelid single domain antibodies (sdAbs) are small and highly stable recombinant antibody fragments with activity and specificity equivalent to standard monoclonal antibodies. We present data on the isolation, properties and adaptability of alpaca sdAbs to cardiac troponin I. Randox can offer a custom sdAb isolation, humanization and engineering service.

15:05 Refreshment Break in the Exhibit Hall with Poster Viewing

TARGETING THE IMMUNE RESPONSE (continued)

15:45 Targeting Cancer with BiTE Molecules
Roman Kischel, M.D., BiTE Technology, Amgen Research (Munich) GmbH
The recent clinical success in harnessing the immune system to fight cancer has demonstrated the potential of this approach. Here we will give an overview of the BiTE (Bispecific T-cell Engager) technology, which drives directed T cell mediated tumour cell killing, and describe our target discovery platform.

16:15 Targeting Immune Checkpoints in Cancer: Novel Mechanistic Insights on the Role of Fc Receptors and the Tumour Microenvironment
Sergio A. Quezada, Ph.D., Professorial Research Fellow, Research Haematology, University College London Cancer Institute
The immunological balance in cancer is often characterized by dominant infiltration of regulatory T cells. Antibodies against CTLA-4, a key immune modulatory receptor expressed on T cells, efficiently modify this balance promoting tumour elimination. Surprisingly, changes in Teff/Treg ratio and tumour rejection depend on the depletion of tumour-infiltrating Treg cells expressing high levels of CTLA-4. Depletion is driven by FcγRIV expression on tumour infiltrating myeloid cells illustrating the impact of Fc Receptors and the tumour microenviroment on the final outcome of antibody-based immune-modulatory therapies.

16:45 Discovery and Development of Fusion Proteins and Antibodies Modulating the Immune Response in Malignancy and Enhancing Overall Effector Function
Sol Langerman, Ph.D., CSO, Research and Development, Amplimmune, Inc.
AMP-224 binds to inhibitory receptor PD-1. It was extensively tested in a CT26 colon carcinoma model, prior to human studies and found to be maximally active (60% tumour free survival) when administered once or twice a week, after receiving a single, low dose of cyclophosphamide (CTX). This promoted a functional anti-tumour immune response. A variety of clinical correlative studies were run to assess biological activity of the molecule, using real-time immune-monitoring assays and readouts.

17:15 End of Day One

17:15 Dinner Short Course Registration

17:30 – 20:30 Dinner Short Courses

Recommended Short Courses*

SC6: Troubleshooting and Engineering of Antibody Constructs

SC7: Immunotherapy Approaches

SC8: Recent Advances in Antibody-Drug Conjugates

*(*Separate Registration Required. Please see page 2 for more details.)*

FRIDAY, 7 NOVEMBER

08:00 Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

BISPECIFIC ANTIBODIES FOR CANCER

08:30 Chairperson's Remarks
Rakesh Dixit, Ph.D., Vice President, Research and Development, Safety Assessment, MedImmune LLC

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08:35 Mix and Match: Making Bispecific and Bivalent Antibody Fragments with Next Generation Maleimides (NGMs)

Kerry Chester, Ph.D., Professor, Molecular Medicine, University College London Cancer Institute

A robust, developable and manufacturable bispecific platform will be discussed as the foundation to engineer novel anti-solid tumour antibodies. Unlike combination therapies, these bispecifics demonstrate enhanced tumour decoration, tumour diffusion and retention, internalization, and effector functions. Supported with IND-enabling *in vivo* efficacy studies, Zymeworks' lead bispecific and bispecific ADC programs will be presented.

09:05 Preclinical Developments with a Fully-Human Bispecific Antibody Platform

Eric Smith, Ph.D., Associate Director, Bispecific Antibodies, Regeneron Pharmaceuticals, Inc.

This presentation will describe a platform technology to generate fully human bispecific antibodies through the combination of Fc modifications that allow selective protein A purification and VelocImmune® derived antibodies that utilize a single defined light chain. Molecular characterisation and initial *in vitro* efficacy data will be discussed. In addition, preclinical findings with proof-of-principle molecules targeting T cells will be presented.

09:35 Problem Solving Roundtable Discussions

Key Features of a Bispecific Antibody Platform

Moderator: David Poon, Ph.D., Director, External R&D and Alliances, Zymeworks, Inc.

Antibody-Drug Conjugates: Linkers and Payloads

Moderator: Gonçalo Bernardes, Ph.D., Royal Society, University Research Fellow, Chemistry, University of Cambridge

Safety Concerns with Immunotherapy

Moderator: Rakesh Dixit, Ph.D., Vice President, Research and Development, Safety Assessment, MedImmune LLC

Strategies for Entering the Clinic

Moderator: Sol Langerman, Ph.D., CSO, Research and Development, Amplimmune, Inc.

Fc Engineering to Enhance Complement Activation

Moderator: Janine Schuurman, Ph.D., Vice President, Research, Genmab

10:35 Coffee Break

DEVELOPMENTS WITH ADCs

11:00 Discovery of Novel Linkers, Payloads and Antibody-Drug Conjugates for the Treatment of Cancer

Edmund I. Graziani, Ph.D., Associate Research Fellow, Oncology Medicinal Chemistry, Pfizer, Inc.

Antibody-drug conjugates (ADCs) are an emerging modality for the treatment of cancer. Presently, three classes of cytotoxic payloads have been successfully employed on these modalities in clinical settings, namely the auristatins, maytansines and calicheamicins. This talk will focus on Pfizer's chemistry strategy to discover and develop new linker-payload classes and conjugation technologies that will yield more efficacious and potentially better tolerated conjugates that we are advancing to the clinic.

11:30 Producing Homogeneous ADCs with Single or Combination Warheads

Aaron Sato, Ph.D., Vice President, Research, Sutro Biopharma, Inc.

Using Xpress CF+, hundreds of non-natural amino acid antibody variants are made within a day. Using fast, quantitative conjugation chemistries, e.g. Click Chemistry/Reverse Diels-Alder, antibodies are conjugated within hours with low molar excess of linker warhead. The best sites are selected based on expression, cell binding, conjugation efficiency (DAR), and cell killing. *In vivo* efficacy, PK/PD, and stability studies further winnow to our best ADC candidates. Multiple ADC examples will be provided that illustrate the power of this platform.

12:00 Targeted Delivery of Cytotoxic Agents for Cancer Treatment

Gonçalo Bernardes, Ph.D., Royal Society, University Research Fellow, Chemistry, University of Cambridge

Our work explores the interplay between effector molecules, targeting ligands and site-selective protein conjugation chemistry to create safer, more selective and efficient cancer therapeutics. This lecture will cover recent examples of emerging areas in our group in (i) targeted drug conjugates construction with an emphasis on traceless antibody-drug conjugates and (ii) use of carbon monoxide (CO) as an immunomodulator signalling molecule for applications in cancer therapeutics.

12:30 Improving Product Homogeneity of Next Generation Biotherapeutics

Thomas Müller-Späth, Ph.D., ChromaCon AG

Safety and efficacy of next generation biotherapeutics such as Antibody drug conjugates (ADCs), bispecific antibodies and biobetter mAbs are strongly linked to the homogeneity of the product. Most 1st generation ADCs are manufactured with little control of drug-antibody-ratios (DARs) leading to sub-optimal drug safety and efficacy profiles. DAR ratios are particularly relevant for those 1st generation ADCs in the drug pipeline that are based on un-specific coupling chemistries. In this presentation we demonstrate how homogenous product profiles and a good product definition can be obtained for biotherapeutics using an advanced counter-current chromatography technology including case studies for 1st generation ADCs, bispecific antibodies and biobetter mAbs.

13:00 Luncheon Presentation *(Sponsorship Opportunity Available)* or Lunch on Your Own

COMPLEMENT ACTIVATION, SYNERGISTIC MECHANISMS, ENHANCED ADCC, AND CLINICAL DEVELOPMENTS

14:00 Chairperson's Remarks

Sergio A. Quezada, Ph.D., Professorial Research Fellow, Research Haematology, University College London Cancer Institute

» KEYNOTE PRESENTATION

14:05 The Mechanism of Complement Activation by IgG Antibodies

Janine Schuurman, Ph.D., Vice President, Research, Genmab

Complement activation by antibodies is an important mechanism in immune defense and immunotherapy. Using X-ray crystallography, mutagenesis studies and cryo-EM tomography, we revealed that IgG antibodies form hexamers on the cell surface following antigen binding. Enhancing hexamerisation on the cell surface by using the HexaBody platform potentiated the intrinsic killing capability of antibodies in *in vitro*, *in vivo* and *ex vivo* models.

14:35 IgA as a Novel Antibody Isotype for the Treatment of Cancer, Potential Synergy with IgG Antibodies

Jeanette Leusen, Ph.D., Associate Professor, Translational Immunology, University Medical Center, Utrecht

Our lab has recently shown that IgA can induce efficient killing of EGFR-positive tumour cells *in vivo*, in mice transgenic for the human receptor for IgA, FcaR. We are now studying the combination of IgG and IgA antibodies against Her2 and EGFR, and find that they work synergistically. It is hypothesized that the combination of effector cells and mechanisms is responsible for this synergy.

15:05 ARGX-111, a Defucosylated Antagonistic Anti-MET Antibody, Displays Potent Anti-Tumour Activity through Enhanced ADCC

Natalie de Jonge, Ph.D., Senior Scientist, arGEN-X

Signaling through MET, the hepatocyte growth factor (HGF) receptor, plays a key role in tumour progression and metastasis. In cancer patients, molecules blocking HGF/MET induce incomplete blockade of MET, are primarily associated with cytostatic activity, and result in modest clinical effects. To overcome this limitation, we developed a defucosylated anti-MET antibody that blocks both HGF-dependent and independent MET activation mechanisms, and kills MET-expressing cancer cells through enhanced ADCC.

15:35 Clinical Development of Tanibirumab and its Next Generation of Bispecific Antibody

Jin-San Yoo, Ph.D., CEO and President, PharmAbcine, Inc.

Tanibirumab, a novel anti-KDR neutralizing fully human IgG has completed a Phase I study. In contrast to other KDR pathway antagonists, Tanibirumab does not cause hypertension, hemorrhage and bleeding side effects, and due to its cross-species cross reactivity, it has been assessed in *in vivo* efficacy studies. These allow precise design of clinical trial protocols. Currently we are planning Phase II trials, and developing bispecific next-generation products to enable Tanibirumab to reach its full potential.

16:05 End of PEGS Europe

> "I had a great time at PEGS Europe and learned a lot."
>
> ***Germaine F, M.S., Senior Scientist, Antibody Engineering, Genentech, Inc.***

Recommended Short Courses*

SC1: Engineering of Bispecific Antibodies

SC2: Mutation and Selection Strategies for Multi-Parameter Antibody Optimisation

SC6: Troubleshooting and Engineering of Antibody Constructs

*(*Separate Registration Required. Please see page 2 for more details.)*

MONDAY, 3 NOVEMBER

12:00 Conference Registration

PLENARY SESSION

13:45 PEGS Europe Team Welcome

13:50 Chairperson's Opening Remarks
William Finlay, Ph.D., Director, Global Biotherapeutic Technologies, Pfizer, Inc.

14:00 The Impact of the New Regulatory Guidance Landscape on the Validation of the Manufacturing Process and the Characterisation of Starting Materials, Drug Substance and Drug Product
Steffen Gross, Ph.D., Head, Monoclonal and Polyclonal Antibodies, Paul-Ehrlich-Institut
The regulatory guidance landscape regarding biological products changes rapidly. Documents overseeing process validation is currently facing major overhauls. New guidelines are published defining the requirements for starting materials and excipients. This might have a deep impact not only on the process development of traditional monoclonal antibody type products but also on new antibody formats such as conjugates as well as on new developed formulations.

14:45 Current Progress with Armed Antibody Products
Dario Neri, Ph.D., Professor, Chemistry and Applied Biosciences, ETH Zurich
There is an emerging trend in Pharmaceutical Biotechnology to "arm" antibodies, capable of selective localization at the site of disease, with suitable therapeutic payloads (e.g., drugs, cytokines, radionuclides, a second antibody moiety, hence producing a bispecific product). This strategy aims at concentrating therapeutic agents in diseased part of the body, while sparing normal tissues. In this lecture, I will present a comparative evaluation of different classes of armed antibody products, developed in my laboratory in collaboration with Philogen. In particular, I will present preclinical and clinical data of armed antibodies in the field of cancer, of chronic inflammation and of endometriosis.

15:30 Refreshment Break

OPTIMISATION OF POTENCY, BINDING, STABILITY, AND RESISTANCE TO AGGREGATION

16:00 Chairperson's Opening Remarks
William Finlay, Ph.D., Director, Global Biotherapeutic Technologies, Pfizer, Inc.

16:05 Differential Co-Engagement of TLR4 and FcγRs Modulates the Potency of NI-0101
Jeremy Loyau, Scientist, Antibody Engineering Unit, Research, Novimmune SA
NI-0101 is a monoclonal antibody directed against TLR4 with a neutralizing mechanism enhanced by FcγR interactions. The antagonistic activity of NI-0101 can be modified based on valency, i.e., the level of co-engagement with different receptor types at the cell surface. The hierarchy for increased avidity is: TLR4 alone < TLR4 + FcγRII < TLR4+ FcγRI. This mode of action could be exploited in order to more efficiently or selectively neutralize other cell surface targets on cells expressing FcγRs.

16:35 Development and Application of TwoB-Ig: A Novel Engineered Fc Variant with Selectively- Enhanced Binding to FcγRIIb
Hitoshi Katada, Ph.D., Research Scientist, Discovery Research, Chugai Pharmaceutical Co. Ltd.
We have developed a novel engineered Fc platform named TwoB-Ig which has complete selectivity to FcγRIIb, an only inhibitory FcγR, over activating FcγR including both allotypes of FcγRIIa. This unique selectivity is important to exploit FcγRIIb for various applications. *In vitro* and *in vivo* data for the application of TwoB-Ig technology to improve pH-dependent antigen binding antibody and enhance agonistic activity of anti-TNFR antibody will be presented.

17:05 Dual-Affinity Re-Targeting DART Proteins for Oncology
Syd Johnson, Ph.D., Vice President, Antibody Engineering, MacroGenics, Inc.
Bispecific antibodies that recruit effector cells to tumours represent a highly potent class of immunotherapeutic agents that may outperform or complement traditional chemotherapy, naked antibodies and ADCs. MacroGenics' Dual-Affinity Re-Targeting (DART) proteins are among the most stable and potent biologics in this therapeutic class. An update will be presented on several DART candidates in different stages of development for treatment of hematological or solid tumours. Applications of half-life extended and non-extended DARTs will be discussed, as well as methods for their production.

17:35 Recent Advances and Successes in Computational Antibody Modeling Using BioLuminate
Sponsored by SCHRÖDINGER.
David A. Pearlman, Ph.D., Senior Principal Scientist, Schrödinger
We describe recent studies demonstrating the power of theoretical structure-based protein design tools as applied to antibodies, as well as our performance in a recent multi-institution blinded antibody structure prediction assessment, and demonstrate how computational tools can be used to perform analyses such as hot spot identification.

17:50 Veltis® Innovative Technology for Half-Life Extension and Optimisation of Biotherapeutics
Sponsored by novozymes
Filipa Antunes, Msc, Ph.D., Research Scientist, Novozymes A/S
Short circulatory half-life represents a major obstacle for many protein and peptide-based therapeutic agents, resulting in increased dosing with the consequent risk of side effects and reduced patient compliance. It has been demonstrated that the pharmacokinetics of small drugs, peptides and proteins can be significantly improved by conjugation, association or fusion to albumin. This extended circulatory half-life derives from both the size of albumin and recycling of the molecule via the neonatal Fc receptor, FcRn. Using advanced protein engineering expertise, human serum albumin has been modified to enhance its affinity for FcRn. This increase in affinity for the FcRn receptor translates into improved pharmacokinetic properties of the albumin molecule and ultimately the therapeutic candidate that is fused or conjugated to it. The application of these novel albumin variants to improve the pharmacokinetic properties of a number of therapeutic candidates, including proteins and small peptides will be presented and discussed.

18:20 Welcome Reception in the Exhibit Hall with Poster Viewing

19:20 End of Day One

TUESDAY, 4 NOVEMBER

07:30 Registration

07:45 Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

OPTIMISATION OF MANUFACTURABILITY, RESISTANCE TO AGGREGATION AND SOLUBILITY

08:30 Chairperson's Remarks

08:40 Engineering Aggregation-Resistant Antibody Fragments

Peter Tessier, Ph.D., Associate Professor, Chemical & Biological Engineering, Center for Biotechnology & Interdisciplinary Studies, Rensselaer Polytechnic Institute

We are investigating how antibody fragments can be engineered to possess extremely high solubility without altering binding activity. We have developed a novel approach for engineering the edges of hydrophobic CDRs with charged insertion mutations that dramatically increases antibody solubility without reducing binding affinity. Our studies reveal that the location of charged mutations within CDRs as well as the polarity of such mutations dramatically impact their solubilizing activity.

09:10 Engineering, Purification and Optimisation of Bispecific Heavy Chain Heterodimers for T Cell Redirection

Stanislas Blein, Ph.D., Director & Head, Antibody Engineering, Biologics, Glenmark Pharmaceuticals

By combining FAB and scFv formats with a unique concept of bio-mimicry, we have developed a heavy chain heterodimerization platform wherein antibodies from different sources can be paired without any restrictions and subsequently manufactured. Bottlenecks such as achieving high levels of heterodimerization, removal of homodimer traces during scale-up, or scFv instability and aggregation have been solved to create an efficient and scalable process

09:40 Antibody v-Domain Optimisation for Subcutaneous Dosing Strategies

William Finlay, Ph.D., Director, Global Biotherapeutic Technologies, Pfizer, Inc.

While myriad molecular formats for bispecific antibodies have been examined, the simplest structures are often based on the scFv. Issues with stability and manufacturability in scFv-based bispecific molecules, however, have been a significant hindrance to their development, particularly for high-concentration, stable formulations that allow subcutaneous delivery. Using a novel CDR-based engineering strategy, we have generated a tetravalent bispecific molecule for subcutaneous administration. New insights into structure-function relationships will be presented.

10:10 Coffee Break in the Exhibit Hall with Poster Viewing

DATA MANAGEMENT FOR ANTIBODY DISCOVERY

10:50 GSK's Antibody Discovery Database (ADD), a Comprehensive System to Manage, Share and Exploit Antibody Discovery Processes and Format Information

Trevor Wattam, Ph.D., Manager, Biopharm Discovery Group, GlaxoSmithKline

I will present an overview of a comprehensive R&D data management system referred to as the GSK's Antibody Discovery Database (ADD), a comprehensive system used to manage, share and exploit the large amount of relevant and complex information from all our Antibody discovery processes (yeast display, phage display, hybridoma/humanization) and GSKs biopharm formats, including domain antibodies (dAbs), mAbs and bispecifics.

11:20 Fast and Easy Generic Anti-CHO HCP Analysis, 96-Samples Assay-To-Data in 65 Minutes

Sponsored by PALL Life Sciences / forteBIO A Division of Pall Life Sciences

Darick Dayne, Ph.D., Senior Product Manager, ForteBio, A Division of Pall Life Sciences

Pall ForteBio has teamed up with Cygnus Technologies to jointly develop an Anti-CHO HCP detection kit. While ForteBio Octet systems are the industry standard in easy and rapid high throughput analysis, Cygnus HCP ELISA kits are known for their broad HCP recognition and sensitivity. The new ForteBio-Cygnus Anti-CHO HCP kit will embody the best of both worlds. Users will achieve unparalleled time-to-results, streamlined and automated* workflow, enhanced dynamic range, and excellent precision and assay robustness.

*Complete hands-off automated workflow achieved with the Octet HTX system

11:50 Problem Solving Roundtable Discussions

Optimisation of Manufacturability

Moderator: Stanislas Blein, Ph.D., Deputy Director & Head, Antibody Engineering, Biologics, Glenmark Pharmaceuticals

Measures to Avoid Off-Target Toxicity

Moderator: Klaus Bosslet, Ph.D., Head, Discovery Oncology, Roche Pharmaceuticals, Penzberg

Engineering of Bispecific Antibodies

Moderator: Ton Logtenberg, Ph.D., CEO, Merus

Measures for Getting Biologically Active Antibodies

Moderator: Yanay Ofran, Ph.D., Founder, Biolojic Design, Ltd.; Goodman Faculty of Life Sciences, BarIlan University

12:50 pm Luncheon Presentation: High Throughput Multimode Stability Measurements Accelerate Formulation Screening and Facilitate the Characterisation of Biologics

Sponsored by Avacta ANALYTICAL

Geoff Platt, MSc, Ph.D., Head, Optim Applications, Avacta Analytical, UK

Optim delivers high throughput measurements of protein samples that provide information on both their conformational stability and propensity to aggregate. The presentation will include examples of its use in screening biologics formulations and demonstrate its capacity to afford predictive information for long-term stability. The ability of this technology to aid optimisation and development of biologics by characterising degradation mechanisms of monoclonal antibodies, antibody-drug conjugates and membrane proteins will also be highlighted.

14:00 Dessert Break in the Exhibit Hall with Poster Viewing

PRECISION ONCOLOGY, EPITOPE-SPECIFIC ANTIBODIES, AND MANAGEMENT OF TOXICITY

14:30 Chairperson's Remarks

Julian Bertschinger, Ph.D., CEO, Covagen

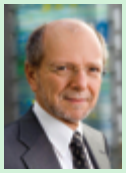
KEYNOTE PRESENTATION

14:35 Next-Generation Cancer Treatment Using Multi-Specific Darpins

Michael Stumpp, Ph.D., Molecular Partners, AG

Precision oncology is an emerging treatment paradigm by which well-chosen targeted therapeutics will inhibit the specific tumour drivers of each patient. Such an approach will require the combination of several targeted therapeutics, which may be hampered by overlapping off-target toxicities and economic reasons, or ideally the availability of multi-specific therapeutics - a natural setting for DARPins given their high specificity and modular architecture. We have generated multi-specific DARPin drug candidates against various tumour drivers, which compare favorably in preclinical models to available standards of care. Insights on the rationale for target choice, drug format, mechanism of action and differentiation will be provided.

KEYNOTE PRESENTATION



15:35 RG7787 - A Cytolytic Fusion Protein Based on a De-Immunised Variant of Pseudomonas Exotoxin (PE)

Klaus Bosslet, Ph.D., Head, Discovery Oncology, Roche Pharmaceuticals, Penzberg

Development of immunotoxins into actual drugs has been hampered by their immunogenicity and off-target toxicity, particularly vascular leak syndrome. Together with Ira Pastan's lab at NCI we have developed a new cytolytic fusion protein format that is de-immunized and has much reduced off-target toxicity. Cell viability assays show that RG7787 has similar cytotoxic potency in a variety of cell lines as well as similarly strong efficacy as the immunogenic Mesothelin targeted PE38 from NCI (SS1P) even in slow growing tumour xenograft systems.

15:35 The Shark Strikes Twice: Generation of Mono- and Bispecific High-Affinity vNAR Antibody Domains via Step-Wise Affinity Maturation

Stefan Zielonka, Scientist, Department of Biochemistry, University of Darmstadt

16:05 Creating Focused Libraries for Protein Engineering

Sponsored by CHEMICAL COMPUTING GROUP

Andrew Henry, Principal Scientist, Chemical Computing Group

Protein engineering plays a pivotal role in modulating the function, activity and physical properties of biologics. Representative strategies employed in protein engineering include directed evolution and rational protein design. Although both approaches are effective at identifying and optimizing protein therapeutic candidates, efficient search and evaluation of an excessively large sequence design space becomes challenging and requires multiple experimental rounds to reasonably assess the sequence space. Here we have developed a computational approach which predicts mutation probabilities for given residue sites in specified sequences. In assessing the probabilities at given residue sites, the sequence search space can be efficiently sampled to design and produce focused mutant libraries.

16:20 Sponsored Presentation *(Opportunity Available)*

16:35 Refreshment Break in the Exhibit Hall with Poster Viewing

PRECLINICAL DEVELOPMENT AND CLINICAL VALIDATION

17:15 COVA322: A Novel Bispecific TNF/IL-17A Inhibitor for the Treatment of Inflammatory Diseases

Julian Bertschinger, Ph.D., CEO, Covagen

We present the discovery and preclinical development of COVA322, a potent bispecific TNF/IL-17A inhibitor which is about to enter clinical trials. COVA322 consists of an anti-IL-17A Fynomer fused to a fully human anti-TNF antibody and exhibits excellent biophysical properties. COVA322 was produced under GMP conditions with a yield of 3.3 g/l and was well tolerated in preclinical safety studies.

17:45 Preclinical and Clinical Developments with Nanobodies

Catelijne Stortelers, Ph.D., Senior Scientist, Discovery, Ablynx

Nanobodies are protein therapeutics based on the smallest functional fragments of naturally-occurring heavy-chain antibodies and enable straight-forward multimeric drug targeting across several formats and target classes. Examples from our drug pipeline candidates in clinical and preclinical development show that this formatting flexibility allows fine-tuning of valency, avidity, specificity for two or more targets, mechanism of action and half-life. In combination with favorable physicochemical properties, the Nanobody platform has the potential to bring biologics therapy beyond what's possible with antibodies and will be exemplified by the development of ALX-0171, an inhaled Nanobody for the treatment of Respiratory Syncytial Virus infection in infants.

18:15 Discovery and Development of Human Bispecific Antibodies with Potent Anti-Tumour Activities

Mark Throsby, Ph.D., CSO, Merus

This presentation will describe the use of a platform technology for the generation and high-throughput functional selection of heterodimerized human bispecific antibodies sharing a common light chain. These products, specific for combinations of receptor tyrosine kinases showed superior tumour cell killing activity, whereas CMC at 2000L scale was reminiscent of regular IgG antibodies. First-in-patient studies are planned in 2015.

18:45 End of Optimisation & Development

> "The quality of the talks was extremely good in terms of both speakers and content. The meeting was very well organized and the schedule was great as well as the location."
>
> ***Alessandro A., Ph.D., Scientist, Koch Institute for Integrative Cancer Research, MIT***

Inaugural

Protein Aggregates & Particles

Prevent • Detect • Minimise • Eradicate

Recommended Short Course*

SC5: Aggregation and Immunogenicity: How Do Formulation, Process and Delivery Influence Immunogenicity of Therapeutic Proteins?

*(*Separate Registration Required. Please see page 2 for more details.)*

WEDNESDAY, 5 NOVEMBER

07:45 Registration and Morning Coffee

MECHANISM OF AGGREGATES AND ENGINEERING TO IMPROVE DEVELOPABILITY

08:30 Chairperson's Opening Remarks

Murali Bilikallahalli, Ph.D., Associate Director, Biopharmaceutical Development: Vaccines & Non-mAb Biologics, MedImmune LLC

KEYNOTE PRESENTATION

08:35 Cell and Process Engineering Strategies to Cure Cellular Aggregation of a Difficult to Express Fusion Protein

David C. James, Ph.D., Professor, Chemical & Biological Engineering, University of Sheffield

Based on kinetic modeling of the cellular synthetic process, we compared different strategies (cell engineering, modulation of culture environment) to alleviate cellular aggregation and the associated poor expression of a recombinant Fc-fusion protein by CHO cells. Our analysis serves as a paradigm for multivariate optimisation of DTE protein production.

09:05 Kinetic and Thermodynamic Correlations of Protein Folding & Stability to Aggregate & Particle Formation

Murali Bilikallahalli, Ph.D., Associate Director, Vaccines & Biologics, Biopharmaceutical Development, MedImmune LLC

Cofactors often have the ability to interact specifically with the unfolded polypeptides. Developing cofactor bound/free protein/protein conjugates is challenging since cofactors in most cases play direct role in structure, stability and activity. Fundamentals of protein folding pathways, cofactors assisted protein folding & stability, and some of the stability challenges in developing metal bound protein as a therapeutic drug will be addressed in this presentation.

09:35 A3D: Towards the Design of Aggregation-Resistant Biotherapeutics

Salvador Ventura, Ph.D., Prof Biochemistry & Molecular Biology, Institute of Biotechnology & Biomedicine, University Autonoma of Barcelona

The molecular complexity of protein therapeutics makes them sensitive to stress during production and delivery. A major problem is the formation of aggregates in protein solutions, which impact the product properties and result in adverse immunogenic reactions. Therefore, tools to design aggregation-resistant proteins are receiving increasing interest. Here we introduce A3D which is able to predict and assist the redesign of the aggregation propensity of protein 3D-structures.

10:05 Determining the Stability and Structure of Therapeutic Proteins

Sponsored by Malvern

E. Neil Lewis, CTO, Malvern Instruments & Head, Malvern Bioscience Development Initiative

Aggregation and native-state unfolding of therapeutic proteins is of critical importance to manufacturers and patients alike. The use of hybrid techniques lends itself to more thorough characterization of particulates in therapeutics. An approach that combines dynamic light scattering with Raman spectroscopy can measure the high-order structure of proteins while concurrently monitoring aggregation. Another hybrid technique, the combination of optical microscopy with Raman spectroscopy, allows for both the detection and identification of particulates in protein suspensions.

10:35 Coffee Break in the Exhibit Hall with Poster Viewing

11:15 *In silico* Engineering to Improve Antibody Developability

Bojana Popovic, Ph.D., Senior Research Scientist, Antibody Discovery and Protein Engineering, MedImmune

Due to mutations introduced during affinity maturation MEDI-1912 displayed an increase propensity to aggregate. Using an *in silico* spatial aggregation propensity tool we identified surface exposed hydrophobic amino acids responsible for aggregation. These amino acids were reverted to the parental sequence, resulting in a stable antibody without compromising potency or affinity for NGF. By improving the stability of MEDI-1912, we also improved the serum half-life *in vivo*.

11:45 Aggregation of Therapeutic Proteins in Human Plasma and Human Blood: A New Research and Development Field

Tudor Arvinte, Ph.D., Chairman & CEO, Therapeomic, Inc.

After injection of a clear, not-aggregated protein solution, aggregation can form at the injection site in tissue or in the blood stream. The talk will present new data on characterisation of the aggregates formed *in vitro* when different formulations of therapeutic proteins are mixed with human plasma and blood. A model for the aggregation will be presented and some clinical implications of the aggregation induced by biopharmaceuticals will be discussed.

12:15 Identification of High MW Species using diSPR® Pulse Method

Sponsored by sensiQ

Eric Reese, Ph.D., Vice President, Marketing, Sales and Marketing, SensiQ Technologies Inc.

The detection and subsequent analysis of protein aggregation is of hallmark importance in the discovery and development of biotherapeutic drugs. Standard methodologies used to detect aggregation can either be time consuming or cumbersome. This presentation describes how the diSPR® technique designated Pulse OneStep® can detect and measure simulated aggregation in proteins or other biomolecules. In addition we demonstrate that by monitoring the diffusion coefficient, aggregation events can be defined in bulk sample. Further research is underway to define the limits of detection. OneStep® marks a quantum innovation in the detection and analysis of sample aggregation by SPR biosensors.

12:45 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

CHARACTERISING, PREDICTING AND DETECTING AGGREGATES AND PARTICLES

14:00 Chairperson's Remarks

Pete M. Tessier, Ph.D., Associate Professor, Chemical & Biological Engineering, Rensselaer Polytechnic Institute, USA

KEYNOTE PRESENTATION

14:05 Characterising and Release Testing of Protein Aggregates in Biologics

Ewa Marszal, Ph.D., CMC Reviewer, Division of Hematology Research and Review, Center for Biologics Evaluation and Research, U.S. Food & Drug Administration

Protein aggregates in biologics present a quality issue and raise safety concerns. Thus, their content should be minimized and controlled. This presentation will cover recent guidelines for particulate matter control and the advancements in particulate matter detection and metrology.

14:35 Using *in silico* Tools for Prediction of Propensity for Aggregation and for Viscosity

Bernhard Helk, Ph.D., Head, New Technologies, Novartis Pharma AG

Three *in silico* tools and their practical application to the prediction and characterisation of protein-protein-interaction are demonstrated: SAP (Spatial Aggregation Propensity) identifies hydrophobic patches and is applied to engineer mAbs and ADCs with increased stability. DI (Developability Index) predicts aggregation propensities based on SAP and net charge. SCM (Spatial Charge Map) ranks mAbs according to viscosity. Case studies for predicting crystallization and viscosity of mAbs are presented.

15:05 Emerging Technologies for Characterising and Detecting Sub-Visible and Visible Particles

Andrea Hawe, Ph.D., CSO, Coriolis Pharma Research

Within the last years emerging technologies such as nanoparticle tracking analysis, resonant mass measurements, flow imaging microscopy or semi-automated visual inspection have been introduced for (sub-) visible particle analysis in biopharmaceutical products. An overview on emerging technologies for sub-visible and visible particle analysis will be given, challenges pointed out and highlighted with relevant examples and case-studies.

15:35 Refreshment Break in the Exhibit Hall with Poster Viewing

16:15 Optimising Monoclonal Antibody Selection and Formulation Using Self-Interaction Nanoparticle Spectroscopy

Pete M. Tessier, Ph.D., Associate Professor, Chemical & Biological Engineering, Rensselaer Polytechnic Institute, USA

Improving selection of highly soluble antibody candidates early in the discovery process requires biophysical methods capable of assaying mAb self-association that are robust for handling hundreds to thousands of samples at extremely dilute antibody concentrations (microgram per mL) and in the presence of contaminants (cell culture supernatants). We report a method (affinity-capture self-interaction nanoparticle spectroscopy) for addressing these challenges and discuss its use in the discovery of new, highly soluble antibodies.

16:45 Stability Challenges for Protein Therapeutics: Structure Alteration and Aggregation Propensity

Joel Richard, Ph.D., Senior Vice President, Peptides, Head, CMC & Engineering Dreux Site, IPSEN

This talk will present biophysical analytical techniques to characterise protein aggregation as well as their aggregation propensities. Appropriate combination of biophysical methods will illustrate structural modifications of the protein in the formulations, display the effect of excipients on these modifications and the subsequent mechanism of formation of sub visible particles. Clinical impact will also be discussed, under the angle of potential safety issues, as identified by the regulatory agencies.

17:15 Problem Solving Roundtable Discussions:

Engineering Aggregate-Resistant Biotherapeutics
Moderator: Prof Salvador Ventura, Full Professor, Protein Folding and Conformational Diseases Lab (PFCD), Institute of Biotechnology and Biomedicine, Department of Biochemistry and Molecular Biology, Universitat Autònoma de Barcelona

Protein Folding in Relation to Stability and Aggregate Formation
Moderator: Murali Bilikallahalli, Ph.D., Associate Director, Vaccines & Biologics, Biopharmaceutical Development, MedImmune LLC

Biophysical Development and Characterisation in Early Drug Discovery
Moderator: Bojana Popovic, Ph.D., Senior Research Scientist, Antibody Discovery and Protein Engineering, MedImmune

Strategies for Analytical Characterisation of Sub-Visible Particles in Various Stages of Development
Moderator: Andrea Hawe, Ph.D., CSO, Coriolis Pharma Research

18:15 Networking Reception in the Exhibit Hall with Poster Viewing

19:15 End of Day One

THURSDAY, 6 NOVEMBER

08:00 Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

08:30 Chairperson's Remarks

Tudor Arvinte, Ph.D., Chairman & CEO, Therapeomic, Inc.

AGGREGATES AND IMMUNOGENICITY

08:35 Testing the Immunogenic Potential of Aggregates – *In silico, in vitro* and *in vivo*

Melody Sauerborn, Ph.D., Senior Expert Immunogenicity, Bioanalysis, TNO Triskelion

Although the precise characteristics of an aggregate responsible for immunogenic behavior are not known yet, efforts are made to predict the intrinsic probability of a biologic to form aggregates and the impact of aggregates in the clinics. This presentation will give an update on the latest tools and technologies to characterise, predict and test aggregates *in silico*, *in vitro* and *in vivo*.

09:05 Induction of T Cell Responses by Protein Aggregates: A Key Stage for the Immunogenicity of Biologics

Mark Fogg, Ph.D., Immunology Group Leader, Antitope Limited, an Abzena Company

This presentation will provide case study examples of how preclinical methods measuring drug induced T cell responses can be applied to select drugs with a reduced risk of clinical immunogenicity. Furthermore new data will be presented on how aggregates in some formulations can trigger innate responses that ultimately enhance immunogenicity. The clinical relevance to these findings will be discussed.

ENHANCING STABILITY AND OPTIMISING FORMULATION TO MINIMIZE AGGREGATES & IMMUNOGENICITY

09:35 Investigation of Reversible Self-Association during Early Stage Development of a Low Concentration Antibody-Drug Conjugate

Elizabeth Bartlett, Ph.D., Scientist, Analytical & Pharmaceutical Sciences, Immunogen, Inc.

Reversible self-association is often present in high concentration antibody products, but may also occur in lower concentration preparations. In the case of antibody-drug conjugates (ADC), a novel class of molecules for the treatment of cancers, this property can present substantial challenges to successful formulations. In this study, a multi-technique approach was used to identify and investigate the effects of various excipients on reversible self-association in a low concentration ADC.

10:05 Reproducible and Fast Exosome Detection - The "Zeta View" System from Particle Metrix GmbH is the Answer!

Sponsored by PARTICLEMETRIX

Rainer Muehlbacher, DI (FH), MBA, Sales and Marketing Global Manager, Particle-Metrix GmbH

Exosomes can potentially be used for prognosis, therapy, and biomarkers for health and disease but the characterization was challenging; Particle Tracking Analysis (NTA/PTA) is a technique where single particles of the sample are visualized and traced. By analysis of the particle traces, the NTA/PTA device (ZetaView®, Particle Metrix, Germany) performs the measurement of particle size, concentration and zeta potential of exosomes in one experiment.

10:20 Sponsored Presentation *(Opportunity Available)*

10:35 Coffee Break in the Exhibit Hall with Poster Viewing

11:15 High hydrostatic pressure as a novel method for characterization, identification and mitigation - Building a better IFN-beta-1b

Amber Fradkin, Ph.D., Director, Analytical Characterization, Barofold, Inc.

Particles are known to form during purification, process, shipping and handling procedures. Particles may be stress induced or could be resultant of formulation issues. In addition, the presence of proteinaceous nanoparticles has potential to lead to subvisible and visible particle formation with storage over shelf life. We demonstrate how high hydrostatic pressure can be used as a novel tool to purify protein products as well as identify and trouble shoot root cause for particle formation, minimizing immunogenicity. Case studies based on IFN-beta-1b will be presented.

11:45 NaCl-Induced Aggregation of Monoclonal Antibodies at Low pH: Prevention by Additives

Fabian Bickel, MSc, Ph.D., Student, Institute of Applied Biotechnology, Biberach University of Applied Science

Aggregation is a known phenomenon in downstream processing of monoclonal antibodies. Here we investigated a model system where mAb aggregation is induced by increasing the ionic strength at low pH. Aggregation can be partially reverted by lowering the ionic strength. The effect of protective osmolyte additives on aggregation kinetics and final aggregate concentration is investigated. The system has potential for buffer optimisation and formulation development.

12:15 End of Protein Aggregates and Particles conference

> "All in all, the PEGS meeting was, again, very informative and an excellent occasion to meet colleagues working on similar subjects."
>
> ***Hubert K, Ph.D., Principal Scientist, Large Molecule Research, Roche Diagnostic***

THURSDAY, 6 NOVEMBER

12:30 Conference Registration

13:00 Dessert Break in the Exhibit Hall with Poster Viewing

ANALYTICAL METHOD DEVELOPMENT AND QUALIFICATION

13:30 Chairperson's Opening Remarks
Jonas V. Schaefer, Ph.D., Head, High-Throughput Laboratory, Department of Biochemistry, University of Zurich

» KEYNOTE PRESENTATION

13:35 Development of High-Throughput Selection and Screening Methods
Jonas V. Schaefer, Ph.D., Head, High-Throughput Laboratory, Department of Biochemistry, University of Zurich
With the help of technology developments, a robust pipeline could be established that already generated valuable DARP in binders (Designed Ankyrin Repeat Proteins, an alternative scaffold), not just covering a variety of different targets but also meeting the high quality criteria important for most scientific projects: monomeric binders that specifically recognize different, non-overlapping epitopes at their targets with high affinities and which can be expressed at high levels in bacterial systems.

14:05 Development of High-Throughput mAb Developability Screening Assays through Detection of Self- and Cross-Interaction
Yingda Xu, Associate Director Protein Analytics Adimab
Self- and cross-interaction of an antibody usually leads to developability issues, such as low expression, poor solubility, high viscosity, aggregation and fast serum clearance. Development of high-throughput assays targeting detection of antibody self- and cross-interaction allows elimination of problematic candidates early in the discovery process, minimizing downstream risks.

14:35 Detection of Anti Drug Antibodies to a Therapeutic Using a Photonic Ring Immunoassay
Sponsored by Genalyte
Alex Batchelor, General Manager, Europe, Sales and Marketing, Genalyte, Inc.
Recent data demonstrates the exceptional growth in biologic therapeutics across all phases of development. Often, patients taking infused or injected therapeutics can develop antibodies against the drug (ADAs). These ADAs can cause a decrease in efficacy, increased clearance rate, or adverse events. Genalyte has developed an assay capable of detecting and isotyping ADAs with sensitivity and drug tolerance levels exceeding regulatory guidelines. The assay demonstrated concordance with orthogonal technologies while yielding multiplex isotyping profiles, including IgG4.

15:05 Refreshment Break in the Exhibit Hall with Poster Viewing

CHARACTERISATION AND DEVELOPMENT OF ADCs, BISPECIFICS AND OTHER NOVEL BIOTHERAPEUTICS

15:45 Polysorbate Degradation and Particulates in Biotherapeutic Formulations: Characterization Challenges and Risk Mitigation Strategies
Sandeep Yadav, Ph.D, Scientist, Late Stage Pharmaceutical Development, Genentech, Inc., a member of Roche Group

16:15 Analytical Characterisation of the RNA-Polymerase II inhibitor Amanitin and Amanitin-Based ADCs
Andreas Pahl, Ph.D., CSO, Heidelberg Pharma
New generations of payloads enter the area of ADC therapeutics including Heidelberg Pharma's amanitin, a highly effective inhibitor of the eukaryotic RNA Polymerase II. Due to its hydrophilic nature the physicochemical properties differ from well-known tubulin inhibitor based ADCs. This presentation will summarize the current status of Amanitin based ADCs and appropriate methods for their analytical characterisation.

16:45 Characterisation and Comparability Studies for Antibody-Drug Conjugates
Gayathri Ratnaswamy, Ph.D., Director, Analytical and Formulation Development, Agensys, Inc.
This presentation will focus on the characterisation of ADCs derived from IgG1 and IgG2 isotypes (derived from hybridoma or CHO cell lines) when conjugated to cytotoxic drugs at the inter-chain disulfides. The results show that the mAb isotypes influence drug loading profiles and this in turn leads to differences in the structure, physico-chemical properties and stability of the resulting conjugates.

17:15 End of Day One

17:15 Dinner Short Course Registration

17:30 – 20:30 Dinner Short Courses

Recommended Short Course*

SC5: Aggregation and Immunogenicity: How Do Formulation, Process and Delivery Influence Immunogenicity of Therapeutic Proteins?
*(*Separate Registration Required. Please see page 2 for more details.)*

FRIDAY, 7 NOVEMBER

08:00 Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

CHARACTERISATION AND DEVELOPMENT OF ADCs, BISPECIFICS AND OTHER NOVEL BIOTHERAPEUTICS (cont'd)

08:30 Chairperson's Remarks
Vivian Lindo, Ph.D., Associate Director, Product Characterisation, MedImmune

08:35 Analytical Strategies for Characterisation of Non-mAbs

Vivian Lindo, Ph.D., Associate Director, Product Characterisation, MedImmune

Case studies of non-mAb characterisation strategies will include:

- Approaches to primary sequence characterisation
- Approaches to glycosylation characterisation
- Higher order structure characterisation for non-mAbs

9:05 Functional Assay Strategies for Bispecific Antibodies and Fusion Proteins

Joerg Moelleken, Ph.D., Senior Scientist, Large Molecule Research, Roche Pharmaceutical Research & Early Development, Roche Innovation Center Penzberg

The increasing complexity of novel biotherapeutics comprising of Bispecific antibodies and fusion proteins raise new challenges for functional characterisation as compared to standard antibodies. Besides addressing new technical aspects like multi-specificity, and poly-valency, additional biological viewpoints like exclusive or simultaneous target binding need to be considered now. This presentation shows points to consider relevant from lead identification until lead characterisation.

09:35 Problem Solving Roundtable Discussions

Specification Setting for ADCs

Moderator: Gayathri Ratnaswamy, Ph.D., Director, Analytical and Formulation Development, Agensys, Inc.

What are the Biggest (Common) Challenges in Analytical Characterisation of Next-Generation Biotherapeutics?

Moderator: Samadhi Vitharana, Ph.D., Senior Scientist, Core Sciences and Technologies, Takeda California

Analytical Characterisation for Product Comparability

Moderator: Daotian Fu, Ph.D., Executive Vice President, Livzon Mabpharm

Comparability for Process Changes throughout Product Lifecycle

Moderator: Alain Bernard, Ph.D., Vice President, Technical Operations GPS, UCB Pharma

10:35 Coffee Break

11:00 Developing Quality Product Attributes Using Cell Line Selection Strategies and High-Throughput Analytics

Silke Hansen, Ph.D., Large Molecule Research, Roche Pharmaceutical Research & Early Development, Roche Innovation Center Penzberg

Bispecific antibodies and complex antibody fusion proteins consisting of up to four different polypeptide chains in a single CHO cell line at high quality has been shown to be possible. Diligent cell line selection strategies, supported by high-throughput analytical methods, were keys to the success of identifying cell clones with well characterised cell properties, a stable product profile giving rise to the production of clinical grade API.

11:30 Comprehensive Optimisation of a Single-Chain Variable Domain Antibody Fragment as a Targeting Module for a Cytotoxic Nanoparticle

Kathy Zhang, M.D., MSc, Scientist, Antibody Technology Team, Merrimack Pharmaceuticals

Antibody-targeted nanoparticles increase the therapeutic index of cytotoxic anti-cancer therapies by directing them to tumour cells. We present a case study of iterative engineering of a single chain variable fragment for use as a targeting arm of a liposome-based cytotoxic nanoparticle. Our studies demonstrate that a comprehensive engineering strategy may be required to develop a scFv with optimal characteristics for nanoparticle targeting.

12:00 Multi-Parametric Optimisation and Characterisation of Antibody Binding Domains for Chronic Dosing

Orla Cunningham, Ph.D., Associate Director, Global Biotherapeutic Technologies, Pfizer

Our aim was to generate a tetravalent bispecific molecule targeting two inflammatory mediators for synergistic immune modulation. Phage displayed mutagenesis libraries were aggressively selected and screened using tailored approaches to identify truly potent AND manufacturable scFv-based bispecifics suitable for subcutaneous administration. Subsequent structural analysis revealed how a very restricted number of CDR-based mutations effectively modulated significant changes in potency and stability.

12:30 Advances in Antibody Characterization and Collaborative Workflows

Sponsored by accelrys BIOVIA

Anne Goupil, Principal Field Applications Scientist, Pre-Sales, BIOVIA (formerly Accelrys)

Antibody discovery is driven by complex time consuming experimental processes involving numerous teams. Evolving technologies enable researchers to make more informed decisions early in the process. Here we suggest collaborative and comprehensive capabilities in antibody characterization and development: capabilities to analyze annotate, predict 3-dimensional structures, mutation energies for stability and binding affinity, electrostatics properties, aggregation propensity, developability and more. Collaborative environments for registration, workflow and sharing will be discussed.

13:00 Luncheon Presentation *(Sponsorship Opportunity Available)* or Lunch on Your Own

CHARACTERISING FOR COMPARABILITY

14:00 Chairperson's Remarks

Hans-Martin Mueller, Ph.D., Director, Bioprocess Development, Merck & Co.

14:05 Comparability for Process Changes throughout Product Lifecycle

Alain Bernard, Ph.D., Vice President, Technical Operations GPS, UCB Pharma

This presentation will describe strategies to implement major process changes during clinical development or after launch of a product on the market. A common denominator to all strategies is to set as an absolute key objective the improvement of product quality. We will illustrate how, a cell line change, or major changes in cell culture media or purification steps can be safely implemented with positive impacts for the patients.

14:35 Analytical and Quality Considerations to Support Product Characterisation Comparability

Daotian Fu, Ph.D., Executive Vice President, Livzon Mabpharm

With wide implementation of QbD in the biotech industry and recent advances in analytical technologies, strategies of analytical characterisation and product comparability continues to evolve. In this presentation, we will discuss implications of QbD applications in process development, and how it may be best used to support process characterisation and product comparability.

15:05 Forced Degradation: A Modern Analytical Tool for Demonstrating Comparability and Similarity

Hans-Martin Mueller, Ph.D., Director, Bioprocess Development, Biologics and Vaccines, Merck MSD

Just recently, forced degradation studies became a "super trend" in industry. As an analytical tool, forced degradation studies were applied very successfully to demonstrate comparability of novel biologics and biosimilars. Today, the inclusion of forced degradation studies is just an expectation of regulatory agencies like the FDA when it comes to filing of comparability studies for biologics.

15:35 Product Stability Profiling for Bioprocess Development

Christine P. Chan, Ph.D., Principal Scientist/Technical Lead, Global Manufacturing Science & Technology, Genzyme – a SANOFI company

Development of complex glycoproteins requires an array of analytical techniques to adequately understand and control product quality and stability during the bioproduction process as well as storage through the end of shelf-life. This presentation will discuss strategies in product testing and review case studies on characterisation of different proteins in support of process development.

16:05 End of PEGS Europe

MONDAY, 3 NOVEMBER

12:00 Conference Registration

PLENARY SESSION

13:45 PEGS Europe Team Welcome

13:50 Chairperson's Opening Remarks
William Finlay, Ph.D., Director, Global Biotherapeutic Technologies, Pfizer, Inc.

14:00 The Impact of the New Regulatory Guidance Landscape on the Validation of the Manufacturing Process and the Characterisation of Starting Materials, Drug Substance and Drug Product
Steffen Gross, Ph.D., Head, Monoclonal and Polyclonal Antibodies, Paul-Ehrlich-Institut
The regulatory guidance landscape regarding biological products changes rapidly. Documents overseeing process validation is currently facing major overhauls. New guidelines are published defining the requirements for starting materials and excipients. This might have a deep impact not only on the process development of traditional monoclonal antibody type products but also on new antibody formats such as conjugates as well as on new developed formulations.

14:45 Current Progress with Armed Antibody Products
Dario Neri, Ph.D., Professor, Chemistry and Applied Biosciences, ETH Zurich
There is an emerging trend in Pharmaceutical Biotechnology to "arm" antibodies, capable of selective localization at the site of disease, with suitable therapeutic payloads (e.g., drugs, cytokines, radionuclides, a second antibody moiety, hence producing a bispecific product). This strategy aims at concentrating therapeutic agents in diseased part of the body, while sparing normal tissues. In this lecture, I will present a comparative evaluation of different classes of armed antibody products, developed in my laboratory in collaboration with Philogen. In particular, I will present preclinical and clinical data of armed antibodies in the field of cancer, of chronic inflammation and of endometriosis.

15:30 Refreshment Break

ENGINEERING BETTER HOSTS

16:00 Chairperson's Opening Remarks

» 16:05 KEYNOTE PRESENTATION

Production of Protein Tools in Support of R&D Pharma Projects
Jacques Dumas, Ph.D., Head, Protein Production, Global Biotherapeutics, sanofi
The genomic era of the 90's is culminating in the identification and production of novel protein targets for drug discovery. Increasing numbers of "high value" proteins are used for crystallography and High Throughput Screening (HTS). Proteins are produced by recombinant technology and purified to homogeneity using platform strategies. In the last 10 years, strategies have evolved to adapt to difficult to express proteins, such as kinases. In addition, the revival of biotherapeutic proteins has generated the need for new protein tools.

16:35 High-Yield, Zero-Leakage Expression System in Escherichia coli
Yusuke Kato, Ph.D., Senior Researcher, Genetically Modified Organism Research Centre, National Institute of Agrobiological Sciences
We designed a high-yield, zero-leakage expression system using a transcriptional-translational double-regulation for toxic protein production in *E. coli*. "Translational switches" were constructed using site-specific unnatural amino acid incorporation at the amber stop codons that were inserted in target genes. Under repression conditions, leakage-expression was completely abolished by a synergistic repression both at the transcriptional and translational levels. In contrast, both transcription and translation were fully activated under induction conditions.

17:05 Addressing Challenges for Production of Human Proteins and Multi-Protein Complexes Using the Baculovirus Expression System (BEVS)
Arnaud Poterzman, Research Director, Integrated Structural Biology, IGBMC/CNRS
We present here recent advances for the production of multi-subunit complexes in the baculovirus expression system using human multi-subunit transcription factors as model systems: Vector development for parallel expression/co-expression screening, use of Lambda red recombination in *E. coli* for manipulation and improvement of the baculoviral genome and assembly of multi-gene constructs from synthetic biology approaches. We will also discuss use of fluorescent proteins as infection makers and of baculovirus-infected insect cells (BIIC) for storage and standardization.

17:35 Sponsored Presentation *(Opportunity Available)*

18:20 Welcome Reception in the Exhibit Hall with Poster Viewing

19:20 End of Day One

TUESDAY, 4 NOVEMBER

07:30 Registration

07:45 Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

NOVEL STRATEGIES

08:30 Chairperson's Remarks

Andrias O'Reilley, Ph.D., Lecturer/Senior Lecturer, Natural Sciences and Psychology, Liverpool John Moores University

08:40 Higher Yield – An Ultimate Goal for Biological Product Development: A Case Study about Use of Process Intensification Technology for a Difficult to Express Glycoprotein

Mallika Singh, Ph.D., Associate Director, Upstream Development & Manufacturing, Teva Biopharmaceuticals USA, Inc.

The case study will show the use of an emerging technology (process intensification technology using Alternating Tangential Flow, ATF) which will perhaps be the direction of cell culture manufacturing process for biologics in near future.

09:10 Exploring Codon Optimisation Strategies for Production of Membrane Proteins

Morten Nørholm, Ph.D., Academic Entrepreneurial Research Group Leader, DTU Biosustain; Technical University of Denmark, Novo Nordisk Foundation Center for Biosustainability

Using a library of GFP-tagged membrane proteins, we have compared different codon optimisation strategies including synonymous mutations in the 5´end, complete re-coding using multiparameter optimisation algorithms and complementing rare codon usage with additional copies of the corresponding low-concentration tRNAs.

09:40 Chaperones Enable Native Folding of a Disulfide-rich Scorpion Toxin in the *E.coli* Periplasm

Andrias O'Reilley, Ph.D., Lecturer/Senior Lecturer, Natural Sciences and Psychology, Liverpool John Moores University

Animal neurotoxin peptides are valuable probes for studying ion channel pharmacology. Misfolding through formation of incorrect disulfide isomers has hindered recombinant toxin expression in *E.coli*. We report that co-secretion of a suite of protein disulphideisomerases and peptidyl-prolylcis/trans-isomerases into the *E.coli* periplasm boosts expression and produces correct folding of an insecticidal scorpion toxin, as validated by X-ray crystallography.

10:10 Coffee Break in the Exhibit Hall with Poster Viewing

10:50 A *S. cerevisiae*-Based High Yield Expression System for Efficient Purification of High Quality Human/Eukaryotic Membrane Proteins for Structural Studies

Per Armstrup Pedersen, Ph.D., Professor, Department of Biology, University of Copenhagen, Copenhagen, Denmark; Center for Microbial Biotechnology, Department of Systems Biology, Technical University of Denmark

We have managed to develop a *S. cerevisiae*-based platform with the capacity to deposit eukaryotic membrane proteins to a density of up till 8% of total membrane protein content and identified conditions that allow efficient purification of high quality eukaryotic membrane proteins. We believe that our expression platform is of relevance for any membrane protein as we have managed to express and purify, 7TM receptors, P-type ATPases, K-channels, amino acid/hexose transporters/tranceptors.

10:05 ESETEC® 2.0: A Powerful *E. coli* Secretion Technology for the High-Yield Production of Fabs

Sponsored by WACKER

Nicole Peuker, Ph.D., Scientific Specialist, Process Development, Wacker Biotech GmbH

WACKER BIOTECH is now introducing ESETEC® 2.0, an enhanced version of its *E. coli* based secretion technology. ESETEC® 2.0 combines a newly engineered host and optimized fermentation to produce even higher titers of secreted Fabs in several grams per liter, thus enabling the cost-convenient production of correctly assembled and bioactive antibody fragments.

11:50 Problem Solving Roundtable Discussions

Using Codon Optimisation to Facilitate Expression of Membrane Proteins

Moderator(s): Morton Nørholm, Ph.D., Academic Entrepreneurial Research Group Leader, DTU Biosustain; Technical University of Denmark, Novo Nordisk Foundation Center for Biosustainability

Recombinant Expression of Toxins and Peptides

Moderator: Jacques Dumas, Ph.D., Head, Protein Production Vitry, Biologics SCP, Vitry Research Center, sanofi

Overcoming Challenges in Protein Expression with Baculovirus

Moderator: Arnaud Poterzman, Research Director, Integrated Structural Biology, IGBMC/CNRS

12:50 Luncheon Presentation *(Sponsorship Opportunity Available)* or Lunch on Your Own

14:00 Dessert Break in the Exhibit Hall with Poster Viewing

MODULAR APPROACHES, CO-EXPRESSION AND PARTNERS

14:30 Chairperson's Remarks

Stefan Schmidt, Ph.D., Vice President, Downstream Processing, Rentschler Biotechnology

14:35 Modular Approaches to Express Complex Therapeutic Proteins

Stefan Schmidt, Ph.D., Vice President, Downstream Processing, Rentschler Biotechnology

Difficult to express proteins represent an increasing amount of therapeutic molecules. This causes bioprocessing challenges such as controlling glycosylation, increasing titers and yields, suppressing aggregation and purification without specific affinity resins. Here we demonstrate how to develop modular quasi-platform processes solving these issues. The case studies with examples from various molecule classes highlight successful process design, optimisation strategies and critical manufacturing parameters. Additionally practical advice will be given what to consider when designing a novel molecule.

15:05 Enhancing Protein Secretion of Clinically-Important Proteins

Tsafi Danieli, Ph.D., Head of Protein Expression Facility, Wolfson Centre for Applied Structural Biology, Alexander Silberman Institute of Life Sciences

The ability to improve recombinant protein secretion has significant biological and commercial benefits; Based on high throughput screening experiments, followed by bioinformatics analysis of protein databases of secreted vs. non-secreted proteins, we have developed an algorithm that can predict whether a protein will be poorly or efficiently secreted. We have tested our algorithm on several poorly secreted proteins, and found they all contained specific motifs that we predicted to impair translocation. We then demonstrated that disruption of these motifs by conserved replacement of a few amino acids resulted in a dramatic (up to 15 fold) enhancement of protein secretion in E.coli, insect cells and mammalian cells.

15:35 Heterologous Expression and Purification of an Active Human TRPV3 Ion Channel

Stefan Kol, Ph.D., Protein Biochemist, Novo Nordisk Foundation Centre for Biosustainability, Danish Technical University

In spite of great progress in the TRP-channel characterization, very little is known about their structure and interactions with other proteins at the atomic level. This is mainly caused by difficulties in obtaining functionally active samples of high homogeneity. I will present here the high-level Escherichia coli expression of the human TRPV3 channel, which retains its current inducing activity.

16:05 Sponsored Presentation *(Opportunity Available)*

16:35 Refreshment Break in the Exhibit Hall with Poster Viewing

STUDIES IN SUCCESS

17:15 Expression of Soluble and Active Interferon Consensus in SUMO Fusion Expression System in *E. coli*

Karolina Peciak, Ph.D., Senior Researcher, BioAnalysis, PolyTherics Ltd.

Here we describe the expression of soluble and active recombinant IFN-con in *E. coli*. The IFN-con gene sequence was optimised for expression in *E. coli*, which was then cloned into the Champion™ pET SUMO expression vector downstream of the SUMO fusion protein and under strong T7lac promoter allowed us to use a simple, two-step purification process to yield highly pure and active IFN-con which is more efficient than obtaining IFN-con from inclusion bodies.

17:45 A Technology for the Consistent Generation of Functional Antibody-Drug Candidates to Membrane Proteins

C. Davis Farmer, Jr., Chairman, MSM Protein Technologies

MSM Protein Technologies has developed proprietary methods for generating cell lines that over-express complex membrane proteins. We also have displays to present these proteins in their native conformation, highly purified for use in antibody discovery. To date we have generated fully human antibodies to several GPCRs that have met very stringent criteria as drug candidates. We will present an overview of the platforms and examples of antibodies that we have generated.

18:15 Expression of USP18 (UBP43) for Enzymatic and Structural Analysis using a Trigger Factor Fusion System in E.Coli and Baculovirus Expression

Klaus Peter Knobeloch, Ph.D., Head, Liebniz Institute for Molecular Pharmacology

Protein modification by ISG15 represents an interferon effector system counteracted by USP18. In mice, we selectively inactivated USP18 protease activity. Enhanced ISGylation increased resistance against influenza-virus infections qualifying USP18 inhibition as a potential antiviral strategy. Using a trigger factor fusion system in E.Coli and baculovirus expression we overcame poor USP18 expression yields, weak enzymatic activity and limited solubility, enabling us to perform inhibitor screens and solve the USP18/ISG15 complex crystal structure.

18:45 End of Difficult to Express Proteins

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SC4: Solving Problems in Eukaryotic Expression Systems

SC5: Analytical Strategies for Comparability in Bioprocess Development

*(*Separate Registration Required. Please see page 2 for more details.)*

WEDNESDAY, 5 NOVEMBER

07:45 Registration and Morning Coffee

NOVEL METHODS

08:30 Chairperson's Opening Remarks

Colin Harwood, Ph.D., Professor, Molecular Microbiology, University of Newcastle Upon Tyne

» 08:35 KEYNOTE PRESENTATION

Playing Catch-Up with Escherichia coli: Using Yeast to Increase Success Rates in Recombinant Protein Production Experiments

Roslyn M. Bill, Ph.D., Professor, School of Life and Health Sciences, Aston University Birmingham

This presentation highlights the benefits of using yeast for more challenging targets such as membrane proteins. We've seen advances in understanding how a yeast cell responds to the stress of producing a recombinant protein and how this information can be used to identify improved host strains in order to increase functional yields. I argue that *S. cerevisiae* and *P. pastoris* should be considered at an early stage in any serious strategy to produce proteins.

09:05 In Search of Expression Bottlenecks in Recombinant CHO Cell Lines: A Case Study

David Reinhart, Ph.D., Vienna Institute of BioTechnology, Department of Biotechnology, University of Natural Resources and Life Sciences

We applied several different techniques to investigate a previously generated cell line (4B3-IgA), which expressed recombinant immunoglobulin A (IgA) with an unusually low specific productivity. Results were compared to the host cell line and to another recombinant CHO cell line (3D6-IgA) expressing another IgA that binds to an overlapping epitope. Our studies suggest that the primary amino acid sequence and consequently the resulting structure of an expressed protein need to be considered as a factor influencing a cell's productivity.

09:35 Proteomic Analysis of Bacillus Subtilis Strains Engineered for Improved Production of Heterologous Proteins

Colin Harwood, Ph.D., Professor, Molecular Microbiology, University of Newcastle Upon Tyne

10:05 Scalable Electroporation for the Rapid Production of Complex and Difficult to Express Proteins

Sponsored by MaxCyte

Peer Heine, Ph.D., Field Application Scientist, MaxCyte, Inc.

Flow electroporation provides rapid, fully scalable transient (co)transfection. This universal technology is compatible with a range of cells including CHO, MDCK, BHK-21, Vero, NS0, CAP-T™, insect cells, and others used for large-scale production of proteins, including simple recombinant antigens, complex antibodies, antibody-like molecules, VLPs, and vaccines. High transfection efficiencies and cell viabilities enable production of gram quantities of antibodies within days of a single transfection. The ease of the scale-up/scale-down allows for aligning protein yields and resource usage with the stage of candidate development. Flow electroporation also can be used to generate stable pools and stable clones.

10:35 Coffee Break in the Exhibit Hall with Poster Viewing

11:15 Exploring the Protein Expression Space with pCoofy Vectors

Sabine Suppmann, Ph.D., Head, Recombinant Protein Production, Max-Planck Institute of Biochemistry

We previously reported the design of a "pCoofy" expression vector series that combines a variety of N- and C-terminal tags with a variety of backbones for several expression hosts. The parallel design allows to navigate easily between the systems in order to identify successful expression parameters. Cloning is based on SLIC plus ccdB counter selection. This presentation will highlight recent advances and new tools.

11:45 Periplasmic Chaperones Used to Enhance Functional Secretion of Proteins in *E. coli*

Martin Schlapschy, Ph.D., Lehrstuhl für Biologische Chemie, Technische Universität München

We have developed the helper plasmid pTUM4, which effects overexpression of four established periplasmic chaperones and/or folding catalysts: the thiol-disulfide oxidoreductases DsbA and DsbC, which catalyze the formation and isomerization of disulfide bridges, and two peptidyl-prolylcis/trans isomerases with chaperone activity, FkpA and SurA. We present a detailed protocol how to use this system for the bacterial secretion of recombinant proteins, including human EGF as a new example, and we give hints on optimisation of the expression procedure.

12:15 PURExpress®: A Next-Generation of Reconstituted Cell-Free Protein Synthesis System

Sponsored by kaneka GeneFrontier

Takashi Kanamori, Ph.D., Director, Business Development, GeneFrontier Corporation

PURExpress® is a reconstituted cell-free protein synthesis system which can provide highly pure proteins in a fast and easy way. We will present our recent developments regarding the increase of the productivity and also show our application to the expression of some difficult targets and Ribosome Display.

12:30 Corynex®: A Gram-Positive Microbial Protein Secretion System that Delivers Better Results

Sponsored by AJINOMOTO

Yoshimi Kikuchi, Ph.D., Principal Researcher, AJINOMOTO CO., Inc.

Corynex® is a powerful protein expression system based on the gram-positive bacteria *C. glutamicum* that can secrete various active proteins directly into media with high purity. These advantages enable less downstream time and costs compared to traditional methods. Our newly-developed enzymatic protein modification technologies will also be introduced.

12:45 Lunch on Your Own

SCALING UP WITH AN EYE TOWARDS THE CLINIC

14:00 Chairperson's Opening Remarks

Nicole Borth, Ph.D., Professor, Biotechnology, University of Natural Resources & Applied Life Sciences, Institute of Applied Microbiology

14:05 The Relevance of the Kinome on the Optimisation of a Human Production Cell Line

Andreas Wagner, Researcher, Institute for Applied Biotechnology, University of Applied Science Biberach

We identified genes and pathways of the kinome that are important for recombinant protein expression bioprocess performing a high-throughput screening. Using RNAi technology employing a novel transfection agent CAP®-SEAP cells were transfected in complex production media and evaluated for modulated proliferation, productivity and apoptosis. Inhibition of 128 relevant genes was further characterized using an antibody-producing CAP® cell line. Genetically engineered cell lines with enhanced phenotypically characteristics for a bioprocess were established.

14:35 Optimizing the Solubility of a Recalcitrant Protein for Structural Studies: Lessons from the Papillomavirus Oncoprotein E6

Gilles Trave, Ph.D., Group Leader, Ecole Supérieure de Biotechnologie de Strasbourg

The papillomavirus E6 oncoprotein is aggregation-prone and has resisted structural analysis for almost 30 years. Through the years, we analyzed the multiple causes of E6 aggregation and developed strategies against them, to finally obtain its 3D structure by NMR and crystallography (Zanier, Charbonnier et al., Science 2013). I will summarize the project's history and the lessons we learnt, notably about the use of solubilizing tags and of solubilizing mutations.

15:05 High-Throughput Cell Line and Process Optimisation of Mammalian Cell Culture Processes: About Small (50 ml) Tubes and Large Bioreactors

Maria De Jesus, Ph.D., COO, ExcellGene SA

Process and cell line optimisations will continue to be necessary requiring study of thousands of interacting parameters - a true dilemma. Small tubes as bioreactors have proven to be true predictors of cell line performance - even for large scale operation. My talk will indicate key insights and will show how multi-gram/l processes can be developed with minimal resources.

15:35 Refreshment Break in the Exhibit Hall with Poster Viewing

OVER-EXPRESSION AND HIGH DENSITY

16:15 The Impact of microRNA Expression on Growth and Productivity in CHO Cells

Nicole Borth, Ph.D., Department of Biotechnology, University of Natural Resources and Life Sciences, Vienna, Austria; Austrian Centre of Industrial Biotechnology GmBH

Overall biogenesis of miRNAs is dependent on growth rate and many miRNAs are differentially regulated depending on growth and productivity in a variety of CHO cell lines. Compared to other engineering strategies, the manipulation of miRNA expression does not burden the translational machinery of cells and provides the capability of global phenotypic control. The recent availability of genome sequence information has enhanced our ability to rapidly and efficiently optimise and fine-tune the properties of CHO cells.

16:45 Recombinant Production of Human Aquaporin-1 to an Exceptionally High Membrane Density in *Saccharomyces cerevisiae*

Julie Bomholt, MSc, Researcher, Aquaporin A/S

We explore the capacity of yeast *Saccharomyces cerevisiae* as host for heterologous expression of humanAquaporin-1.Aquaporin-1 cDNA was expressed from a galactose-inducible promoter situated on a plasmid with an adjustable copy number. Human Aquaporin-1 was C-terminally tagged with yeast enhanced GFP for quantification of functional expression, determination of sub-cellular localization, estimation of *in vivo* folding efficiency and establishment of a purification protocol.

17:15 Problem Solving Roundtable Discussions

MicroRNA Expression to Improve CHO Cell Expression

Moderator(s): Nicole Borth, Ph.D., Department of Biotechnology, University of Natural Resources and Life Sciences, Vienna, Austria; Austrian Centre of Industrial Biotechnology GmBH

Challenges for Determining and Improving Catalytic Activities of Therapeutic Enzymes

Moderator: Manfred Konrad, Ph.D., Head, Enzyme Biochemistry Research Group, Max-Planck-Institute for Biophysical Chemistry; Goettingen University Ph.D. Program Faculty Member

Issues with Transient Expression

Moderator: Peer Heine, Field Application Scientist, MaxCyte

18:15 Networking Reception in the Exhibit Hall with Poster Viewing

19:15 End of Day One

THURSDAY, 6 NOVEMBER

08:00 Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

NOVEL SOLUTIONS FOR CHALLENGING PROBLEMS

08:30 Chairperson's Remarks

Manfred Konrad, Ph.D., Head of Research, Enzyme Biochemistry, Max Planck Institute for Biophysical Chemistry

08:35 Nitrogen Catabolite Repressible GAP1 Promoter: A New Tool for Efficient Recombinant Protein Production in *S. cerevisiae*

Fabien Debailleul, Ph.D., Université Libre de Bruxelles

Our work shows that the nitrogen catabolite repressible GAP1 promoter can be used to obtain high levels of recombinant protein while allowing for large biomass production in *S. cerevisiae*. This approach can be used to express membrane and soluble proteins from higher eukaryotes (from yeast to human). Therefore, this system stands as a promising alternative to commonly used expression procedures in yeasts.

09:05 Solving Problems of Recombinant Production of Two Human L-asparaginases

Manfred Konrad, Ph.D., Head, Enzyme Biochemistry Research Group, Max-Planck-Institute for Biophysical Chemistry; Goettingen University Ph.D. Program Faculty Member

Asparaginases hydrolyzes L-asparagine in the blood, thus depriving leukemic cells from the external source of this natural amino acid. To replace therapeutically used bacterial enzymes, we pursue the design of human asparaginases. We developed a co-expression system to expose the catalytically critical threonine residue at the N-terminus of the b-subunit.

09:35 Protein Expression Screening in Mammalian Suspension Cells

Michael R. Dyson, Ph.D., Group Leader, IONTAS Ltd.

High throughput protein expression screening in mammalian suspension cells is an important step in the process of recombinant antibody selection and optimisation. This is both to select an optimal antigen expression construct and to screen IgG and Fab clones that can be expressed in high yield to provide antibodies for cell-based functional assays. Methods will be presented for high-throughput antibody expression in HEK293, CHO and stem cells including case studies for the selection of functionally active antibodies.

10:05 Sponsored Presentation *(Opportunity Available)*

10:35 Coffee Break in the Exhibit Hall with Poster Viewing

11:15 HTP Affinity-Based Identification and Ranking of the Human PDZ Domains Targeted by HPV E6 Oncoprotein

Coordinator of the IBiSA Structural Genomics Facility, Architecture et Fonction des Macromolécules Biologiques (AFMB), CNRS/Marseille University

Using our *E. coli* HTP protein production pipeline (Saez et al, jove 2014), we over-expressed most of the 266 human PDZ domains and analyzed their binding profile for the viral oncoprotein E6 using the holdup assay, a novel automated quantitative approach for HTP measurement of domain-peptide affinities. The protocols and results of this study will be exposed during the seminar.

11:45 Cell Line Engineering Using the Potential of microRNAs

Kerstin Otte, Ph.D., Professor, Pharmaceutical Biotechnology, University of Applied Sciences Biberach

miRNA technology is a highly innovative and novel engineering tool available to the optimise production cells. miRNAs are involved in virtually all cellular processes, and thus have recently gained much attention as valuable tools for cell engineering. The revelation of the CHO genome and transcriptome as well as the CHO miRnome substantially accelerated miRNA research in this industrially relevant cell type.

12:15 End of Optimizing Protein Expression

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THURSDAY, 6 NOVEMBER

12:30 Conference Registration

13:00 Dessert Break in the Exhibit Hall with Poster Viewing

CELL LINE DEVELOPMENT

13:30 Chairperson's Opening Remarks

» 13:35 KEYNOTE PRESENTATION

CHO Cells and Processes for Antibody Manufacturing: Convoluted History and Insights

Florian Wurm, Ph.D., Dr. rer. nat., Professor of Biotechnology, Swiss Federal Institute of Technology Lausanne (EPFL)

"Superstar" CHO are THE production system for therapeutic rec-proteins. Sequencing of one CHO cell genome (2013) has extended our knowledge established in the 1960s and 70s. What made CHO cells so popular? The talk will cover the "prehistory" of CHOs as well as key insights and key opportunities that have emerged during the 30 + year biotech history of these cells.

14:05 Studying Design Principles for Bispecific Antibodies: The H-L Pairing Challenge

Itai Benhar, Ph.D., Professor, Department of Molecular Microbiology and Biotechnology, Tel-Aviv University

We present a solution for the correct H-L chain pairing of bispecific IgGs: an engineered disulfide bond between the antibodies' variable domains. This approach termed disulfide stabilization, replaces the natural disulfide bond between the CH1 and CL domains. By combining Knobs into holes for heavy chains heterodimerization and disulfide stabilization for H-L chain pairing, we efficiently produced several bsAbs in bacteria and in mammalian cells.

14:35 Superior Protein Yields in CHO and HEK-293 Cells Using Novel, Highly Efficient Transfection Reagent

Sponsored by Polyplus transfection

Jelena Vjetrovic, Ph.D., Bioproduction Technical Support Specialist, Polyplus-transfection

Low transfection efficiency of CHO cells is a major bottleneck hampering protein production in Transient Gene Expression (TGE). With its 10+ year expertise in transfection, Polyplys-transfection will present superior results obtained in CHO and HEK-293 cells with its novel technically advanced reagent - FectoPRO.

14:50 Sponsored Presentation *(Opportunity Available)*

15:05 Refreshment Break in the Exhibit Hall with Poster Viewing

15:45 Antibody Membrane Switch (AMS) Technology for Facile Cell Line Development

Bo Yu, Ph.D., Co-Founder and CSO, Antibody Research, Larix Bioscience, LLC

Antibody Membrane Switch (AMS) technology is a novel, FACS-based cell line development technology. It utilizes a unique switch mechanism of alternative splicing and site-specific DNA recombinase to turn cells from expressing membrane-anchored antibodies into production cells secreting the antibody. Utilizing AMS technology can reduce cell line screening time from 6-8 months to 2-3 months.

16:15 Bispecific Antibodies in *E. coli*: It Takes Two to Tango

James Giulianotti, Ph.D., Senior Research Associate, Early Stage Cell Culture, Genentech

Bispecific antibodies (bisAbs) are being developed by companies in an attempt to address complex disease states. The production of bisAbs in *E. coli* requires the optimisation of a number of cellular processes within two distinct compartments (cytoplasm and periplasm) and across a single membrane. A number of technologies have been tested and implemented at Genentech that aid in the production of bisAbs in *E. coli*. This talk will discuss some of our recent work in this area.

16:45 Selection of Nanobodies That Neutralize the Binary Clostridium difficile Toxin CDT

Anna Marei Eichhoff, Immunology and Molecular Biology , University Medical Center, Hamburg-Eppendorf

17:15 End of Day One

17:15 Dinner Short Course Registration

17:30 – 20:30 Dinner Short Courses*

Recommended Short Courses*

SC4: Solving Problems in Eukaryotic Expression Systems

SC5: Analytical Strategies for Comparability in Bioprocess Development

*(*Separate Registration Required. Please see page 2 for more details.)*

FRIDAY, 7 NOVEMBER

08:00 Breakfast Presentation *(Sponsorship Opportunity Available)* **or Morning Coffee**

SEEING THE END FROM THE BEGINNING

08:30 Chairperson's Remarks

Raphael Levy, Ph.D., Senior Scientist, Preclinical Research and Development, XOMA Corp.

08:35 Application of Cell-Based Assays in Biologics Drug Discovery

Liz England, Scientist 1, Antibody Discovery and Protein Engineering, MedImmune

Cell-based assays can allow identification of therapeutics against complex targets that provide challenges in soluble protein expression such as GPCRs, ion channels and multimeric complexes. In addition therapeutics can be identified with multiple mechanisms of action and screening for function can lead to identification of the right epitope in a shorter time frame. For these reasons cell-based assays have been used extensively for High-Throughput Screening (HTS) within the pharmaceutical industry.

09:05 A Robust High-Throughput Platform to Generate Functional Recombinant Monoclonal Antibodies Using Rabbit B Cells from Peripheral Blood

Stefan Seeber, Ph.D., Principal Scientist, Cell Line and Molecule Development, Roche Pharma Research and Development (pRED)

We have developed a new two-step technology involving the isolation and cloning of single B cells from rabbit blood samples after immunization, screening of the B cell supernatants, followed by automated and high-fidelity B cell PCR of the antibody coding sequences. The antibodies are then directly sequenced and expressed or genetically engineered to create chimeric antibodies as well as bispecific antibodies, antibody fragments and other scaffolds. We will present an example of generating antibodies against a human interleukine receptor.

09:35 Problem Solving Roundtable Discussions

Fine Tuning Cell-Based Assays for Drug Discovery

Moderator: Liz England, Scientist 1, Antibody Discovery and Protein Engineering, MedImmune

Solving Bi-Specific Antibody Expression Problems in *E. coli*

Moderator: James Giulianotti, Ph.D., Senior Research Associate, Early Stage Cell Culture, Genentech

Using the Antibody Membrane Switch to Produce Better Production Cell Lines

Moderator: Bo Yu, Ph.D., Co-Founder and CSO, Antibody Research, Larix Bioscience, LLC

10:35 Coffee Break

11:00 Determinants and Impact of Antibody Aggregation on Production and Application

Joost Schymkowitz, Ph.D., Principal Investigator, VIB Switch Laboratory, KU Leuven

As most proteins, antibodies have a propensity to aggregate that is determined by their primary sequence and aggregation acts as a bottleneck on both production and application. Accurate prediction of antibody quality is currently lacking but would be of value to help identify good antibodies. I will discuss a number of key determinants and how to employ them for this purpose.

11:30 Improved Panning Output and Antibody Fragment Production by Co-Expression with the Peptidyl-Prolylisomerase, FkpA, in the Cytoplasm of Escherichia coli

Raphael Levy, Ph.D., Senior Scientist, Preclinical Research and Development, XOMA Corp.

Bacterial cytoplasmic expression of cytFkpA, a variant of peptidyl-prolylisomeraseFkpA, improved secretion of functional Fab fragments into the periplasm, exceeding the benefits of Fab co-expression with the native periplasmic FkpA. Panning and subsequent screening of large naïve phage antibody libraries in the presence of cytFkpA significantly increased the number of unique clones selected, their functional expression levels, and diversity.

12:00 High-Level Secretion of Recombinant Monomeric Murine and Human Single-Chain Fv Antibodies from Drosophila S2 Cells

Felix A. Rey, Ph.D., Head, Département de Virologie, Unité de Virologie Structurale, Institut Pasteur

We report here a system allowing for easy and efficient cloning of (i) scFvs selected by phage display and (ii) individual heavy and light chain sequences from hybridoma cDNA into expression plasmids engineered for secretion of the recombinant fragment produced in Drosophila S2 cells. The suitability of the produced recombinant fragments for structural studies was demonstrated by crystallization and structure determination of one of the produced scFvs, derived from a broadly neutralizing antibody against the major glycoprotein E2 of the hepatitis C virus.

12:30 Application of Label-Free Technology for Biologics Discovery

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Frances Neal, MSc, Scientist I, MedImmune, LLC.

ForteBio's Octet RED384 is a label free system that uses BioLayer Interferometry (BLI) to understand biomolecular interactions in real time. The Octet RED384 system can be applied to evaluate a number of key characteristics of protein interactions to aid biologics discovery. These include: antibody and antibody fragment quantification from crude and purified samples; competition assays for characterisation of receptor – ligand neutralising antibodies or distinguishing different epitopes; and kinetic screens for antibody affinity and antibody fragment off rate ranking. Here we present examples for these different biologics applications, demonstrating the versatility of this system, and its utility in the discovery of biologic therapeutics.

13:00 Luncheon Presentation (Sponsorship Opportunity Available) or Lunch on Your Own

CASE STUDIES IN SUCCESS

14:00 Chairperson's Remarks

14:05 Predicting the Expression of Recombinant Monoclonal Antibodies in Chinese Hamster Ovary Cells Based on Sequence Features of the CDR3 Domain

Leon P. Pybus, Ph.D., ChELSI Institute, Department of Chemical and Biological Engineering, University of Sheffield

We have developed a new computational tool that enables prediction of MAb titer in Chinese hamster ovary (CHO) cells based on the combinant coding sequence of the expressed MAb. Our data suggest that engineering intervention strategies to improve the expression of DTE recombinant products can be rationally implemented based on an identification of the sequence motifs that render a recombinant product DTE.

14:35 Expression of Single-Chain Variable Fragments Fused with the Fc-Region of Rabbit IgG in *Leishmania tarentolae*

Peter Kristensen, Ph.D., Associate Professor, Department of Engineering, Aarhus University

To our knowledge, this is the first time that antibody fragments with intact Fc-region of immunoglobulin have been produced in *L.tarentolae*. This system provides an alternative in cases where antibody constructs express poorly in standard prokaryotic systems. Furthermore, in cases where bivalent Fc-fused antibody constructs are needed, using *L. tarentolae* for expression provides an efficient alternative to mammalian expression.

15:05 T-Cell Dependent Bispecific Antibodies (TDBs)

Teemu Junttila, Ph.D., Antibody Engineering, Genentech, Inc.

TDBs are full-length IgG1 antibody molecules with a long half-life that are able to recruit T cells to selectively eliminate target-expressing tumour cells. TDBs exhibit robust preclinical activity in the treatment of pre-established tumours in immunocompetent transgenic mice. Our studies reveal a general resistance mechanism for T cell recruiting molecules with significant potential as a predictive diagnostic marker and demonstrated that direct polyclonal recruitment of T cell activity together with blockage of T cell inhibitory signaling results in enhanced and durable long-term responses.

15:35 Recombinant Barley-Produced Antibody for Detection and Immunoprecipitation of the Major Bovine Milk Allergen, β-Lactoglobulin

Anneli Ritala, Ph.D., Pharm., Docent, Principal Scientist, Project Manager, IPMA C, Plant Biotechnology, VTT Technical Research Centre of Finland

16:05 End of PEGS Europe

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MONDAY, 3 NOVEMBER
SC1: Engineering of Bispecific Antibodies
SC2: Mutation and Selection Strategies for Multi-Parameter Antibody Optimisation
~~SC3: Alternate Display Technologies~~
THURSDAY, 6 NOVEMBER
~~SC4: Analytical Strategies for Comparability in Bioprocess Development~~
SC5: Aggregation and Immunogenicity: How Do Formulation, Process and Delivery Influence Immunogenicity of Therapeutic Proteins?
SC6: Troubleshooting and Engineering of Antibody Constructs
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5-6 November	1B: Constructs & Scaffolds	2B: Aggregates & Particles	3B: Optimising Protein Expression
6-7 November	1C: Cancer Biotherapeutics	2C: Characterising Biotherapeutics	3C: Antibody Expression

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