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SAVE up to €300, Register by 30 September

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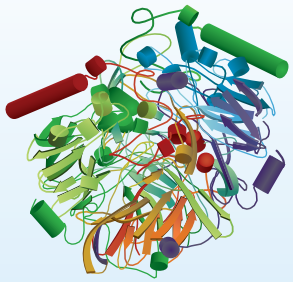
Final Agenda



Eighth Annual

PEGS EUROPE

Protein & Antibody Engineering Summit

31 October – 4 November 2016 | EPIC SANA Lisboa Hotel | Lisbon, Portugal

Plenary Keynotes

Paul Adam, Ph.D.,
Boehringer Ingelheim

Christian Klein, Ph.D.,
Roche Pharmaceutical Research and Early Development

Sandra S. Diebold, Ph.D.,
National Institute for Biological Standards and Control

- **Be part of a growing event - attendance has increased more than 60% since 2013**
- **Network with 700 colleagues from 30+ countries at Europe's largest protein engineering event**
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- Protein Expression Technologies
- Introduction to Protein Engineering

ENGINEERING
- Display of Antibodies
- Engineering Antibodies
- Engineering Bispecifics
- Engineering Next-Generation ADCs

THERAPEUTICS
- Novel Immunotherapy Strategies
- Advancing Bispecifics
- Novel Therapies for Cancer

ANALYTICAL
- Optimisation & Developability
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EXPRESSION
- Protein Expression Technologies
- Optimising Expression Platforms
- Protein Purification Technologies

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CONFERENCE-AT-A-GLANCE

	Monday - Tuesday 31 October - 1 November		Wednesday - Thursday (am) 2-3 November	Thursday (pm) - Friday 3-4 November
Cambridge Healthtech Training SEMINARS	Pre-Conference Short Courses*	TS1: Basic Technologies in a Core Protein Expression Lab TS2: Introduction to Protein Engineering		Dinner Short Courses*
ENGINEERING STREAM		1A: Display of Antibodies 4A: Engineering Next-Generation Antibody-Drug Conjugates	1B: Engineering Antibodies	1C: Engineering Bispecifics
THERAPEUTICS STREAM		2A: Novel Immunotherapy Strategies	2B: Advancing Bispecifics and Combination Therapy to the Clinic	2C: Novel Therapies for Cancer and Emerging Targets
ANALYTICAL STREAM		3A: Optimisation & Developability	3B: Analytical Characterisation of Biotherapeutics	3C: Protein Aggregates & Particles
EXPRESSION STREAM		TS1: Basic Technologies in a Core Protein Expression Lab	4B: Optimising Expression Platforms	4C: Protein Purification Technologies

** Separate registration required for short courses*

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- Rakesh D., Ph.D., Vice President, R&D, MedImmune

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Maximize your educational and networking opportunities by adding a short course.

MONDAY, 31 OCTOBER | 09:00 – 12:00

SC1: Cancer Immunotherapy

Fred Arce, Ph.D., University College London Cancer Institute
Andrea van Elsas, Ph.D., CSO, BioNovion B.V.

Distinct from other paradigms in medical oncology, cancer immunotherapy aims to treat the patient's immune system. During the past few years, antibodies targeting T cell checkpoint proteins have demonstrated unprecedented clinical responses and long-term benefit in patients diagnosed with melanoma and other advanced cancers. Beyond anti-PD-1 and anti-CTLA-4, other pathways and therapeutic agents are rapidly being translated to clinical practice alone or in combination approaches.

SC2: Mutation and Selection Strategies beyond Affinity Optimisation

Orla Cunningham, Ph.D., Associate Director, Global Biotherapeutic Technologies, Pfizer, Inc.
Matthew Lambert, Ph.D., Principal Scientist, Global Biotherapeutic Technologies, Pfizer, Inc.

This course will begin with an introduction to the multiple display technology platforms, mutagenesis strategies and library generation options that exist to enable antibody optimization. In the simplest application, generated libraries can be selected for improved antigen binding. However, increasingly these strategies are being used for more complex applications from humanization to ortholog cross-reactivity, stability, solubility and specificity optimizations. This workshop will use case studies to help attendees navigate the complex workflows and technological options available to ensure success.

SC3: Designing Antibodies for Function and Low Risk of Immunogenicity

George Octavian Badescu, Ph.D., Senior Director Scientific Affairs, Abzena plc
Maria Gonzalez-Pajuelo, Ph.D., Chief Scientific Officer, FairJourney Biologics
Matthew Baker, Ph.D., Chief Scientific Officer, Abzena plc

Increased knowledge of elements that contribute to enhancing the immunogenicity of protein therapeutics has enabled the development of a preclinical 'toolkit' that can be used to assess and mitigate against the risk of immunogenicity during the early stages of drug development. For antibody therapeutics a variety of *in silico*, *in vitro* and *in vivo* immunogenicity selection/testing technologies are available and these can be used at various stages during antibody development from discovery through to lead optimisation. This workshop will provide an introduction to antibody immunogenicity, assessment of the technologies available for lead selection, rational sequence design through engineering, and a look at how these tools can be integrated with optimising antibodies for desired function.

SC4: Transient Protein Expression: A Key Tool to Enable Rapid Protein Engineering

Richard Altman, MS, Scientist, Protein Technologies, Amgen, Inc.
Henry C. Chiou, Ph.D., Associate Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific
Dominic Esposito, Ph.D., Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research, Leidos Biomedical Research, Inc.

This short course introduces both the fundamental concepts and technologies needed to establish transient protein production in mammalian cells, which has become an essential tool to enable rapid protein engineering. Transient expression allows for the rapid generation, purification and characterization of milligram-to-gram quantities of secreted or intracellular recombinant proteins for therapeutic, functional and structural studies. The course combines instruction and case studies in an interactive environment.

THURSDAY, 3 NOVEMBER | 17:30 – 20:30 (DINNER)

SC5: Troubleshooting and Engineering of Antibody Constructs

Jonas Schaefer, Ph.D., Head, High-Throughput Binder Selection Facility, Biochemistry, University of Zurich
Julia Neugebauer, Ph.D., Associate Director, Leader Discovery Programs, MorphoSys AG

Recombinant antibodies vary widely in their biophysical characteristics. In particular, antibody variable domains differ in their intrinsic thermodynamic stability and may require labour-intensive engineering. It is essential to implement antibody engineering strategies in screening and initial characterisation project phases in order to avoid time and cost consuming optimisation strategies in later development. Moreover, it is critical to understand how poor stability of individual variable domains can limit the biophysical properties of small fragments, and also affect production yield, stability and homogeneity of full-length IgGs containing these domains.

SC6: Engineering of Bispecific Antibodies

Nicolas Fischer, Ph.D., Head, Research, Novimmune SA
Michaela Silacci, Ph.D., Director, Discovery Research, Covagen AG, part of J&J

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.

SC7: Protein Purification Strategies: Dealing with Proteins that Are Prone to Aggregate

Mario Lebendiker, Ph.D., Head, Protein Purification Facility, Wolfson Centre for Applied Structural Biology, Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem

This course will provide a comprehensive and detailed outline of hands-on issues for purifying proteins. We will first address general considerations about the protein we want to produce, including issues of activity, solubility, homogeneity, purity, and proper oligomeric conformation. Aggregation is one of the main obstacles in protein production, so we will look at how to monitor for aggregation and comprehend its mechanism. We will also discuss how to check for the optimal solubility conditions at the expression level, and our comprehensive approach for optimizing solubility during purification. We will also discuss expression screening methodology, environmental factors to consider during purification, families of additives, and screening for additives. Lastly, we will address ways to avoid aggregation, as well as setting up protein concentration and storage.

SC8: Protein Aggregation: Mechanism, Characterisation and Consequences

Thomas Laue, Ph.D., Professor, Molecular, Cellular & Biomedical Sciences, University of New Hampshire

Protein aggregation is recognized by regulatory agencies and industry as a key quality attribute of biotherapeutic products. Various aggregates hold the potential for adversely impacting production and patients. This in-depth workshop reviews origins and consequences of aggregation in biotherapeutics, and then examines strategies for predicting and quantifying it. It benefits scientists engaged in development, production, analytical characterization and approval of biotherapeutics and who require a good working knowledge of aggregation.

**** Separate Registration required***

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Introduction to Protein Engineering

Cambridge Healthtech Training SEMINARS
Comprehensive and Practical Training

Day 1: 31 October 13:40 – 18:25
Day 2: 1 November 08:30 – 18:45

Instructor:

David Bramhill, Ph.D.,
Founder, Bramhill Biological Consulting, LLC

CHI's Introduction to Protein Engineering training seminar offers a comprehensive tutorial in the concepts, strategies and tools of protein engineering – and explains the role of this discipline in the progression of biotherapeutic research and development. The class is directed at scientists new to the industry or working in support roles, academic scientists and career protein scientists wanting a detailed update on the current state of the field.

Today's wealth of knowledge of protein structures is reviewed, along with the genetics of diversity generation of antibodies, to give insights into the best strategies for improving protein function. There is particular emphasis on the selection of functional assays to monitor effectively the changes in desired properties.

Display technologies such as phage display and yeast display are described and the advantages and disadvantages of each compared. Design strategies are presented for constructing libraries of variant proteins for display, and panning strategies for enriching proteins with the desired properties considered.

The course details the engineering and enhancement of traditional antibodies and also cytokines, antibody fragments and emerging antibody-like scaffolds. Also included is a discussion of the roles of protein engineering in the discovery, design and development of new therapeutic modalities including antibody-drug conjugates (ADCs), bispecific antibodies and Chimeric Antigen Receptor (CAR) constructs.

This class will discuss the expression platforms used for producing proteins for testing and for manufacture, along with the rapidly emerging role of protein engineering in optimizing antibody and other protein therapeutics.

A background in biochemistry and molecular biology is useful, as the course is designed to progress rapidly from simple to advanced concepts. Links and references will be provided with the course materials to provide a glossary and other useful resources.

What is Protein Engineering?

- Functions amenable to engineering: Affinity, specificity, catalysis, stability, solubility, immunogenicity, serum half-life

Tools and Techniques

- The measure of success: Functional assays
- Engineering by design
- Engineering by random mutation
- Designed libraries
- Display technologies

Production and Manufacturing

- Evaluating biotherapeutic developability
- Improving manufacturing by protein engineering methods
- Glycosylation engineering – Function and homogeneity
- Other protein modifications
- Immunogenicity engineering
- Expression of antibodies and fragments for discovery and testing
- Manufacturing platforms for antibodies and fragment

Emerging Molecule and Product Formats

- Bispecific antibodies/binders
- Antibody-drug conjugates (ADCs)
- CAR T strategies
- Other emerging constructs

Each CHI Training Seminar offers 1.5 Days of instruction with start and stop times for each day shown above and on the Event-at-a-Glance published in the on-site Program & Event Guide. Training Seminars will include morning and afternoon refreshment breaks, as applicable, and lunch will be provided to all registered attendees on the full day of the class.

Each person registered specifically for the training seminar will be provided with a hard copy handbook for the seminar in which they are registered. A limited number of additional handbooks will be available for other delegates who wish to attend the seminar, but after these have been distributed no additional books will be available.

Though CHI encourages track hopping between conference programs, we ask that Training Seminars not be disturbed once they have begun. In the interest of maintaining the highest quality learning environment for Training Seminar attendees, and because Seminars are conducted differently than conference programming, we ask that attendees commit to attending the entire program, and NOT engaging in track hopping, as to not disturb the hands-on style instruction being offered to the other participants.

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3rd Annual

Display of Antibodies

Empowering Novel Biologics

Recommended Short Course*

SC2: Mutation and Selection Strategies beyond Affinity Optimisation

**Separate registration required, please see page 4 for details.*

MONDAY 31 OCTOBER

12:00 Registration

PLENARY KEYNOTE SESSION

13:40 Welcome from PEGS Europe Team

13:45 Chairperson's Opening Remarks

Ana Barbas, Ph.D., Coordinator, Bayer Satelite Laboratory at iBET, iBET and Bayer Portugal SA

13:50 Biotherapeutic Programs that Re-Direct Cytotoxic Lymphocytes to Cancer Cells

Paul Adam, Ph.D., Executive Director, Immune Modulation and Biotherapeutics Discovery, Boehringer Ingelheim

Cytotoxic lymphocytes such as NK and T cells have the capability to control cancer development and progression. Harnessing this cytotoxic potential with biotherapeutic agents is predicted to become a future pillar of cancer therapy in light of recent clinical successes. This presentation will describe novel biotherapeutics whose mode of action involves the engagement and re-direction of NK and T cells to hematological tumors.

14:30 Antibody-Based Combination Cancer Immunotherapy at Roche pRED

Christian Klein, Ph.D., Distinguished Scientist, Head, Oncology Programs, Cancer Immunotherapy Discovery, Roche Pharmaceutical Research and Early Development, Roche Innovation Center Zurich

This presentation will introduce novel antibody cancer immunotherapies developed at Roche pRED including novel IL2 variant immunocytokines and T cell bispecifics as well as preclinical data for their optimal combination and scheduling.

15:10 Safety Concerns Associated with Immunotherapy and Novel Biotherapeutics and Challenges in Investigating Their Immunotoxicity

Sandra S. Diebold, Ph.D., Principal Scientist, Immunotoxicology, Biotherapeutics, National Institute for Biological Standards and Control (NIBSC)

The pre-clinical assessment of the risks associated with immunotherapy and novel biotherapeutics is challenging since the bioassays have to be individually tailored to the investigated reagent. The immunotoxic activity and adverse responses that may be observed in patients are depending to a large degree on the mechanism of action of the biotherapeutic. The specific set-up of *in vitro* assays plus the identification of suitable animal models is critical for obtaining predictive pre-clinical data.

15:50 Refreshment Break in the Exhibit Hall with Poster Viewing

USING DISPLAY TO ADVANCE IMMUNOTHERAPY

16:50 Chairperson's Remarks

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

16:55 FEATURED PRESENTATION: Optimisation of Chimeric Antigen Receptors for T Cell Cancer Therapy

Martin Pule, Ph.D., Clinical Senior Lecturer, University College London

17:25 Combinatorial Display in Development of T Cell Vaccines

Andrew Sewell, Ph.D., Professor, Division of Infection and Immunity, Cardiff University School of Medicine

Several uses of combinatorial display will be described including: (1) Quantification of extremely high levels of T-cell cross-reactivity, (2) Definition of causal epitopes/pathogens during autoimmune disease, (3) Generation of optimal epitopes for given T-cell clonotypes, (4) Ligand discovery for dominant 'orphan' T-cell clones following successful tumour-infiltrating lymphocyte therapy for malignant melanoma and, (5) Generation of acid and protease stable non-biologic T-cell ligands that can be orally administered. These exciting studies are providing new ubiquitous targets for cancer vaccination and open up the possibility of oral vaccination and/or induction of tolerance.

17:55 Development and Validation of llamdA, a Synthetic Domain Antibody Library

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Guy Hermans, Ph.D., CSO, Isogenica Ltd.

llamdA is a synthetic library design based on natural camelid antibody repertoire analysis, manufactured to the highest fidelity standards using Isogenica's COLIBRA library synthesis technology. The use of CIS cell-free display technology allows for the selection of libraries with orders of magnitude greater diversity than competing technologies. We will discuss various validation studies where a high diversity of low single digit nanomolar binders could be rapidly isolated to different therapeutically relevant targets.

18:25 Welcome Reception in the Exhibit Hall with Poster Viewing

19:25 End of Day

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TUESDAY 1 NOVEMBER

07:45 Registration and Morning Coffee

USING DISPLAY TO ADVANCE IMMUNOTHERAPY (CONT.)

08:30 Chairperson's Remarks
Kerry Chester, Ph.D., Professor, Molecular Medicine, University College London Cancer Institute

08:40 How Display and Signaling of CAR Molecules Can Be Used to Redirect the Specificity of Human T Cells
Hinrich Abken, Ph.D., Professor, Genetics & Immunology, Center for Molecular Medicine Cologne, University of Cologne
Adoptive therapy with engineered T-cells with an antigen-specific chimeric antigen receptor (CAR) is achieving impressive efficacy in early phase trials, in particular in hematologic malignancies, strongly supporting the notion that the immune system can control cancer. Such CAR T-cells can substantially reduce the tumor burden as long as the targeted antigen is present on the cancer cells and recognized by the antibody domain of the CAR.

09:10 Inclusion of Strep-Tag II in Design of Antigen Receptors
Stanley R. Riddell, M.D., Professor, Immunology & Clinical Research, Fred Hutchinson Cancer Institute

09:40 Problem-Solving Breakout Discussions*
**See website for details.*

10:40 Coffee Break in the Exhibit Hall with Poster Viewing

ANTIBODIES TO GPCRs AND ION CHANNELS

11:15 Chairperson's Remarks
John McCafferty, Ph.D., Co-Founder, Director and CEO, IONTAS Ltd

11:20 Using Stabilised Receptors as Antigens to Generate Therapeutic Antibodies to GPCRs
Catherine Hutchings, Ph.D., Consultant, Antibody Alliance Management & Strategic Partnering, Heptares Therapeutics Ltd.
Stabilized receptors offer a breakthrough solution to the central challenge of reliably making pharmacologically active antibodies against GPCRs. They enable the production of purified, properly folded and functional protein when removed from the cell membrane for use as an antigen. This presentation provides several examples that provide important validation of this solution, including data from our MorphoSys and AstraZeneca collaborations, demonstrating that StaR antigens preserve biologically relevant epitopes. This enables the generation of diverse panels of functional antibodies directed to this important target class for use as therapeutics.

11:50 Pathological Autoantibodies to Ion Channels
Angela C. Vincent, Ph.D., Emeritus Professor of Neuroimmunology, Nuffield Department of Clinical Neurosciences, University of Oxford
For many years it was thought that the blood brain barrier prevented antibodies or B cells reaching the brain. Over the last 15 years it has become very clear that they can. The talk will show how many rare but treatable diseases of the nervous system are associated with autoantibodies to neuronal proteins, and emphasise the importance of testing for binding to extracellular domains on native proteins, or of establishing quicker and cheaper methods for routine testing and searching for new antibodies.

12:20Deeper Profiling of Antibodies During High Throughput Antibody Discovery
Niccolo Pengo, Ph.D., Senior Scientist, UCB-Celltech

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12:35 Protein-Protein Docking with Sequential Coarse-Grained Minimization
Nels Thorsteinson, MSc, Scientific Services Manager, Biologics, Chemical Computing Group

Sponsored by CHEMICAL COMPUTING GROUP

Protein-protein docking is an important tool for predicting affinity, optimizing properties and exploring druggable sites. This work presents a novel protein docking method for predicting protein-protein binding. The output protein poses are shown to produce high-quality structures. The applicability of the docking program to antibody optimization will also be discussed.

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

13:20 Session Break

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

COMPETITIVE TECHNOLOGIES FOR IMMUNOTHERAPY AGAINST MAJOR AUTOIMMUNE DISEASE

14:30 Chairperson's Remarks
Ahuva Nissim, Ph.D., Reader, Molecular Targeting, Biochemical Pharmacology, William Harvey Research Institute, Queen Mary University of London

14:35 DIPIC: Di-Iodotyrosinated Peptide Imaging of Cartil
Ngee Han Lim, Ph.D., Research Fellow, Kennedy Institute of Rheumatology, University of Oxford
The insensitive nature of X-ray based imaging techniques precludes the use of antibodies to obtain targeted radiocontrast agent which can serve as imaging biomarkers for diseases such as osteoarthritis. In a generalisable method for other targeting peptides, the peptide identified by phage display to target the type II collagen present in cartilage was modified to carry out preclinical *in vivo* DIPIC using micro-computed tomography (micro-CT). The ease and speed of this modification should spark a renaissance in the development of contrast agents based on peptides for the widely used CT imaging modality.

15:05 Overview on the Current Antibody Treatment of Multiple Sclerosis
David Baker, Ph.D., Professor, Neuroimmonology, Centre for Neuroscience and Trauma, Blizard Institute, Barts and the London School of Medicine and Dentistry
Multiple sclerosis is a putative autoimmune disease of the central nervous system that is characterised pathologically by inflammation, demyelination and variable degrees of axonal loss. Numerous immunomodulatory therapies have been licensed, or are in late stage development, to treat multiple sclerosis including several monoclonal antibodies. Dissecting out the mode of action of the targeted monoclonal antibodies is providing interesting insights into the pathogenesis of MS.

15:35 Targeted-Cytokines for the Treatment of Rheumatoid Arthritis
Mattia Matasci, Ph.D., Head, Cell Line Development, Philochem
Antibody-cytokine fusion proteins (immunocytokines) are being mainly developed for cancer therapy applications. However, certain immuno-

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modulatory cytokine payloads can also be considered for the treatment of patients with chronic inflammatory conditions. I will present work of the Philogen group, in collaboration with the Swiss Federal Institute of Technology (ETH Zürich), which has led to the development of potent immunocytokines for the treatment of rheumatoid arthritis.

15:50 Targeting Therapeutic and Regenerative Biomedicine Specifically to Arthritic Joints

Ahuva Nissim, Ph.D., Reader, Molecular Targeting, Biochemical Pharmacology, William Harvey Research Institute, Queen Mary University of London

We developed a panel of human scFv that bind specifically to collagen type II post-translationally modified by oxidants which: binds specifically to arthritic cartilage from patients with RA and OA or from murine models of inflammatory arthritis and OA, localises and target payload drug in the arthritic joints in a mouse model of arthritis (inflammatory and OA). Our development will have a significant impact on treatment of arthritic conditions.

16:05 F-star: Advancing Novel Bispecific Antibody Biologics using the iQue Screener Platform

Frederick Akele, Senior Research Associate, F-star Biotechnology Ltd

F-star develops novel bispecific antibodies (called mAb2) based on a unique modular approach. Using this cutting-edge technology, F-star is building a product pipeline focused on immuno-oncology. This talk will highlight the pivotal role the iQue Screener played in increasing the screening throughput of Fcab (antigen-binding Fc domain) candidates against several antigens.

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

ANTIBODY GENERATION

17:10 Chairperson's Remarks

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

17:15 CDR-Restricted Engineering beyond Affinity Maturation

Orla Cunningham, Ph.D., Director GBT, Pfizer

CDR mutagenesis has been used successfully for many years across multiple display platforms for antibody affinity maturation. However, approaches to other aspects of antibody engineering, such as humanization, stability and solubility, tend to maintain the CDR loops and their interaction with antigen as sacrosanct. This talk will use a number of case studies to demonstrate that CDR-restricted engineering can be used for multi-parameter optimization with the benefit of maintaining 100% germline framework content.

17:45 Nanobodies as a Versatile and Clinically Validated Drug Platform

Antonin de Fougerolles, Ph.D., CSO, Ablynx

An outline of the Nanobody®platform and clinical experience will be presented. The flexibility of Nanobody formatting is used to create differentiated drugs, and examples of mono-specific and multi-specific Nanobody drugs will be shared.

18:15 Toward Single Cell Proteome Analysis Using Phage Display of Recombinant Antibodies

Peter Kristensen, Ph.D., Associate Professor, Molecular Engineering, Aarhus University

In recent years the importance of cellular heterogeneity has become increasingly clear. In developing therapies for important diseases, such as cancer, the ability to isolate and characterize rare cell populations will be important. We have advanced the phage display technology, thus allowing the isolation of specific antibodies binding to one or few identified cells in a heterogeneous mixture such as blood or a tissue section.

18:45 End of Display Of Antibodies

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Engineering Antibodies

Inspiring Next-Generation Biologics Discovery and Development

Recommended Short Course*

SC5: Troubleshooting and Engineering of Antibody Constructs
**Separate registration required, please see page 4 for details*

WEDNESDAY 2 NOVEMBER

07:45 Registration and Morning Coffee

TECHNOLOGIES AND STRATEGIES TO IMPROVE TARGETING AND BIOACTIVITY OF THERAPEUTICS

08:30 Chairperson's Remarks
Claudio Sustmann, Ph.D., Head, Molecular Design & Engineering, Large Molecule Research, Roche Diagnostics GmbH

08:35 KEYNOTE PRESENTATION:
Using Nanobody Bi-Specifics to Improve the Targeting of Therapeutics
Antonin de Fougerolles, Ph.D., CSO, Ablynx
This presentation will provide an outline of the Nanobody® platform and will illustrate the flexibility of Nanobody formatting to rapidly make multi-specific drugs. Examples of multi-specific Nanobody drugs that improve targeting of therapeutics will be presented.

09:20 Protease-Activated Antibody Derivatives - Engineered bsAbs with Prodrug-Like Functionality
Ulrich Brinkmann, Ph.D., Expert Scientist, Large Molecule Research, Roche Pharma Research & Early Development
Bispecific and engineered antibody derivatives have been generated in a multitude of formats. Many of these are in preclinical stages for a variety of applications, some in clinical development, and a few are approved. The presentation will provide an overview of the concepts and status of engineered bispecific antibodies at Roche and cover novel formats and applications including bispecific antibody derivatives with prodrug-like functionalities.

09:50 Characterizing and Optimizing Glycostructures by Targeted Cell Engineering
Claus Kristensen, Ph.D., Associate Professor, Copenhagen Center for Glycomics, University of Copenhagen
Using targeted gene editing of mammalian cells we modify sugars on glycoproteins. The technology involves knock-out and/or knock-in of glycogenes to modify cellular glycosylation pathways and generate arrays of different glycans on glycoproteins produced by the cell. Application includes glycooptimization of biologics for improving bioactivity and/or obtain more homogeneous product.

Sponsored by ABZENA Enabling better biopharmaceuticals

10:20 A Deimmunised Form of the Ribotoxin, α-sarcin, Lacking CD4+ T Cell Epitopes and Its use as an Immunotoxin Warhead
Rob Holgate, Ph.D., Head, Protein Engineering, Abzena
Fungal ribotoxins that block protein synthesis are useful warheads. Peptide mapping using an ex-vivo human T cell assay determined that α-sarcin contained two T cell epitopes. Mutations within each epitope were designed, tested and combined to isolate deimmunised α-sarcin variants with the desired properties of silencing T cell epitopes whilst retaining the ability to inhibit protein synthesis. The results represent the first fully deimmunised fungal ribotoxin.

10:50 Coffee Break in the Exhibit Hall with Poster Viewing

11:30 Highly Efficient Elimination of High Concentration Soluble Antigen from Plasma by Novel Sweeping Antibody Technology
Meiri Shida-Kawazoe, Ph.D., Research Scientist, Biologics Discovery, Chugai Pharmaceutical Co., Ltd.
In this presentation, we will introduce novel sweeping antibody technology that enables highly efficient elimination of soluble antigen from plasma. The novel technology has been applied to various antigens, which are present at high concentration in plasma and therefore difficult to target by conventional antibodies, and we will show that these antibodies can efficiently eliminate various soluble antigens from plasma in cynomolgus monkey.

12:00 Antibody Engineering in Drug Discovery & Development at Roche
Claudio Sustmann, Ph.D., Head, Molecular Design & Engineering, Large Molecule Research, Roche Diagnostics GmbH
Bispecific antibodies are an important drug class in oncology but also beyond. Identification of the best candidates for a certain application is a challenging task. These aspects as well as selected examples of Roche development candidates will be the focus of the presentation. In particular, application of the IgG-like bispecific CrossMab technology in different disease areas will be addressed.

Sponsored by GYROS

12:30 Rapid Affinity Measurements Using Gyrolab Immunoassay Platform
Johan Engström, Senior Scientist, Research & Development, Gyros AB
Real-time, surface-based analytical methods often have difficulty in analyzing the slow dissociation kinetics associated with high-affinity KD's. Gyrolab systems enable rapid determination of KD's down to low picomolar levels. This will be illustrated with the KD determination for three TNF-α antagonists and the active binding concentration of the antagonists.

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12:45 Antibody Protein *De Novo* Sequencing with LC-MS/MS

Sponsored by RAPID NOVOR

Mingjie Xie, MSc, MBA, Co-Founder, CEO, Rapid Novor Inc

Many applications in antibody engineering require the direct sequencing of antibody proteins. At Rapid Novor (rapidnovor.com) we have developed a robust workflow and routinely sequenced antibody proteins. Here we share the success experiences, examine common mistakes novices make, and present our practices to ensure the correctness of every amino acid.

13:00 Talk Title to be Announced

Sponsored by PALL Life Sciences / fortéBIO

Marie Gagnaire, Research Scientist, Protein Biochemistry, Biologics Research, Sanofi

13:30 Session Break

ANTIBODY DISCOVERY FOR EMERGING AND CHALLENGING TARGETS

14:00 Chairperson's Remarks

Claus Kristensen, Ph.D., Associate Professor, Copenhagen Center for Glycomics, University of Copenhagen

14:05 Efficient Mining of the Natural Antibody Repertoire – Finding Rare Molecules with Desirable Characteristics

Dale Starkie, BSc., Research Scientist, Antibody Discovery, UCB Celltech

UCB's core antibody discovery technology combines high throughput B cell culture screening and a proprietary technique called the "fluorescent foci method" to identify and isolate single, antigen-specific, IgG-secreting B cells from which variable region genes are isolated and cloned. The talk will describe case studies on the application of the platform to a number of antibody projects.

14:35 Discovering Antibodies to a Moving Target

Elizabeth England, Scientist I, Antibody Discovery and Protein Engineering, MedImmune Ltd.

MedImmune has shown that IL-33 forms disulphide bonds, resulting in large conformational changes. This occurs rapidly, posing a challenge in identifying antibodies that inhibit the action of IL-33. Through innovative use of mutant forms of IL-33 and appropriate design of screening campaigns, a highly potent inhibitor of IL-33 was identified, a testament to how understanding of target structure and biology is key to the identification of potential therapeutic drug candidates.

15:05 Antibodies Targeting Peptide/HLA Complexes for Cancer Therapy

Julia Neugebauer, Ph.D., Associate Director/Leader, Discovery Programs, Morphosys AG

Tumor-specific peptide / HLA complexes make intracellular targets accessible to antibodies. However, the generation of therapeutic antibodies, which recognize a particular peptide / HLA complex specifically, is highly challenging. By identifying and applying appropriate counter-targets we generated fully human, high affinity antibodies against a WT1 peptide / HLA complex. These antibodies bind to target-positive cancer cell lines and outperform similar state-of-the-art antibodies regarding target specificity and binding affinity.

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

16:15 Strategies to Identify High Potency Therapeutic Antibodies for Multi-TM Targets

Peter Ertl, Ph.D., Manager, Biopharm Molecular Discovery, GlaxoSmithKline

Cellular targets such as G-protein coupled receptors (GPCRs) are typically very challenging for therapeutic antibody discovery due to their complex nature and limited antigen availability. This presentation will describe the strategies implemented by GSK to successfully identify high potency neutralising antibodies for such targets, using both *in vitro* antibody presentation technologies and *in vivo* immunisation approaches.

16:45 Integration of High Throughput Omic's Platforms into Antibody Discovery

John Castle, Ph.D., Senior Director, Bioinformatics, Agenus & 4-Antibody

In pursuit of lead structures, omic technologies are revolutionizing the discovery and development of novel biological lead structures. However, omic platforms are first and foremost data generation instruments that require careful integration into workflows. Here, we demonstrate how we have applied next-generation sequencing, big data, biostatistics, and computational immunology to the discovery and development of novel antibody lead structures.

17:15 Problem-Solving Breakout Discussions*

**See website for details.*

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

19:15 End of Day

THURSDAY 3 NOVEMBER

08:00 Registration and Morning Coffee

COMPUTATIONAL AND *IN SILICO* DESIGN AND ENGINEERING

08:30 Chairperson's Remarks

David Melvin, Ph.D., Director, Informatics, Kymab Limited

08:35 Engineering Protein-Protein Interactions *in silico*: Lessons from the Affibody Scaffold

Samuel Coulbourn Flores, Ph.D., Group Leader, Structural Bioinformatics and Computational Structural Biology, Uppsala Universitet

Altering protein-protein interface properties is key to biologic design, but experimental directed evolution introduces many mutations, leading to immunogenicity and off-target effects. We have created an *in silico* method which predicts single mutations with a clear mechanism, to modify charge and binding properties and remove functionalization sites. We engineer properties of the Affibody – IgG interaction. I briefly discuss how to apply this to important oncology and autoimmune disease targets.

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09:05 Beyond Binding: How to Design Biologically Active, Developable Antibodies against Difficult Targets

Yanay Ofran, Ph.D., Founder & CEO, Biolojic Design; Head, Lab of Systems Biology and Funcional Genomics, Bar Ilan University

It is fairly straightforward to obtain antibodies that specifically bind almost any protein. However, further screenings and analyses typically reveal that most of these binders are not biologically active or not developable. This is because existing methods for antibody engineering select for binding, while drug development requires function and developability. We show how computational design and *in vitro* evolution can be combined to design developable antibodies with specific, predefined function.

09:35 Rational Design of Antibody Solubility and Complementarity Determining Regions

Pietro Sormanni, Ph.D., Researcher, Chemistry, Centre for Misfolding Diseases, University of Cambridge

I will present a computational strategy for the design of soluble binding proteins as well as experimental validations and applications. I will introduce the CamSol method of designing protein variants with improved solubility, and a method for the *de novo* design of protein-protein interactions, which we used to design domain antibodies and molecular-chaperones binding to linear epitopes and able to inhibit the disease-related aggregation of their target proteins.

10:05 Engineering Next-Generation Biotherapeutics: Developability & Manufacturability

Maria Wendt, Ph.D., Head, Science, Biologics, Genedata

Next-generation biotherapeutics, specifically bi- and multi-specifics, alternative scaffolds, and ADCs, provide significant advantages over traditional IgG-based molecules. However, as highly engineered molecules they pose new design, cloning, expression, purification, and analytics challenges. Our workflow platform automates engineering, production, and testing of large panels of these candidate therapeutic molecules. We demonstrate the platform's capability to explore the huge combinatorial space of novel molecule-specific designs, its high-throughput capability, and its built-in tools for developability and manufacturability assessments.

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

HIGH THROUGHPUT SCREENING AND SELECTION

11:15 High-Throughput Screening of Monoclonal Antibodies to Multiplexed Antigens

Benjamin Hoffstrom, Ph.D., Director, Antibody Technology, Fred Hutch Cancer Research Center

We have a high-throughput platform for simultaneous screening of monoclonal antibodies to 5 different antigens. The target identification assay is 25-50 times more sensitive than traditional ELISA-based screens, which allows for rapid ranking of several thousand antibodies based on target affinity and isotype. We have validated the platform for modified peptide targets, small molecules, recombinant proteins, and cell surface receptors. A general overview of the workflow will be outlined and specific projects will be highlighted.

11:45 Advances in Kymab's Fully Integrated, B-Cell Repertoire Analysis and Hit Selection Capabilities

David Melvin, Ph.D., Director, Informatics, Kymab Limited

Kymab have developed an advanced technology to visualise and deeply explore the Kymouse™ antibody repertoire. We can identify candidate-quality molecules with exceptionally broad diversity and with the quality of fully human antibodies. Our platform allows rapid, detailed and efficient exploration of the B-cell response to immunisation as well as informing and supporting decision making process throughout our discovery program. We will present our work with the Bill and Melinda Gates foundation.

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12:15 Luncheon Presentation: Generating More Relevant Data: High Titer Antibody Production in a Range of Host Cells using Scalable Electroporation

Payal Roychoudhury, Ph.D., Field Applications Scientist, EU, MaxCyte, Inc.

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

13:30 End of Engineering Antibodies

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8th Annual

Engineering Bispecifics

New Approaches and Platform Refinements

Recommended Short Course*

SC2: Mutation and Selection Strategies beyond Affinity Optimisation

**Separate registration required. Please see page 4 for details.*

THURSDAY 3 NOVEMBER

12:30 Registration

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

NEW MODES OF ACTION / T CELL ENGAGEMENT

13:30 Chairperson's Opening Remarks

Christoph Spiess, Ph.D., Senior Scientist, Antibody Engineering, Genentech, Inc.

13:35 KEYNOTE PRESENTATION:
Protein Engineering for New Modes of Action

Andreas Plückthun, Ph.D., Director and Professor, Biochemistry, University of Zurich

The engineering of very robust binding proteins gives new opportunities for achieving novel modes of action of biotherapeutics. These can exploit a very strict control of receptor geometries, the opportunity to attack intracellular targets and the opportunity to engineer cell-specific virus entry. The basis for these development is a reliable engine to generate high-affinity specific binding proteins.

14:20 Pfizer's T Cell Engaging Full Length Bispecific Antibody Platform: From Bench to NHS

Javier Chaparro-Riggers, Ph.D., Senior Director, Protein Engineering, Rinat Pfizer, Inc.

The recent clinical success of blinatumomab (anti-CD19/CD3) spurred the development of a variety of T cell engaging bispecific antibody architectures. Pfizer developed a T cell engaging antibody platform, which allows the formation of full length human IgG1 and IgG2 antibodies *in vitro* or *in vivo*. The effect of IgG isotype and affinities of the T cell- and tumor antigen-targeting arm were explored and optimized.

14:50 Computational Approaches in Antibody Design: Identifying and Reducing Liabilities early in the Discovery Process

David Pearlman, Ph.D., Senior Principle Scientist, Schrödinger

Computational tools that can be used in the optimization process for antibody drug candidates have greatly improved in the past. These tools are finding increasing acceptance for liability assessment and reduction in the discovery process. We describe how these calculations can be utilized for workflowed triage among multiple candidates, and how tools such as FEP are used to suggest sequence engineering that can ameliorate identified liabilities such as aggregation propensity while maintaining affinity and stability.

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15:20 Refreshment Break in the Exhibit Hall with Poster Viewing

ENGINEERING BISPECIFICS FOR T CELL ENGAGEMENT

16:05 Engineering of CD3 Bispecific FynomAbs

Julian Bertschinger, Ph.D., Vice President, Janssen R&D, Managing Director, Covagen

I will describe the development of bispecific FynomAbs by fusing human Fynomer binding proteins to antibodies, resulting in bispecific protein therapeutics with novel modes-of-action and enhanced efficacy for the treatment of inflammatory diseases and cancer. We will present case studies demonstrating that FynomAbs with tailored architecture overcome limitations encountered with other therapeutic protein formats, such as suboptimal efficacy of lack of tumour selectivity.

16:35 High Affinity T Cell Receptor-Based Bifunctional Biologics for Redirected Tumour Killing

Milos Aleksic, Ph.D., Team Lead, Protein Engineering, Immunocore

ImmTACs are bispecific reagents that target tumours via a soluble monoclonal TCR with exceptionally high sensitivity and specificity and redirect host polyclonal T cells via an anti-CD3 antibody fragment. The selection and validation of appropriate target antigens and the testing of ImmTACs for specificity is critical. Using appropriate tumour and primary human cell lines, the *in vitro* pre-clinical package can be predictive of *in vivo* clinical observations.

17:05 End of Day

17:00 Dinner Short Course Registration

Recommended Dinner Short Course*

SC6: Engineering of Bispecific Antibodies

**Separate registration required. Please see page 4 for details.*

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FRIDAY 4 NOVEMBER

08:00 Registration and Morning Coffee

FOCUS ON BISPECIFIC ENGINEERING FOR TARGETING

08:30 Chairperson's Remarks

Ulrich Brinkmann, Ph.D., Expert Scientist, Roche Innovation Center

08:35 Epitopes Matter: Strategies to Generate and Analyse Binders to Different Epitopes

Jonas Schaefer, Ph.D., Head, High-Throughput Binder Selection Facility, Biochemistry, University of Zurich

Several characteristics determine the true value and potential of affinity reagents for most applications. However, while amongst other the lead candidate's affinity can be matured after it has been identified, scientists still are not able to routinely and reliably design these binders for specific epitopes. Thus, special considerations have to be taken into consideration both in the selection and screening processes, which will be presented in this presentation.

09:05 Engineered Fab Domains Promote Efficient Production of Bispecific Antibodies in a Single Cell

Christoph Spiess, Ph.D., Senior Scientist, Antibody Engineering, Genentech, Inc.

Bispecific antibodies have gained increased relevance in research and therapeutic settings despite the complexities in their production and challenges in finding the right combination. The presentation will discuss strategies and consideration to screen for the best bispecific antibody pair. In addition, a novel approach to produce a bispecific antibody with natural surface architecture in a single cell will be discussed. The technology now simplifies bispecific production for research and development.

09:35 A Novel Highly Versatile Multi-Specific Antibody Format

Sebastian Meyer, Ph.D., VP, Protein Engineering & CMC, Numab

We present the MATCH, a novel modular antibody format that utilises a pair of split variable domains to drive defined assembly of heterodimeric complexes with up to six specificities. This architecture offers the unique advantage of rapidly screening permutations of binder panels to identify ideal combinations of affinities, potencies and specificities in the final molecular format. This format offers unprecedented opportunities for fine-tuning binding properties for targeting complex pathologies.

10:05 Coffee Break in the Foyer with Poster Viewing

PLATFORM DEVELOPMENT AND REFINEMENT

10:35 CrossMAb Version 2: A Versatile Toolbox for Bispecific Antibody Engineering

Joerg Thomas Regula, Ph.D., Head, Functional Characterisation, Large Molecule Research, Roche Pharmaceutical Research and Early Development

The CrossMAb technology (Schäfer et al., 2011) can be used to generate a bispecific antibody from two independent parental antibodies by immunoglobulin domain exchange. Additional modifications can be introduced in these different CrossMAb designs. This enables their use as well suited building blocks for the generation of bispecific antibodies with 1+1, 2+1 or 2+2 target binding sites.

11:05 Efficient Generation of Bispecific Mouse Antibodies for Preclinical Investigations

Aran F. Labrijn, Ph.D., Principal Scientist, Antibody Sciences, Genmab BV

Complex therapeutic concepts are often studied using (surrogate) mouse antibodies in immunocompetent mice to ensure optimal interaction with tumour associated immune cells and the microenvironment. We recently described controlled Fab-arm exchange (cFAE) as a versatile and robust method for the generation of therapeutic human IgG1 bispecific antibodies (bsAb). To facilitate the study of dual-targeting concepts in immunocompetent mice, we have now applied and optimised our method for the efficient generation of murine bsAbs.

11:35 Platform Refinements for Bispecifics for Oncology Targets

John de Kruif, Ph.D., CTO, Merus

12:05 Achieving Optimal Bispecific Antibodies Assembly by Codon De-Optimization

Nicolas Fischer, Ph.D., Head, Research, Novimmune SA

Bispecific antibodies often rely on the co-expression of three or more chains and maximal bispecific antibody production is achieved when their expression is relatively balanced. We have investigated different approaches to control and balance the relative expression levels of light chains and the effect on assembly of native bispecific antibodies. We found that codon de-optimization - instead of optimization - of an over expressed chain led to significant increase in yield. This approach to tune the ratio of different polypeptides can be applied to improve assembly of other protein complexes.

12:35 Problem-Solving Breakout Discussions with a Light Snack in the Foyer*

**See website for more details.*

13:35 Session Break

NOVEL APPROACHES

14:00 Chairperson's Remarks

Joseph Dukes, Ph.D., Head, Pre-Clinical Biology, Cell Biology, Immunocore

14:05 Using Alphabodies to Generate Bispecifics with Optimal *in vitro* and *in vivo* Characteristics

Yvonne McGrath, Ph.D., CSO, Complix NV

CMPX-1023 is an Alphabody that has been engineered to bind the p19 chain of IL-23, a cytokine of therapeutic importance in autoimmune disease. By fusing CMPX-1023 to different anti-TNFα antibodies at various positions, we have generated a panel of therapeutic bispecific proteins. CMC characteristics, *in vitro* potencies and *in vivo* pharmacokinetics of this panel of bispecifics will be presented.

14:35 Hapten-Bispecific Antibodies for Drug Discovery and Delivery Applications

Ulrich Brinkmann, Ph.D., Expert Scientist, Roche Innovation Center

Many bispecific and engineered antibody derivatives are in preclinical stages for a variety of applications, some in clinical development, and a few are approved. The presentation will provide an overview of the concepts and status of engineered bispecific antibodies at Roche with a focus on novel formats and bsAb-applications for discovery applications. This includes the

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application of Hapten-binding antibody derivatives for delivery of payloads to, into, as well as across tissues and cells.

15:05 Cellular FRET Assay for the Determination of Simultaneous Binding of Bispecific Antibodies

Stefan Seeber, Ph.D., Principal Scientist, Cell Line and Molecule Development, Roche Innovation Center Munich/Large Molecule Research

To demonstrate simultaneous binding to two cell surface expressed receptor targets, we developed a robust, one-vial, FRET-based system, allowing for parallel testing of 2 independent pathways (not necessarily cross-talking). We engineered cell lines expressing the two receptors with FRET tags inserted proximal to the cell membrane. Possible applications as a screening tool or potency assay will be discussed.

15:35 Novel Strategy for a Bispecific Antibody: Induction of Dual Target Internalisation and Degradation

Ji Min Lee, Ph.D., Principal Scientist, Open Innovation Team, Samsung Bioepis

Cancers show well aligned multifaceted properties, and there is cross-talk and convergence of signaling pathways of RTKs. Consequently, many therapeutic interventions have been actively developed to overcome inherent or acquired resistance. To date, no BsAb have shown complete depletion of dual RTKs from the plasma membrane and efficient dual degradation. Leveraging the anti-Met mAb, we generated the BsAbs for Met/EGFR and Met/HER2 to induce an efficient EGFR or HER2 internalisation and degradation.

16:05 Engineering and Manufacturing of Bispecific Antibodies for T-Cell Redirection

Stanislas Blein, Ph.D., Senior Director, Antibody Engineering, Glenmark Pharmaceuticals

Over the past two decades various functional bispecific antibody formats have been designed with only few molecules reaching clinical trials due to an inherent lack of manufacturability. Herein we describe a versatile bispecific antibody format that fits industrial-scale manufacturing processes and enables the rapid design and making of T-cell redirecting molecules. Engineering, preclinical and phase-one manufacturing data will be presented.

16:35 End of Conference

"As in past years, PEGS Europe again proved to be a stimulating conference with distinguished speakers from both industry and academia, covering the hot topics of the field. A great source of food for thought"

- Jonas S., Ph.D., Head, High-Throughput Binder Selection Facility, Department of Biochemistry, University of Zurich

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Engineering Next-Generation Antibody-Drug Conjugates

Into the Clinic and Beyond

Recommended Short Course*

SC3: Designing Antibodies for Function and Low Risk of Immunogenicity

**Separate registration required, please see page 4 for details.*

MONDAY 31 OCTOBER

12:00 Registration

PLENARY KEYNOTE SESSION

13:40 Welcome from PEGS Europe Team

13:45 Chairperson's Opening Remarks

Ana Barbas, Ph.D., Coordinator, Bayer Satelite Laboratory at iBET, iBET and Bayer Portugal SA

13:50 Biotherapeutic Programs that Re-Direct Cytotoxic Lymphocytes to Cancer Cells

Paul Adam, Ph.D., Executive Director, Immune Modulation and Biotherapeutics Discovery, Boehringer Ingelheim

Cytotoxic lymphocytes such as NK and T cells have the capability to control cancer development and progression. Harnessing this cytotoxic potential with biotherapeutic agents is predicted to become a future pillar of cancer therapy in light of recent clinical successes. This presentation will describe novel biotherapeutics whose mode of action involves the engagement and re-direction of NK and T cells to hematological tumors.

14:30 Antibody-Based Combination Cancer Immunotherapy at Roche pRED

Christian Klein, Ph.D., Distinguished Scientist, Head, Oncology Programs, Cancer Immunotherapy Discovery, Roche Pharmaceutical Research and Early Development, Roche Innovation Center Zurich

This presentation will introduce novel antibody cancer immunotherapies developed at Roche pRED including novel IL2 variant immunocytokines and T cell bispecifics as well as preclinical data for their optimal combination and scheduling.

15:10 Safety Concerns Associated with Immunotherapy and Novel Biotherapeutics and Challenges in Investigating Their Immunotoxicity

Sandra S. Diebold, Ph.D., Principal Scientist, Immunotoxicology, Biotherapeutics, National Institute for Biological Standards and Control (NIBSC)

The pre-clinical assessment of the risks associated with immunotherapy and novel biotherapeutics is challenging since the bioassays have to be individually tailored to the investigated reagent. The immunotoxic activity and adverse responses that may be observed in patients are depending to a large degree on the mechanism of action of the biotherapeutic. The specific set-up of *in vitro* assays plus the identification of suitable animal models is critical for obtaining predictive pre-clinical data.

15:50 Refreshment Break in the Exhibit Hall with Poster Viewing

DEVELOPING EFFICACIOUS ADCs

16:50 Chairperson's Remarks

Jens Lohrmann, Ph.D., Senior Global Program Manager, Translational Clinical Oncology, Novartis Institutes for BioMedical Research

16:55 Chemical Pharmacology of Protein Conjugates

Gonçalo J.L. Bernardes, Ph.D., Principal Investigator, Chemistry, University of Cambridge

Our work centers on reaction engineering for site-selective chemical protein modification to provide insight into biology and for the development of protein therapeutics. This lecture addresses recent research in: (i) site-selective chemical modification of proteins and antibodies at cysteine and lysine, and (ii) the development of CO-releasing artificial metalloproteins that are able to deliver CO in a targeted and controlled manner to tumor tissues leading to potent CO-mediated immunomodulation.

17:25 Platform Technologies for Homogeneous and Versatile Full Antibody and Antibody Fragment Modification

Vijay Chudasama, Ph.D., Lecturer, Chemistry, University College London

There is clear demand for the construction of novel antibody-drug conjugate (ADC) platforms that offer greater stability, homogeneity and flexibility. A significant step towards the ideal platform for next generation antibody-based therapeutics is presented. Our technology provides decorated antibody constructs that are highly stable, with complete retention of antibody binding/structure post-modification. It combines site-specific functionalisation with exceptional versatility via the functional re-bridging of interchain disulfide bonds native to antibodies.

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17:55 POSTER SPOTLIGHT:

Antibody-Drug Conjugates Screening Platform for Selection of Novel Biologics at the National Research Council of Canada
Maria Jaramillo, Ph.D., Senior Research Officer & Project Leader, Primary Assays, Biotechnology Research Institute, National Research Council Canada

18:25 Welcome Reception in the Exhibit Hall with Poster Viewing

19:25 End of Day

TUESDAY 1 NOVEMBER

07:45 Registration and Morning Coffee

FULFILLING THE PROMISE OF ADCs

08:30 Chairperson's Remarks
João Tomé, Ph.D., Associate Professor, Chemical Engineering, Instituto Superior Técnico, University of Lisbon

08:40 KEYNOTE PRESENTATION:
Advancement in Antibody Drug Conjugates: A Step Closer to Creating Magic Bullets against Deadly Cancers
Rakesh Dixit, Ph.D., DABT, Vice President, Research & Development, and Global Head, Biologics Safety Assessment, Medimmune (A member of AstraZeneca Group)

- Discuss 5 Rights (target, antibody, linker, warhead and translational strategy) of ADCs
- How to improve and maximize the therapeutic effectiveness of ADCs
- Case studies of a biparatopic ADC for highly resistant low Her2 expressing cancers
- Recent developments in PBD-based ADCs
- Personalized biomarkers-dependent clinical ADC development

09:10 Design, Synthesis and Scale-Up of an ADC Tubulysin Payload
Jeremy S. Parker, Ph.D., Principal Scientist, New Modalities & Tissue Targeting, AstraZeneca
AstraZeneca has designed, synthesized, and manufactured a novel Tubulysin payload that has been successfully used in the production of MedImmune's Biparatopic HER2-Targeting Antibody Drug Conjugate which is currently in Phase I clinical trials.

09:40 Problem-Solving Breakout Discussions*
**See website for details.*

10:40 Coffee Break in the Exhibit Hall with Poster Viewing

SITE-SPECIFIC TECHNOLOGY

11:20 Challenge ADC Therapeutic Index with TG-IPH Site-Specific Technology
Florence Lhospice, Director, Pharmaceutical Operations, Innate Pharma
Here, we describe the *in vitro* and *in vivo* characterization of four novel ADCs that are based on the anti-CD30 antibody cAC10, which has the same polypeptide backbone as ADCETRIS®, and compare the results with the latter. Overall, the results suggest that homogenous ADCs display improved pharmacokinetics and better therapeutic indexes compared to chemically modified ADCs with variable DARs. Of note, equivalent results were confirmed with a panel of drugs and targets as per our current collaborations and our own programs.

11:50 Tub-Tag Labeling – A Novel Chemoenzymatic Approach for the Generation of Site-Specific ADCs
Jonas Helma, Ph.D., Project Group Leader, Biology II, Ludwig-Maximilians University Ludwig-Maximilians Universität
A novel chemoenzymatic approach for simple and fast site-specific antibody conjugation is presented. We repurposed tubulin tyrosine ligase (TTL) to attach various unnatural tyrosine derivatives as small bioorthogonal handles to nanobodies and recombinant antibodies containing a short tubulin-derived recognition sequence (Tub-tag). This novel strategy enables a broad range of chemoselective C-terminal antibody modifications. We foresee a wide field of potential applications throughout the life sciences, including next-generation Antibody-Drug Conjugates.

12:20 Sponsored Presentation *(Opportunity Available)*

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

13:20 Session Break

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

ADVANCING CONJUGATION CHEMISTRY

14:30 Chairperson's Remarks
Jeremy S. Parker, Ph.D., Principal Scientist, New Modalities & Tissue Targeting, AstraZeneca

14:35 Enhancing the Therapeutic Index of ADCs by Conjugation through Glycans with Improved Linkers
Floris Van Delft, Ph.D., Founder & CSO, SynAffix BV
The globally conserved N-glycan provides a superior, natural anchor point for antibody conjugation. By applying a two-stage process involving enzymatic glycan remodeling, and copper-free click attachment of cytotoxic payload, antibody-drug conjugates (ADCs) can be readily prepared from any mAb without protein reengineering. Conjugation of highly hydrophobic payloads is facilitated by applying a short and polar spacer technology, leading to ADCs with improved therapeutic index by increasing *in vivo* efficacy and tolerability.

15:05 Advances in Bio-Orthogonal and Bio-Specific Bond-Forming Reactions for Improved Antibody-Based Conjugates
Alain Wagner, Ph.D., Research Director, Functional ChemosSystem, Strasbourg University and CNRS
The recent development in the fields of bio therapeutics and chemical biology has shed light on the limitations of current bioconjugation and bio-de-conjugation reactions in terms of bio-stability bio-selectivity and biocompatibility. The presentation will focus on some methodological approaches we have implemented to discover novel efficient molecular systems to link and release bioactive compounds and biomolecules.

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15:35 Photo-Immunoconjugates for Targeted Cancer Photodynamic Therapy

João Tomé, Ph.D., Associate Professor, Chemical Engineering, Instituto Superior Técnico, University of Lisbon

The recent development of photo-immunoconjugates as photosensitizers (PSs, photoactive drugs) to target cancer cells open new perspectives for cancer photodynamic therapy (PDT). In this talk, some of our recent work on the synthesis of PSs and PS-antibody conjugates will be shown, as well as highlighting their biological potential against human bladder cancer cell lines.

16:05 POSTER SPOTLIGHT: Abdurin-Drug Conjugates: A New Generation of Targeted Therapeutics

Silvia Peretti, Ph.D., Biochemistry, IRBM Science Park S.p.A.16:35 Refreshment Break in the Exhibit Hall with Poster Viewing

INNOVATING ADC DESIGNS AND PROCESSES

17:15 Novel Linker Chemistries for Antibody-Drug Conjugates

Thomas Pillow, Ph.D., Senior Scientist, Discovery Chemistry, Genentech, a member of the Roche Group

This presentation will focus on our development of a novel disulfide linker where we demonstrate for the first time the ability to decouple stability and release. This linker takes advantage of new sites on cysteine-engineered antibodies that stabilizes both the linker and the payload from metabolism. When applied to PBDs, the disulfide-linked ADC has an improved therapeutic index compared to a peptide-linked ADC.

17:45 Small is Beautiful – Humabodies Drug Conjugates, HDCs a Real Alternative to ADCs

Normann Goodwin, Ph.D., Senior Scientist, Preclinical Development, Crescendo Biologics, Ltd.

Humabodies enable plug and play engineering allowing simple exploration of limitless format options. HDCs demonstrate exceptionally fast tumor penetration. Half-life can be tailored facilitating low systemic and high tumor exposure. Different format of HDCs show high-impact on potency both *in vitro* and *in vivo*. Therefore the versatility of the Humabody™ format enables creation of optimal HDC format and half-life with improved Therapeutic Index.

18:15 Challenges & Lessons Learned in ADC CMC Development & Outsourcing

Jens Lohrmann, Ph.D., Senior Global Program Manager, Translational Clinical Oncology, Novartis Institutes for BioMedical Research

A key decision for achieving stable ADCs is whether to "buy or make" these highly active compounds. Leveraging the know-how of CMOs can be powerful; however, to ensure an effective relationship, communication is key. Technical challenges of site-transfers, especially with concomitant scale-up are to be expected. Case studies will be presented to discuss impact of conjugation process on key product quality attributes, as well as lessons learned from analytical transfers.

18:45 End of Engineering Next-Generation Antibody-Drug Conjugates

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Novel Immunotherapy Strategies

Exciting Developments with Promise in the Clinic

Recommended Short Course*

SC1: Cancer Immunotherapy
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MONDAY 31 OCTOBER

12:00 Registration

PLENARY KEYNOTE SESSION

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13:45 Chairperson's Opening Remarks
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Cytotoxic lymphocytes such as NK and T cells have the capability to control cancer development and progression. Harnessing this cytotoxic potential with biotherapeutic agents is predicted to become a future pillar of cancer therapy in light of recent clinical successes. This presentation will describe novel biotherapeutics whose mode of action involves the engagement and re-direction of NK and T cells to hematological tumors.

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Christian Klein, Ph.D., Distinguished Scientist, Head, Oncology Programs, Cancer Immunotherapy Discovery, Roche Pharmaceutical Research and Early Development, Roche Innovation Center Zurich
This presentation will introduce novel antibody cancer immunotherapies developed at Roche pRED including novel IL2 variant immunocytokines and T cell bispecifics as well as preclinical data for their optimal combination and scheduling.

15:10 Safety Concerns Associated with Immunotherapy and Novel Biotherapeutics and Challenges in Investigating Their Immunotoxicity

Sandra S. Diebold, Ph.D., Principal Scientist, Immunotoxicology, Biotherapeutics, National Institute for Biological Standards and Control (NIBSC)
The pre-clinical assessment of the risks associated with immunotherapy and novel biotherapeutics is challenging since the bioassays have to be individually tailored to the investigated reagent. The immunotoxic activity and adverse responses that may be observed in patients are depending to a large degree on the mechanism of action of the biotherapeutic. The specific set-up of *in vitro* assays plus the identification of suitable animal models is critical for obtaining predictive pre-clinical data.

15:50 Refreshment Break in the Exhibit Hall with Poster Viewing

KEYNOTE PRESENTATIONS

16:50 Chairperson's Remarks
Marie Kosco-Vilbois, Ph.D., CSO, Novimmune SA

16:55 Immunotherapy "From the Inside"
Stefan Dübel, Ph.D., Managing Director, Biochemistry, Biotechnology and Bioinformatics, Technische Universität Braunschweig
We present approaches for inhibition of cell surface receptors or signalling pathways by novel strategies "from the inside". We will inspire the biologics engineering community to start thinking out of the box by opening doors to targets which so far could not be reached inside the cell, and to add extra punch or extra safety to biologics by targeting a combination of two disease specific features.

17:25 Clinical Development of Adoptive T-Cell Therapy in Melanoma and Beyond
Rienk Offringa, Ph.D., Head, Molecular Oncology of Gastrointestinal Tumours, German Cancer Research Centre
Adoptive transfer of tumour-infiltrating T cells has shown striking efficacy in patients with metastatic melanoma, even in late stage patients. T cells targeting neo-epitopes encoded by the tumour mutanome play a dominant role in this respect. Based on this insight, adoptive T-cell therapy can now be further optimised and developed for the treatment of other cancer indications.

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17:55 Quantitative Cell-Based Bioassays for Analysis of mAb Fc Effector and Immune Checkpoint Functions
Gopal Krishnan, Ph.D., Global Product Manager, Cellular Analysis & Proteomics, Promega
Immunotherapy is a promising therapeutic strategy to better fight cancer. We have developed many reporter bioassays for immune checkpoint, co-stimulatory and immunomodulatory receptors including combination bioassays (e.g., PD-1+TIGIT). The assays can quantitatively determine the potencies of candidate antibody drugs or ligand proteins and are valuable tools for antibody screening.

18:10 Sponsored Presentation *(Opportunity Available)*

18:25 Welcome Reception in the Exhibit Hall with Poster Viewing

19:25 End of Day

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TUESDAY 1 NOVEMBER

07:45 Registration and Morning Coffee

IMMUNE CHECKPOINT INHIBITORS

08:30 Chairperson's Remarks

Saar Gill, M.D., Ph.D., Assistant Professor, Medicine, Hematology- Oncology, University of Pennsylvania School of Medicine

08:40 Targeting Immune Regulation at the Tumour Site: Mechanistic Insights on Immune Modulatory Antibodies

Frederick Arce Vargas, Ph.D., Haematology, University College London Cancer Institute

By studying the mechanism of action of anti-CLTA-4 therapy in murine models, we have learned that the effectiveness of immune modulatory antibodies depends on the antibody isotype and not only on blocking or activating the signalling through their targets. Furthermore, a systematic characterisation of the immunological landscape of human cancers has provided more insight on how to translate findings in murine models into clinical application in a rational way.

09:10 Targeted Protein Therapeutics – Alone and in Combination with Immunotherapy

Gregory P. Adams, Ph.D., Chief Development Officer, Viventia Bio

TPTs mediate direct tumour killing and offer the ability to activate anti-tumour immunity. In early phase clinical studies, intra-tumoural injection of Proxinium mediated impressive effects directly on injected tumours and indirectly on uninjected tumours, suggesting the generation of an anti-tumour immune response. Clinical trial results and preclinical studies will be presented both examining the mechanisms underlying the indirect anti-tumour effect and evaluating the potential of combining Proxinium with checkpoint inhibitors.

09:40 Problem-Solving Breakout Discussions*

**See website for details.*

10:40 Coffee Break in the Exhibit Hall with Poster Viewing

PRECLINICAL AND CLINICAL DEVELOPMENTS

11:20 Therapeutic Targeting of B7-H3 in Solid Tumours through Immune Enhanced Abs and DART Molecules

Paul Moore, Ph.D., Vice President, Cell Biology and Immunology, MacroGenics, Inc.

Complementary strategies targeting B7-H3, a B7-family member expressed on solid tumours, are undergoing clinical development. Enoblituzumab, an Fc-enhanced humanized anti-B7H3 mAb, exhibits favorable safety with preliminary evidence of activity and T-cell modulation, supporting further development as monotherapy and combination with checkpoint inhibitors. To leverage the tumor lytic activity of T cells and drive their expansion, we have also developed MGD009, an Fc-bearing B7-H3xCD3 DART molecule, currently in Phase 1 testing.

11:50 FEATURED PRESENTATION: CAR T Cell Immunotherapy Approaches in the Clinic

Renier J. Brentjens, M.D., Ph.D., Director, Cellular Therapeutics, Memorial Sloan-Kettering Cancer

While chimeric antigen receptor (CAR) approaches have resulted in significant clinical benefit with some CD19-B cell malignancies, far more modest outcomes are seen in patients treated with chronic lymphocytic leukemia (CLL). I will present next generation CAR T cell approaches that directly target and kill tumour cells, modulate and overcome the immunosuppressive tumour microenvironment and recruit endogenous anti-tumour immune effector cells to avoid tumour immune escape.

12:20 Cancer Biotherapeutics - Affimers: A Novel Scaffold for Biotherapeutics

Sponsored by Avacta LIFE SCIENCES

Amrik Basran, Ph.D., CSO, Therapeutics, Avacta Life Sciences

Affimers® are a new protein scaffold with great potential for the generation of biotherapeutics. Based on the protease inhibitor Stefin A, large diverse libraries have been created by engineering in peptide loops into the scaffold backbone. Using phage display, we have identified competitive binders to a ranage of targets, including the immune check point, PD-L1. We have shown that the scaffold is amenable to being engineered with a range of half-life extension technologies.

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

13:20 Session Break

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

DEVELOPMENTS WITH CHIMERIC ANTIGEN RECEPTOR-T CELL THERAPY

14:30 Chairperson's Remarks

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

14:35 Clinical Advances in CAR T Cell Therapy with a Focus on Anti-CD19 CARs

Saar Gill, M.D, Ph.D., Assistant Professor, Medicine, Hematology- Oncology, University of Pennsylvania School of Medicine

Currently more than 70 clinical trials using CAR T cells, most of them targeting CD19, are open worldwide. Patients with B-cell malignancies are the first beneficiaries of an exciting and potent new treatment that harnesses the power of the immune system as never before. These patients represent the vanguard of enormous preclinical efforts to develop CAR T therapy into a procedure that hopefully will one day be routine and curative.

15:05 Tumour Models to Investigate CAR T Cell Potency, and Acute and Chronic Toxicity

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

Reports of objective clinical responses and tumour regression in patients receiving Chimeric Antigen Receptor (CAR) -T cell therapy are driving a major surge of interest in the field. CARs are artificial targeting proteins that exploit antibody-based approaches to re-direct the effector function of the T cell to

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virtually any cell surface target. However, it remains unclear whether toxicity resulting from over-activity of the T cell or lack of suitable target specificity is likely to be an issue. Models can provide some answer to this although the relevance of such models remains open to question.

15:35 ErbB-Targeted CAR T cell Immunotherapy of Cancer

Daniela Achkova, Ph.D., Research Associate, Research Oncology, King's College London

We have developed a CAR-based T4 immunotherapy approach targeting 8 of 9 possible ErbB homo- and heterodimers. Efficacy has been demonstrated in established xenograft models of head and neck, ovarian, breast cancer and mesothelioma *in vivo*. Although this immunotherapy also recognises mouse ErbB receptors, toxicity does not occur following intra-tumoural administration. To exploit this, we have initiated a Phase I trial of T4 immunotherapy in patients with locally advanced/ recurrent squamous cell cancer of the head and neck.

16:05 Panel Discussion on Pros and Cons of the Different Approaches: CAR-Ts, Modified TCRs and TILs

Kerry Chester, Ph.D., Professor, UCL Cancer Institute

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

TCR TARGETS/ROLE OF B CELLS/CYTOKINES

17:15 Taking SPEAR T Cells to the Clinic – From TCR Target Selection to Clinical Manufacture

Jo Brewer, Ph.D., Director, Cell Research, Adaptimmune

SPEAR (Specific Peptide Enhanced Affinity Receptor) T-cell therapy, using engineered T-cell receptors (TCRs), is showing clear promise in sarcoma and multiple myeloma trials targeting NY-ESO. Trials are now open with other TCRs: MAGE A10 & AFP – and there will be more to come. I will discuss the lifecycle of a SPEAR T-cell product from target selection, TCR identification and optimization, preclinical safety testing and manufacturing to make a robust, clinical product suitable for commercial use.

17:45 B Cells and Antibody Responses in Solid Tumours

Sophia N. Karagiannis, Ph.D., Senior Lecturer, Translational Cancer Immunology, Head, Cancer Antibody Discovery and Immunotherapy, St. John's Institute of Dermatology, Division of Genetics and Molecular Medicine, King's College London

The nature and contribution of circulating and tumour-infiltrating B cells and the antibodies they produce remain largely unexplored. We report active B-cell immune surveillance and mature memory B cells with distinct immunoglobulin isotype-biased profiles in melanoma. We provide evidence in support of monitoring the humoral immune compartment in cancer to provide new prognostic tools and to inform therapeutic antibody design.

18:15 Bi- and Tri-Functional Antibody-Cytokine Fusion Proteins for Cancer Immunotherapy

Dafne Mueller, Ph.D., Group Leader, Cell Biology and Immunology, University of Stuttgart

IL-15 and costimulatory members of the B7 and TNF superfamily have shown great potential to support the generation and development of an anti-tumour immune response. In order to improve the efficacy of such molecules at the tumour site we designed bi- and tri-functional antibody-fusion proteins, focusing on targeted presentation and combined mode of action of diverse immunomodulatory molecules, demonstrating enhanced immune responsiveness *in vitro* and anti-tumour activity in a mouse model *in vivo*.

18:45 End of Novel Immunotherapy Strategies

> "Once more, PEGS Europe was an outstanding event with great science and a perfect setting for networking. Very nice combination of topics and speakers."
>
> - PHILIPP M., PH.D., PROJECT LEADER, BIOMEDICINE, UNIVERSITY HOSPITAL OF BASEL

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8th Annual

Advancing Bispecifics and Combination Therapy to the Clinic

Including New Focus on Immunotherapy Targets

Recommended Short Course*

SC1: Cancer Immunotherapy
**Separate registration required. Please see page 4 for details.*

WEDNESDAY 2 NOVEMBER

07:45 Registration and Morning Coffee

BISPECIFICS FOR RETARGETING / REPROGRAMMING T CELLS

08:30 Chairperson's Remarks
Janine Schuurman, Ph.D., Vice President, Research, Genmab B.V.

08:35 KEYNOTE PRESENTATION:
Bispecific T Cell Engagers (BiTEs) for the Treatment of Malignant Diseases
Matthias Friedrich, Ph.D., Director, Nonclinical Development, Amgen Research (Munich) GmbH

09:20 Novel T Cell-Redirecting Bispecific Antibody Targeting a Highly Tumour Specific Antigen
Hirotake Shiraiwa, Ph.D., Group Manager, Biologics Discovery, Chugai Pharmaceutical Co., Ltd.
We have generated a T cell-redirecting antibody against a highly tumour specific antigen. This fully bispecific antibody recognises both CD3 and tumour-specific antigens and exerts highly potent anti-tumour efficacy in various *in vivo* models, and its large scale production has been made possible by proprietary engineering technology. The findings observed in non-human primate toxicity studies were manageable and reversible. Optimisation, pharmacology, and toxicity of this antibody will be presented.

09:50 Development of REGN1979, a Fully Human CD20xCD3 Bispecific Antibody
Eric Smith, Ph.D., Associate Director, Bispecific Antibodies, Regeneron, Inc.
This presentation will describe the development of REGN1979, a fully human CD20xCD3 bispecific antibody generated with Regeneron's VelocImmune® technology. Characterization of the in vitro and in vivo properties of this bispecific will be discussed, along with findings from pre-clinical efficacy studies. In addition, an update on the clinical status of REGN1979 and future planned studies will be provided.

10:20 Delivery of CD20 (Rituxan)-Transferrin Receptor VNAR Bispecific Antibody to the Brain for Treatment of MS and Brain Cancer
Krzysztof B. Wicher, Ph.D., Principal Scientist and Group Leader, BBB Group, Ossianix
Penetration of the BBB remains a significant impediment in development of biologics for CNS-related diseases. We fused a transferrin receptor specific VNAR single domain antibody to Rituximab and found that such bi-specifics shuttle to brain significantly better with brain plasma ratios of between 2 to 5%. The hybrid proteins retain their binding to TfR1 and CD20 and mediate an ADCC response on human CD20+ cells. This offers a possible therapeutic approach for B cell mediated disease such as multiple sclerosis and cerebral lymphoma.

10:50 Coffee Break in the Exhibit Hall with Poster Viewing

11:30 Development of a Highly Potent Anti-P-Cadherin / Anti-CD3 Bispecific DART Molecule with Extended Half-Life for the Treatment of Cancer
Adam Root, MSc, Senior Principal Scientist, Global BioTx Technologies, Pfizer, Inc.
We have made an extended-half-life dual-affinity re-targeting (DART) bispecific against P-cadherin and CD3 that demonstrates antibody-like properties. Identified through phage display and affinity-optimised to picomolar affinity, this bispecific molecule elicits P-cadherin-expression level-dependent CTL responses against different tumour lines and induces antigen-dependent T cell activation and cytokine release. PF-06671008 demonstrates potent *in vivo* anti-tumour activity with significant tumour growth inhibition observed across a range of tumour types expressing P-cadherin.

12:00 To the Clinic with T Cell-Engaging and Checkpoint-Inhibiting Bispecific Antibodies - A Modular Approach to Build and Develop Novel Cancer Immunotherapies
David E. Szymkowski, Ph.D., Senior Director, Research, Xencor, Inc.
Bispecific antibody-mediated co-engagement of T cells with tumour antigens is now a validated therapeutic strategy, but manufacturing and dosing concerns have slowed clinical development of such immunomodulatory drugs. We have engineered modular Fc-containing bispecifics by coupling a robust and portable single-chain CD3 domain with full-length antibodies against promising cancer targets, and have also extended this Fc platform to generate multiple-checkpoint inhibiting bispecifics. I will present case studies of several such bispecifics entering clinical development, supported by superior pharmacology and half-life in monkeys coupled with efficient commercial-scale manufacturing.

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12:30 A Novel, Optimized Bispecific Antibody for the Treatment of PSMA-Expressing Cancer

Latifa Zekri, Ph.D., Cancer Immunology and Immunotherapy, German Cancer Consortium DKTK- DKFZ, Tuebingen

T cell recruiting bispecific antibodies (BsAbs) are promising reagents for tumor immunotherapy. However, BsAbs clinical development raised concerns about their low serum half-life, and toxicity due to off-target activation of T cells that prevents the application of higher doses. To overcome these shortcomings we constructed a new PSMAxCD3 antibody, that exhibits reduced off-target T cell activation, increased serum half-life and potent tumor cell killing at limiting effector: target cell ratios.

12:45 Characterization of a Cytomegalovirus-specific BiTE

Charlotte Brey, MSc, Cellular Therapeutics, Children´s Cancer Research Institute, Vienna

Reactivation of human cytomegalovirus (HCMV) in immunocompromised patients after HSCT can still cause life-threatening complications. Therefore, we are investigating a Bispecific T cell engager (BiTE®) directed against the glycoprotein B (gB) of HCMV, which is expressed on the surface of infected cells. The BiTE® was characterized for the first time, which comprised concentration allowing for efficient triggering of T cell effector functions such as degranulation, cytokine release and cytotoxicity.

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

13:30 Session Break

BISPECIFICS THAT TARGET CHECKPOINT REGULATION FOR IMMUNOTHERAPY

14:00 Chairperson's Remarks

Tariq Ghayur, Ph.D., Distinguished Research Fellow, Biologics, Abbvie Research

14:05 Design and Development of Next Generation Bispecific Antibodies for Cancer Immunotherapy

Jinming Gu, Ph.D., Executive Director, Biologics, Shanghai Hengrui Pharmaceuticals Co. Ltd.

Cancer immunotherapy has emerged as one of the major focuses in the pharmaceutical industry. The current limitation of anti-CTLA-4 or anti-PD-1 therapies is low response rate and high toxicity. This presentation will cover a few late stage preclinical bispecific programs in cancer immunotherapy, e.g. CD40/X, OX-40/X, and CD3/X.

14:35 Finding the Right Balance: Selective and Safe Targeting of the Ubiquitous CD47 Checkpoint Receptor on Cancer Cells

Nicolas Fischer, Ph.D., Head, Research, NovImmune SA

The immune checkpoint CD47 represents an attractive target in oncology. However, due to the ubiquitous expressions of CD47, the use of monoclonal antibodies faces safety and pharmacology liabilities. We have developed NI-1701, a bispecific κλ body, that selectively targets CD47 on B cells. CD47 inhibition drives effective phagocytosis of cancer cells *in vitro* and *in vivo* as well as the induction of durable anti-tumour responses in syngeneic animal models.

15:05 Vanucizumab, a Novel Bispecific Antibody Targeting VEGF-A and Angiopoetin-2: Preclinical and Clinical Development, and Preliminary Data on Combining with Cancer Immunotherapy

Oliver Krieter, M.D., Senior Translational Medicine Leader, Pharma Research and Early Development (pRED), Roche

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

T-CELL RETARGETING AND CHECKPOINT REGULATION (CONT.)

16:15 Duokines: A New Class of Bifunctional Immunostimulatory Molecule

Roland Kontermann, Ph.D., Professor, Biomedical Engineering, Cell Biology and Immunology, University of Stuttgart

Duokines are bifunctional fusion proteins of TNF ligand superfamily members expressed either as homotrimer molecules or as single-chain derivatives. They act either in cis or in trans and are capable of amplifying immune responses, e.g. as shown for the anti-tumour activity of T-cell retargeting bispecific antibodies.

16:45 Development of Bispecific DART Molecules to Mobilise Anti-Tumour Immunity

Ezio Bonvini, MD, SVP and CSO, Research, MacroGenics, Inc.

The DART® (Dual-Affinity ReTargeting) scaffold, a covalently-linked diabody-based bispecific module, can be tailored for single or multi-valency as well as fast or prolonged pharmacokinetics. Several DART molecules designed to recruit T cells through co-engagement with cancer antigens are currently in clinical development. Furthermore, the DART platform is ideally suited for immunomodulation via co-checkpoint blockade, such as PD-1xLAG3. Preclinical studies supporting the development of these DART molecules will be presented.

17:15 Problem-Solving Breakout Discussions*

**See website for details.*

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

19:15 End of Day

THURSDAY 3 NOVEMBER

08:00 Registration and Morning Coffee

SYNERGIES: MULTISPECIFIC ANTIBODIES AND COMBINATIONS OF MONO-SPECIFIC ANTIBODIES

08:30 Chairperson's Remarks

Nicolas Fischer, Ph.D., Head, Research, NovImmune SA

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08:35 Functional Aspects of Antigen- and Fc-Dependent IgG Hexamer Formation

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

Monomeric antibodies of the IgG isotype can organise into ordered hexamers after binding their cognate antigen expressed on a cell surface. While unraveling the molecular mechanisms of IgG hexamerisation, we identified point mutations that either inhibited or stimulated the formation of IgG hexamers and complement-mediated cytotoxicity (CDC). Our studies demonstrate that IgG hexamer formation, in addition to potentiating CDC, can induce outside-in signaling and activate intracellular signaling pathways, which we will discuss using two Death Receptor 5 (DR5) specific antibodies.

09:05 Avidity Enhances the Efficacy of EGFR x cMet Bispecific Antibody

Mark Chiu, Ph.D., Associate Director, Structural Biology, Janssen Research and Development

Monovalent bispecific antibodies are typically thought to bind to their respective targets without avidity. However, we show how receptor densities of EGFR and cMet in different lung cancer cell lines can contribute to apparent synergy in targeting both receptors. This impacts the use of an appropriate selection strategy of bispecific antibodies.

09:35 Antibody Mixtures: From Bench to Bedside

Michael Kragh, Ph.D., Senior Director, Preclinical Development, Symphogen

This presentation will outline the receptor internalisation and degradation with two antibodies targeting non-overlapping epitopes, and demonstrate the ability of antibody mixtures to eliminate resistance due to increased ligand production, ectodomain escape mutations, or horizontal receptor cross-talk. It will also describe the MoA and translation into the clinic, and provide examples from development of two antibody mixtures, Sym004 (EGFR) and Pan-HER (EGFR, HER2, and HER3).

10:05 HERA - Hexavalent Receptor Agonists Targeting the TNFR-Superfamily for Cancer Immunotherapy

Oliver Hill, Ph.D., Vice President Molecular Biology, Apogenix AG

TNFRSF targeting compounds with a solely agonistic activity on immune cells are still rare. Apogenix's single-chain-based fusion proteins mimic the three-dimensional organization of the natural ligands (the TNFSF-proteins). In contrast to antibodies, their agonistic activity does not rely on secondary crosslinking events *in vitro* nor *in vivo*. We will present the molecular engineering concept and the current results obtained for the TRAIL-R-, CD40-, GITR-, HVEM- and CD27-agonists.

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

BISPECIFICS IN THE CLINIC: FOCUS ON SAFETY AND EFFICACY

11:15 Clinical Developments with DVD Bispecifics

Tariq Ghayur, Ph.D., Distinguished Research Fellow, Biologics, AbbVie Research

This presentation will discuss: (i) Our efforts at building the DVD-Ig platform, including our preclinical and clinical experience to-date, (ii) our on-going efforts to identify novel target pairs, and (iii) our efforts in designing multi-specific biologics to modulate immune responses.

11:45 Multifunctional DARPin™ Drugs – Next-Generation Oncology and Ophthalmology Treatment

Dan Snell, Ph.D., V.P., Biology, Molecular Partners

The DARPin™ platform enables us to rapidly generate multi-functional drug candidates. Such drug candidates have the potential to improve therapy beyond current standard of care in ophthalmology and oncology. I will present interim data on the first-in-human systemic clinical phase I of MP0250, a multi-domain oncology drug candidate targeting VEGF and HGF.

12:15 Enjoy Lunch on Your Own

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

13:30 End of Advancing Bispecifics and Combination Therapy to the Clinic

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Novel Therapies for Cancer and Emerging Targets

Improving Efficacy for Clinical Success

Recommended Short Course*

SC1: Cancer Immunotherapy
**Separate registration required, please see page 4 for details.*

THURSDAY 3 NOVEMBER

12:30 Registration

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

CHALLENGE OF DISCOVERING NEW TARGETS

13:30 Chairperson's Opening Remarks
Horacio G. Nastri, Ph.D., Senior Director, Antibody Biotherapeutics, Incyte Corporation

13:35 KEYNOTE PRESENTATION: Antibody Functional Diversity as the Key to Unlocking Novel Target Biology
Christophe Blanchetot, Ph.D., Director, Discovery, argenx
Argenx is engaging with academic centers of excellence to secure early access to exciting, novel targets where proof of concept in disease models is yet to be shown. Through its so-called Innovative Access Program, argenx brings its proprietary antibody technologies and know-how to collaborations with target biology specialists, enabling rapid progress into translational studies and creation of novel antibody candidates with therapeutic product potential.

14:20 Immune Checkpoint in Melanoma
Ester Simeone, Ph.D., Director, Medical Oncology, Istituto Nazionale Tumori Napoli
Over the last few years, through numerous clinical trials and real-world experience, we have accumulated a large amount of evidence regarding the potential for long-term survival with immunotherapy agents in various types of malignancy. The results of these studies have also highlighted a number of recurring observations with immuno-oncology agents, including their potential for clinical application across a broad patient population and for both conventional and unconventional response patterns.

14:50 Preclinical Development of Tumor Penetrating Anti-Nucleolin Antibodies with Broad-Spectrum Anticancer Activity
Daniel Fernandes, Ph.D., Chief Scientific Officer, Research Division, CharlestonPharma
Our Company has identified and validated a high value therapeutic target in oncology and has developed first-in-class fully human monoclonal antibodies that bind specifically to this target. A key concept which drove the selection process was that the tumor antigen should be present on the surface of a wide variety of cancer cells with negligible or no expression on the surface of the corresponding normal tissues. In addition, cell surface expression of the therapeutic target should be necessary for the survival of most types of cancer cells.

15:20 Refreshment Break in the Exhibit Hall with Poster Viewing

CHALLENGE OF DISCOVERING NEW TARGETS (CONT.)

16:05 Addressing the Challenges in Effective Cancer Vaccine Development
Pedro Romero, M.D., Professor, Associate Director, Fundamental Oncology, Ludwig Cancer Research Center, Faculty of Biology and Medicine, University of Lausanne
The recent breakthrough with immune checkpoint inhibitors has shown that the adaptive immune system can eliminate a wide range of tumors in a subset of cancer patients. The absence of naturally acquired T-cell responses to cancer antigens may be one of the reasons for failure of immune checkpoint blockade therapy, thus providing a strong incentive to accelerate vaccine development. Rapid optimization of cancer vaccines is urgently needed to attain significant clinical impact.

16:35 Anti-Glycan Monoclonal Antibodies for Cancer Therapy
Lindy Durrant, Ph.D., Professor, Cancer Immunotherapy, Academic Clinical Oncology, University of Nottingham
Glycomic profiling of tumour tissues consistently shows alterations in N- and O-glycosylation profiles of glycoproteins and glycolipids compared to healthy tissues, with important functional implications for cancer cell biology. Despite the attractiveness of the targets, there are very few mAbs recognising glycans as they typically induce low affinity IgM responses. In this talk, we will show how we have overcome this limitation using complex immunisation regimes.

17:05 End of Day

17:00 Dinner Short Course Registration

Recommended Dinner Short Course*

SC5: Troubleshooting and Engineering of Antibody Constructs
**Separate registration required, please see page 4 for details.*

FRIDAY 4 NOVEMBER

08:00 Registration and Morning Coffee

ENGINEERING BISPECIFIC ANTIBODIES FOR CLEVER USE OF THE IMMUNE SYSTEM

08:30 Chairperson's Remarks
Neil Brewis, Ph.D., CSO, F-star

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08:35 Anti-Cytokine Bispecific Antibodies for Asthma: A Brief History of the Ups and Downs

Daniel Rycroft, Investigator, PTS, GlaxoSmithKline

Developing bispecific antibodies that are both manufacturable and clinically developable is challenging. This talk will describe some of the issues we have encountered and what we have learned, focusing on strategies to select the best molecules from the outset, understanding molecule conformation under stress and how we can use this data to build confidence to progress to the clinic.

09:05 *In vivo* Efficacy of Bispecific Antibodies Targeting Two Immune-Modulatory Receptors

Jacqueline Doody, Ph.D., Vice President, Immunology, F-star Biotechnology Ltd.

Combining immunotherapeutic antibodies has shown benefits over single agent in treating cancer patients. Bispecific antibodies are an alternative that not only bring two biologies together but results in novel biological mechanisms. F-star has a unique bispecific format that allows two antigen binding sites to reside within a normal IgG framework. Using this format, several immunomodulatory bispecifics were produced for proof of concept studies in murine tumour models.

09:35 IMCgp100: A Novel TCR-Based Immunotherapy against Malignant Melanoma

Joseph Dukes, Ph.D., Head, Pre-Clinical Biology, Cell Biology, Immunocore

ImmTACs are bi-specific reagents that target tumors via a soluble monoclonal TCR with exceptionally high sensitivity and specificity and redirect host polyclonal T-cells via an anti-CD3 antibody fragment. Emerging data from the first ImmTAC, IMCgp100, to enter Phase I/IIa clinical trials demonstrate durable responses in patients with advanced melanoma and a favorable safety profile. Development of IMCgp100 continues in uveal and cutaneous melanoma and in combination with checkpoint inhibitors.

10:05 Coffee Break in the Foyer with Poster Viewing

HOW TO ENGINEER CAR T THERAPY TO BE MORE EFFECTIVE

10:30 Chairperson's Remarks

Mitchell Ho, Ph.D., Chief, Antibody Therapy Section, Laboratory of Molecular Biology, National Cancer Institute, NIH

10:35 CAR Modified Autologous Cells – CMC of an ATIMP

Christoph Priesner, Qualified Person, Quality Manager, Institute of Cellular Therapeutics, Hannover Medical School

Gene-therapy medicines are re-emerging as promising pharmaceutical candidates for especially haemato-oncological indications. The patient-specific manufacture of genetically modified and expanded cellular therapeutics as investigational medicinal products challenges multi-purpose academic cell processing units as regards biosafety requirements and analytical expertise to regulatory requirements. Highlighting these aspects, we present a case study on the academic-industrial co-development and academic manufacture of an advanced therapy investigational medicinal product.

11:05 CAR T cells: From the Mouse Cage to the Patient's Health

Zelig Eshhar, Ph.D., Professor, Chemical & Cellular Immunology; Chair, Laboratory of Cancer Immunotherapy, Immunology, Weizmann Institute of Science and Tel Aviv Sourasky Medical Center

Along with Eshhar's interest in the molecular recognition in the immune system, his lab. pioneered and developed the "T-Body" unique immune cell approach that involves genetic modifications of T-cells that is called today CAR T-cell, or as he nicknamed it "T body", which is being used to fight cancer. The genetically-engineered T cells have been shown to effectively kill human tumor cells both *in vitro*, and in experimental modes to treat local as well as metastatic disease. Lessons learnt from these pre-clinical trials have been applied end-stage patients with B cell lymphomas and leukemias resulting in a large proportion (>45%) of remission.

11:35 Glypican-3 as a Liver Cancer Target for Antibody-Based Therapies

Mitchell Ho, Ph.D., Senior Investigator and Chief, Antibody Therapy Section, Laboratory of Molecular Biology, National Cancer Institute, NIH

My lab has pioneered the production of inhibitory antibodies that recognize tumor-specific heparan sulfate proteoglycans. These antibodies have been shown to inactivate the Wnt/Yap signaling pathway known to be important for cancer pathogenesis. We have established glypican-3 as an immunotoxin target for the treatment of liver cancer. Its mechanism of action appears to involve both inhibition of cancer signaling (Wnt/Yap) and reduction in protein synthesis. Our ongoing development of chimeric antigen receptors for T-cell immunotherapy will also be discussed.

12:05 A "Trojan Horse" Bispecific Antibody Strategy for Broad Protection Against Ebolaviruses

Elisabeth K. Nyakatura, Ph.D., Senior Research Fellow, Biochemistry, Albert Einstein College of Medicine

Ebolaviruses engage the intracellular late endosome residing receptor Niemann-Pick C1 (NPC1) during host cell entry and infection. This engagement is absolutely required for host cell infection and the receptor-binding site (RBS) on the filovirus glycoprotein is shielded prior to physical sequestration in late endosomes. To target this interaction, we developed a "Trojan Horse" bispecifc antibody strategy, in which the viable domains of NPC-1 or GP-RBS specific antibodies are fused to an antibody that binds to a conserved surface exposed GP-epitope, applying Dual Variable Domain immunoglobulins (DVD-Ig). These bispecific molecules, but not their parental monoclonal antibodies, neutralized all known ebolaviruses by utilizing the viral particle themselves for endosomal delivery, and conferred post exposure protection against multiple filoviruses *in vivo*.

12:35 Problem-Solving Breakout Discussions with a Light Snack in the Foyer*

**See website for more details.*

13:35 Session Break

WHY DOES CAR T THERAPY NOT WORK IN SOLID TUMORS YET?

14:00 Chairperson's Remarks

Soldano Ferrone, M.D., Ph.D., Division of Surgical Oncology, Surgery, Massachusetts General Hospital, Harvard Medical School

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14:05 Why Do CAR T cells Not Work in Solid Tumors Yet?

Attilio Bondanza, M.D., Ph.D., Head, Innovative Immunotherapies Unit, San Raffaele University Hospital and Scientific Institute

While CAR T-cells have demonstrated remarkable antitumor activity in hematological malignancies, they currently struggle to achieve significant results in solid tumors. Target-antigen choice, *in vivo* persistence and the penetration of CAR T-cells in the hostile microenvironment of solid tumors are among the factors potentially limiting their efficacy in other cancer indications. This talk will focus on each of these factors and propose innovative approaches for successfully circumventing them.

14:35 Engineering of ROR1-Chimeric Antigen Receptor (CAR)-Modified T-Cells for Adoptive Immunotherapy of Cancer – Emerging Opportunities and Challenges

Michael Hudecek, M.D., Ph.D., Physician and Research Group Leader, Medicine, Wurzburg University

A current challenge is to establish CAR T-cell therapy in the context of solid tumors. We developed a CAR specific for the antigen ROR1 that is expressed on epithelial cancers and demonstrated the ability of ROR1-specific CAR T-cells to confer anti-tumor reactivity in pre-clinical models. We are in the process of establishing GMP manufacturing in preparation for a clinical trial exploring the safety and efficacy of this therapeutic modality.

15:05 Defects in T Cell Trafficking Within Human Tumors

Emmanuel Donnadieu, Ph.D., Team Leader, Immunology, Inflammation and Infection, Cochin Institute, INSERM

Our projects aim to identify the different obstacles that block T cells in their anti-tumor activities. The role of the extracellular matrix and tumor-associated macrophages is currently investigated. Most of our experiments rely on the use of powerful and original approaches: confocal and two-photon microscopy as well as a preparation of tissue slices kept in live.

15:35 How Can We Make CAR T Cells Able to Activate Bystander Immunity and Resist Immune Suppression?

Magnus Essand, Ph.D., Professor, Immunology, Genetics and Pathology, Uppsala University

The success of CD19 CAR T-cells in treatment of B-cell malignancies has led to hopes that CAR T-cells may also be used to treat solid tumors. The main challenges though are lack of specific and uniformly expressed target antigens and an immunosuppressive microenvironment found in most solid tumors. This presentation will discuss approaches to generate CAR T-cells able to resist immunosuppression and activate bystander effector cells to kill antigen-negative tumor cells.

16:05 CAR T Cell Immunotherapy of Solid Tumors and Hypoxia Induced Escape Mechanisms

Soldano Ferrone, M.D., Ph.D., Division of Surgical Oncology, Surgery, Massachusetts General Hospital and Harvard Medical School

Hypoxia induces changes in T cells and target cells. These changes lead to the development of escape mechanisms utilized by tumor cells to avoid immune recognition and destruction. These escape mechanisms will be described. In addition, the strategies developed to counteract these escape mechanisms will be discussed.

16:35 End of Conference

"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.*

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7th Annual

Optimisation & Developability

Selecting and Enhancing the Best Molecule to Move Forward

Recommended Short Course*

SC2: Mutation and Selection Strategies beyond Affinity Optimisation

**Separate registration required, please see page 4 for details*

MONDAY 31 OCTOBER

12:00 Registration

PLENARY KEYNOTE SESSION

13:40 Welcome from PEGS Europe Team

13:45 Chairperson's Opening Remarks

Ana Barbas, Ph.D., Coordinator, Bayer Satelite Laboratory at iBET, iBET and Bayer Portugal SA

13:50 Biotherapeutic Programs that Re-Direct Cytotoxic Lymphocytes to Cancer Cells

Paul Adam, Ph.D., Executive Director, Immune Modulation and Biotherapeutics Discovery, Boehringer Ingelheim

Cytotoxic lymphocytes such as NK and T cells have the capability to control cancer development and progression. Harnessing this cytotoxic potential with biotherapeutic agents is predicted to become a future pillar of cancer therapy in light of recent clinical successes. This presentation will describe novel biotherapeutics whose mode of action involves the engagement and re-direction of NK and T cells to hematological tumors.

14:30 Antibody-Based Combination Cancer Immunotherapy at Roche pRED

Christian Klein, Ph.D., Distinguished Scientist, Head, Oncology Programs, Cancer Immunotherapy Discovery, Roche Pharmaceutical Research and Early Development, Roche Innovation Center Zurich

This presentation will introduce novel antibody cancer immunotherapies developed at Roche pRED including novel IL2 variant immunocytokines and T cell bispecifics as well as preclinical data for their optimal combination and scheduling.

15:10 Safety Concerns Associated with Immunotherapy and Novel Biotherapeutics and Challenges in Investigating Their Immunotoxicity

Sandra S. Diebold, Ph.D., Principal Scientist, Immunotoxicology, Biotherapeutics, National Institute for Biological Standards and Control (NIBSC)

The pre-clinical assessment of the risks associated with immunotherapy and novel biotherapeutics is challenging since the bioassays have to be individually tailored to the investigated reagent. The immunotoxic activity and adverse responses that may be observed in patients are depending to a large degree on the mechanism of action of the biotherapeutic. The specific set-up of *in vitro* assays plus the identification of suitable animal models is critical for obtaining predictive pre-clinical data.

15:50 Refreshment Break in the Exhibit Hall with Poster Viewing

DEVELOPABILITY & MANUFACTURABILITY ASSESSMENT TO GUIDE CANDIDATE SELECTION

16:50 Chairperson's Remarks

Matthew Traylor, Ph.D., Senior Scientist, Analytical Development, Shire

16:55 Analytical Strategies to Guide Candidate Selection through Optimization and Developability Assessment

Matthew Traylor, Ph.D., Senior Scientist, Analytical Development, Shire

Selecting and optimizing complex recombinant non-mAb molecules can be extremely challenging. Many of these molecules exhibit complex sets of post-translational modifications (PTM) that afford unique challenges for cell line and/or clone selection. With an increasing number of non-mAb molecules in the pipeline an increased reliance on innovative technologies and approaches are being adopted to increase speed, throughput, and quality of the overall analytical support for candidate selection/optimization.

18:15 Preclinical Tools in Formulation Optimization to Improve Biological Performance of Antibodies

Sabine Eichling, Ph.D. Student, NBE Formulation Sciences, Abbvie Deutschland GmbH & Co. KG, University of Heidelberg

Formulation development for biologics has primarily focused on the refinement of physical and chemical stability during shelf-life. Effects of formulation composition following subcutaneous injection and reduced bioavailability were usually not considered. The addition of biological read out parameters enables further improvement in the antibody transport to the target tissue. We develop translatable models to understand the transport of antibodies following subcutaneous injection and predict the effect of the formulation on the bioavailability.

17:55 Precisely Controlled, Highly Diverse Gene Mutant Libraries for Synthetic Biology and Bio-Therapeutic Drug Discovery

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TWIST BIOSCIENCE

Ross Kettleborough, Ph.D., European Field Applications Specialist, Twist Bioscience

Effective synthetic libraries are critical for successful discovery and development. Twist's innovative silicon-based DNA synthesis, reaction volumes are miniaturized by a factor of 1000. By implementing rational design and expertise in synthetic DNA, Twist synthesizes each variant individually. This results in libraries with exceptional representation and diversity and screening efficiency.

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18:25 Welcome Reception in the Exhibit Hall with Poster Viewing

19:25 End of Day

TUESDAY 1 NOVEMBER

07:45 Registration and Morning Coffee

IDENTIFYING VARIATIONS AND ASSESSING DEVELOPABILITY

08:30 Chairperson's Remarks

Mike Molloy, Ph.D., Head, Analytical and Product Characterisation, GlaxoSmithKline

08:40 Fingerprinting Antibody Epitopes: Identifying Even Minor Variations for QC and IP

Michael Szardenings, Dr.rer.nat., Group Leader, Immunology, Ligand Development, Fraunhofer Institute for Cell Therapy and Immunology

Precise and comparative description of antibody binding sites is important for many reasons. Next generation sequencing in combination with a novel peptide phage display setup allows almost automated *in silico* analysis of a plethora of binding peptide variants. This routine procedure reveals not only the epitope, it renders in depth details of mimotope variations. These variations are individual signatures not only of different antibodies but also of batch to batch differences.

09:10 New Capillary Electrophoretic Systems for the Affinity Assessment of Protein Mixture Components

Gerhardus de Jong, Ph.D., Professor, Pharmaceutical Sciences, Utrecht University

We have developed capillary electrophoresis (CE) systems for the study of the affinity of proteins and protein variants to receptors and enzymes. In the first approach, different concentrations of the target protein or ligand are added to the background electrolyte and the affinity of the proteins is assessed by the change of electrophoretic mobility. In the second approach, affinity-specific detection is obtained by the on-line combination of CE and surface plasmon resonance.

09:40 Problem-Solving Breakout Discussions*

**See website for details.*

10:40 Coffee Break in the Exhibit Hall with Poster Viewing

11:20 Novel Approaches for Rapid Degradation Hotspot Profiling of Biotherapeutic Candidates

Bjoern Hueber, Senior Analytical Expert, Novartis Pharma AG

Degradation reactions such as asparagine deamidation and aspartate isomerization can present major risks for the developability of innovative biotherapeutics. Although *in silico* sequence analysis can help to predict potential degradation sites, time- and labor- intense characterization is still required to identify critical degradation hotspots in biologics lead candidates. This talk presents case studies using novel screening assays combined with a new UPLC-IM-MS platform for rapid and higher throughput monitoring of deamidation or isomerization hotspots.

11:50 Developability Assessment of Complex Biologics

Laurent Lariviere, Ph.D., Principal Scientist, Large Molecule Research, Roche Pharma Research and Early Development, Roche Innovation Center Penzberg, Roche Diagnostics GmbH

Complex biologics such as multispecific antibodies or fusion proteins play an increasingly important role as emerging new pharmaceuticals. In contrast to classic monoclonal antibodies, complex biologics can pose additional developability challenges. The talk will focus on our strategies to design and optimize stable, well-behaved drug candidates.

12:20 New Applications for Array-Based SPR Imaging

Sponsored by

Alex van der Kooi, Manager, Interaction Laboratory, IBIS Technologies

12:50 Explore Prometheus: Biologics Stability Screening Has Never Been Faster, Easier & More Fun

Sponsored by

Dennis Breitsprecher, Ph.D., Head, Research and Development – Biochemistry, NanoTemper Technologies, GmbH

Beate Kern, Ph.D., Application Specialist, NanoTemper Technologies, GmbH

Prometheus series instruments allow for rapid and precise high-throughput stability screenings, while providing best-in-class high resolution thermal unfolding data for biologics, independent of buffer or protein concentration. It allows for an exact detection of aggregation onset temperatures and aggregation behavior to find the conditions in which the protein is most stable.

Explore the Prometheus at the live demo and see how instrument and straightforward software solutions bring a whole new experience to your lab!

13:20 Session Break

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

OPTIMISATION FOR IMPROVED PROPERTIES AND MANUFACTURABILITY

14:30 Chairperson's Remarks

Dennis Breitsprecher, Ph.D., Head, R&D - Biochemistry, NanoTemper Technologies GmbH

14:35 Building a Pipeline in Immuno-Oncology: Bispecific Antibodies from Engineering to Optimized In House Phase One Manufacturing

Stanislas Blein, Ph.D., Head, Antibody Engineering, Glenmark Pharmaceuticals

Glenmark Pharmaceuticals' BEAT® platform is a robust and versatile bispecific antibody platform based on a unique heavy chain hetero-dimerization technology. We have produced several T-cell recruiting bispecific antibodies against different cancers, with GBR 1302 being our most advanced development candidate. This BEAT® antibody potently re-directs T-cells to HER2 positive cancer cells with an excellent safety-efficacy margin. GBR 1302 was successfully manufactured and will shortly enter clinical phase. Bioprocess and preclinical data will be presented.

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15:05 New Strategy for an Old Target: How to Make Extremely Potent Anti-ErbB2 Agents

Rastislav Tamaskovic, Ph.D., Researcher, Department of Biochemistry, University of Zurich

We have recently developed a novel approach employing biparatopic anti-ErbB2 Designed Ankyrin Repeat Proteins (DARPins). By creating an intermolecular trap with DARPin agents, which simultaneously target two distinct ectodomain epitopes of ErbB2, the receptors adopt an inactive conformation with kinase domains incapable of productive interactions. This strategy represents a rational approach to engineer anti-ErbB2 agents inducing cell-specific apoptosis based on a structurally and mechanistically understood principle, without using a toxic payload causing potential off-tumor side effects.

15:35 The Importance of Biophysical Screening in Predicting the Perils of UF/DF

Marisa Barnard, Ph.D., Senior Scientist, Biopharm Molecular Discovery, GlaxoSmithKline

16:05 Extending Drug Half-Life to Achieve Monthly Dosing? The Potential of Veltis® Engineered Albumins for Optimized Dosing

Sponsored by Albumedix

Joanna Hay, Ph.D., Science Manager, Customer Solution, Albumedix Ltd.

Short circulatory half-life represents a major obstacle for many protein and peptide-based therapeutics. This can be significantly improved by conjugation or fusion to albumin, due to increased size and recycling via the neonatal Fc receptor (FcRn). The increased FcRn affinity of the Veltis® engineered albumins translates to more than doubling of the already long half-life of native albumin. We will describe rationally engineered albumins and their application to improve the pharmacokinetic properties of therapeutic candidates.

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

17:15 New Solution for Label-Free Biomolecular Interaction Screening

Sponsored by HORIBA Scientific

Chiraz Frydman, Ph.D., Product Manager, Horiba Scientific

Label-free biomolecular interaction analysis is increasingly moving towards screening approaches. The XelPleX platform makes it easier and faster than the conventional techniques. Let's show you how your assay will benefit not only from the advantage of the multiplex but also of the binding affinity determination.

17:30 Improve Productivity of Cell Line Development Using the ClonePix™ 2 and CloneSelect™ Imagers

Sponsored by Molecular Devices

Sarah Rowe, European Application Scientist, Molecular Devices

Molecular Devices offers automated solutions for screening and selection of mammalian clones or microbial colonies. The CloneSelect™ Imager replaces time-consuming, subjective manual inspections of mammalian cells with consistency and objectivity. Re-designed to provide high resolution and fluorescence imaging, all of our CSI models have proven scalable automated use.

17:45 Attribute Tailored Bioprocess Development to Allow 'Designed In' Appropriate Product Quality

Karolina Les, Ph.D., Scientist I, Purification Process Sciences, Biopharmaceutical Development, MedImmune

MedImmune's pipeline has diversified from predominantly antibodies to include many novel molecules of increased complexity. Development of novel biologics can be challenging and often carry higher risks. These can be addressed by early developability assessments and identification of potential critical quality attributes (pCQA). Case studies highlighting challenges encountered during early development of novel molecules are presented, showcasing how quality can be built into the molecules and bioprocesses in a systematic, science-based manner.

18:45 End of Optimisation & Developability

"PEGS Europe and PEGS keep going from strength to strength. One week at a PEGS event can stimulate ideas for a whole year. The presentations were exceptional, covering an extraordinary array of antibody and antibody-alternative technologies. PEGS Europe is unparalleled in both scope and quality."

KEVIN R., PH.D., SCIENTIST, WELLCOME TRUST SANGER INSTITUTE

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3rd Annual

Analytical Characterisation of Biotherapeutics

Harnessing Technologies and Proven Strategies to Improve Analytics

Recommended Short Course*

SC8: Protein Aggregation: Mechanism, Characterisation and Consequences

**Separate registration required, please see page 4 for details*

WEDNESDAY 2 NOVEMBER

07:45 Registration and Morning Coffee

BIOSIMILARITY AND COMPARABILITY ASSESSMENT

08:30 Chairperson's Remarks

Chris R. Cornell, Ph.D., Research Associate, Analytical Chemistry, Genentech, Inc.

08:35 KEYNOTE PRESENTATION:
High Throughput Assays for the Quantification of the Potency and Comparability of Biosimilars and Innovator Products

Michael Tovey, Ph.D., INSERM Director, Research, Laboratory of Biotechnology & Applied Pharmacology, Ecole Normale Supérieure de Cachan

Successful development of biosimilars is dependent upon direct comparisons of the relative potency and comparability of innovator molecules and biosimilars. A validated standardized high throughput 384 assay platform will be described that is applicable to most biopharmaceuticals and that allows direct comparison of drug potency and comparability of innovator molecules and biosimilars in the same assay. Case studies will be presented for products ranging from Neupogen to Remicade and Enbrel.

09:20 Characterization of Filgrastim Using Intact and Top-Down MS

Urs Lewandrowski, Ph.D., Lab Head, Analytical Characterization, Sandoz

The detailed analytical comparison of Zarxio and the reference product Neupogen provided the foundation for FDA's approval of Sandoz's Zarxio as the first biosimilar in the United States. Intact and top-down MS are becoming highly attractive techniques for detailed protein characterization. Using a benchtop Exactive MS, modifications in filgrastim were detected with high sensitivity on the intact level followed by site assignment using all-ion fragmentation mode. Examples of successful top-down MS experiments will be demonstrated.

09:50 Importance of Analytical Characterization for Biosimilar Development - Disulfide Bridging of GP2015/Erelzi

Fabian Higel, Ph.D., Lab Head, PK Profiling, Technical Development Biosimilars, Novartis

Analytical characterization is the foundation of successful biosimilar development. Comprehensive characterization and a deep understanding of the biosimilar candidate and reference product and their variants and modifications can play an important role in different phases of biosimilar development. The unravelling and understanding of disulfide bridging of the biosimilar Erelzi played an important role for the FDA approval and is presented in this talk.

10:20 An Integrated Approach to Managing Immunogenicity Risk and Drug Immune Modulation

Sponsored by PROIMMUNE www.proimmune.com

Jeremy Fry, D.Phil., Director, Sales, ProImmune

Immunogenicity is one of the most complex issues to address in drug design and development. I will provide an overview of the best tools to mitigate immunogenicity risk, including Mass Spectrometry antigen presentation assays; DC-T and T cell proliferation assays for biologic lead selection/ optimization; HLA-peptide binding assays to characterize individual epitopes as well as undiluted whole blood cytokine storm assays.

10:50 Coffee Break in the Exhibit Hall with Poster Viewing

11:30 Overcoming Formulation and Analytical Challenges for Developing Biosimilar Products

Jun Liu, Ph.D., Senior Director, Analytical and Pharmaceutical Science, Coherus Bioscience

Due to the complex nature of biopharmaceuticals, analysis and control of the similarity of biosimilar products to innovators products remains key challenges. Furthermore, critical IP on formulation and process provided additional challenges to introduce biosimilar products into major US and EU markets. In this presentation, we will discuss these challenges on pharmaceutical and analytical development. A case study example will be provided to discuss the strategy to overcome these challenges.

12:00 FTIR Spectroscopy as a Multi-Parameter Analytical Tool for Stability Studies and Batch Consistency Testing of Therapeutic Proteins

Allison Derenne, Ph.D., Researcher, Science-Chemistry, Université libre de Bruxelles

Harnessing the strengths of infrared spectroscopy and recent improvements in chemometric methods, new analytical methods have been developed to study the stability and verify batch-to-batch consistency of therapeutic proteins. The presentation will demonstrate the feasibility, through one quick and direct measurement, to simultaneously obtain information concerning four key characteristics of therapeutic proteins: (i) structural integrity, (ii) quantification of post-translational modifications, (iii) overall protein concentration and (iv) quantification of key excipients.

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12:30 Assessing an Interaction Parameter for Bioformulation Stability in One Measurement, using TDA Concentration Gradients

Sponsored by Malvern

Markos Trikeriotis, Ph.D., Applications Development Scientist, Malvern Instruments Ltd.

The self-association characteristics of molecules in dilute solutions can provide an assessment of stability at an early stage. The diffusion interaction parameter (kD) is a measure of the propensity for self-association, but the determination of this parameter using existing methodologies requires several measurements over a concentration series. Here, we show how Taylor Dispersion Analysis can be used to generate a concentration gradient from which the kD can be extracted in a single, low volume measurement.

13:00 Luncheon Presentation: *In silico* Approaches for Early Assessment of Immunogenicity

Sponsored by BIOVIA

Speaker to be Announced

Unexpected adverse events are reasons of drug development failures that contribute to the attrition rate in the pharmaceutical industry. A possible cause specifically associated to Biotherapeutics (peptides/proteins) is immunogenicity: the ability of some biotherapeutics to trigger immune responses that conduct to the generation of antibodies specifically directed against the drug. This immune response can possibly reduce the treatment efficacy and provoke adverse effects. Predicting immunogenicity is proving difficult because of the complexity of the underlying biological processes. We present here an informatics application based on modeling and simulation approaches that can help pharmaceutical R&D to prioritize promising drugs with respect to the immunogenicity risk.

13:30 Session Break

TOOLS AND TECHNIQUES FOR PRODUCT CHARACTERISATION

14:00 Chairperson's Remarks

Peter M. Ihnat, Ph.D., Principal Research Scientist, Drug Product Development Pre-Formulation, AbbVie Bioresearch Center

14:05 Analytical Characterization of Conjugation-Related Events in the Manufacture of ADCs

Chris R. Cornell, Ph.D., Research Associate, Analytical Chemistry, Genentech, Inc.

The manufacture of cysteine-linked antibody-drug conjugates (ADCs) involves the partial reduction of inter-chain disulfide bonds, and subsequent conjugation of the reduced cysteine residues to a maleimide-containing drug-linker. This presentation will focus on the LC-MS characterization of the products of the conjugation reaction, with an emphasis on how various conjugation process parameters may impact reaction specificity.

14:35 Product Characterization and Control Strategy

Ping Feng, MSc., Director, Analytical Sciences and Operation, Teva Pharmaceuticals

Product characterization should be planned based on knowledge of protein sequence and manufacturing process impact. The level of characterization should be phase-appropriate for an adequate balance between risk and benefit. A well-designed characterization study can be very valuable to support commercial specification with reduced release testing or more robust range of a criterion allowed. Two case studies will be presented: antibody glycan analysis and product variant characterization of a HAS fusion protein.

15:05 Advances in Epitope Characterization Using Label-Free Biosensors

Yasmina Abdiche, Ph.D., CSO, Wasatch Microfluidics

This talk will describe methods used to explore the epitope diversity observed across panels of monoclonal antibodies generated by different *in vitro* and *in vivo* platforms, including chicken immunizations. High throughput epitope binning experiments on label-free biosensors were used to merge large panels of antibodies and compare their epitope outputs. Data will be presented for both, wild-type and transgenic chickens, highlighting the therapeutic potential of chicken-derived antibodies.

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

16:15 Investigating the Interaction between FcRn and IgG Variants by Hydrogen/Deuterium Exchange Mass Spectrometry

Maximiliane Hilger, Ph.D., Senior Scientist, Mass Spectrometry, Large Molecule Research, Pharma Research and Early Development, Roche Innovation Center Munich

The recycling of IgGs by FcRn regulates antibody plasma levels and half-life. Here we study the IgG1–FcRn interaction by HDX-MS to gain deeper molecular understanding that will ultimately allow us to optimize antibody pharmacokinetics, efficacy and safety. Interestingly, our data demonstrate a conformational interplay between the Fab and Fc regions of the antibodies upon FcRn binding and suggest the presence of direct FcRn interaction sites in the Fab region.

16:45 Using Viscosity-Derived Parameters and Thermal Analysis to Evaluate the Solution Properties of Bispecific Dual Variable Domain Immunoglobulins

Peter M. Ihnat, Ph.D., Principal Research Scientist, Drug Product Development Pre-Formulation, AbbVie Bioresearch Center

The Fab regions of dual variable domain immunoglobulins (DVD-Ig) consist of outer and inner complementarity determining regions (CDR) that confer bivalent antigen specificity. The protein – protein interactions (PPI) and protein – solvent interactions (PSI) of DVD-Ig solutions were studied by light scattering and rheological techniques to identify the factors that contribute to achieving stable high concentrations.

17:15 Problem-Solving Breakout Discussions*

**See website for details.*

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

19:15 End of Day

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THURSDAY 3 NOVEMBER

08:00 Registration and Morning Coffee

CHARACTERISING PRODUCT- AND PROCESS-RELATED IMPURITIES

08:30 Chairperson's Remarks
Jihong Yang, Ph.D., Senior Scientist, Bioanalytical Sciences, Genentech

08:35 Enhanced Detection of Product-Related Variants and Impurities in Recombinant Glycoproteins
Francois Griaud, Ph.D., Functional Lead Analytics, Biologics Process Development/Late Phase Analytical Development, Novartis Pharma AG
Monitoring and controlling post-translational modifications (PTMs) in recombinant glycoproteins is a requirement to ensure manufacturing process consistency and product quality. Aside from the example of glycosylation, the analyst may face the challenging task of detecting less predictable post-translational modifications, product-related variants and impurities. This presentation will focus on different mass spectrometry and data analysis approaches to enable the semi-automated detection of such species during technical development.

09:05 Identification and Monitoring of HCPs by Mass Spectrometry in Bioprocess Development
Yan-Hui Liu, Ph.D., Senior Principal Scientist, Merck Research Lab

Sponsored by solvias

09:35 Pyrogen Detection by Monocyte Activation Test in Antibody Formulations
Anya Fritsch, Ph.D., CSO, Confarma France SAS

Sponsored by sensiQ

10:05 Simultaneous Detection of Protein Aggregation and Affinity Measurements in a Single SPR Experiment
Eric Reese, Ph.D., Vice President, Sales and Marketing, SensiQ Technologies, Inc.
SensiQ presents data from a Genentech collaboration highlighting the simultaneous detection of protein aggregation and affinity determination in a single experiment as enabled by Pioneer FE SPR instrumentation with diSPR® injection technology. This is the first presentation of an SPR biosensor capable of both key measurements in a single experiment.

Sponsored by BRUKER

10:20 Semi-Automated, Mass Spectrometric Determination and Evaluation of Glycosylation CQAs at the Bioreactor Level
Catherine Evans, Ph.D., Business Development Manager – Biopharma, Bruker Daltonics
Mass spectrometry is a powerful tool for monitoring CQAs related to bioproduction, providing insights into the design-space and its impact on the product specification. We present here a standalone analytical platform developed for the direct connection of bioreactors to an MS system for real time at-line monitoring of mAb CQAs.

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

CHARACTERISATION OF POTENCY ASSAYS AND ASSAY REAGENTS

11:15 Potency Assays for Biopharmaceuticals: A Regulatory Perspective
Baolin Zhang, Ph.D., Senior Investigator & Product Quality Reviewer, Office of Biotechnology Products, CDER, FDA (Invited)
Because of the complex nature of biopharmaceuticals, it can be scientifically challenging to develop appropriate potency assays for each product. A regulatory evaluation of adequacy of potency assays is made on a case-by-case basis, taking into account multiple factors including, but not limited to, product type, MoA, associated risk, and phases of development. This presentation provides an overview of regulatory expectations regarding potency assays and discusses several case studies that highlight some of the relevant issues commonly seen in the regulatory submissions.

11:45 Robust Characterization Methods to Ensure Quality Bioanalytical Assay Reagents
Jihong Yang, Ph.D., Senior Scientist, Bioanalytical Sciences, Genentech
Bioanalytical assays are critical for the assessment of the exposure-response relationship, safety, and efficacy of biotherapeutics. Robust biophysical and bioanalytical methods can be used to generate important characterization data for critical assay reagents. The talk will highlight some of the emerging analytical and bioanalytical technologies that can be used to characterize assay reagents and describe case studies to demonstrate the application of these methods to support biotherapeutic development.

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12:15 Luncheon Presentation: How Similar is my Biosimilar? A LC and MS Prospective
John C. Gebler, Ph.D., Director, Biopharma Business Development, Waters Corporation
Additional incentive has come from reducing the cost and increasing global access to life-saving therapies for patents.Biologic drugs are inherently homogeneous and innovator products are often a composite of similar species manufactured within a specific range of variability.Drug manufactures and regulators want to reduce risks to patients and ensure that biologics and safe and efficacies.The presentation will report on the use of LC/MS for in-depth, reproducible, and meaningful characterization/comparability between an innovator and biosimilar.

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

13:30 End of Analytical Characterisation of Biotherapeutics

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Protein Aggregates & Particles

Understanding Aggregation Kinetics to Effect Control and Minimise Immunogenicity Risks

Recommended Short Course*

SC8: Protein Aggregation: Mechanism, Characterisation and Consequences

**Separate registration required, please see page 4 for details*

THURSDAY 3 NOVEMBER

12:30 Registration

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

AGGREGATION AND IMMUNOGENICITY RISKS

13:30 Chairperson's Opening Remarks

Jeremy Derrick, Ph.D., Professor, Molecular Microbiology, University of Manchester

13:35 KEYNOTE PRESENTATION:
The Immunogenicity of Antibody Therapeutics: Aggregates and Immune Complexes

Roy Jefferis, Ph.D., MRCP, FRCPAth, D.Sc., Professor Emeritus, University of Birmingham

Many parameters contribute to the development of anti-drug antibodies (ADA) to protein therapeutics; aggregation being considered a particular risk. However, administration of IgG antibody therapeutics results in the formation immune complexes (aggregates!) that may similarly activate pathways leading to ADA production. Individual mAb therapeutics should be evaluated for the propensity of both aggregates and immune complexes to activate downstream effector cascades.

14:20 Understanding the Relationship between Aggregation and Immunogenicity of Biotherapeutic Proteins

Jeremy Derrick, Ph.D., Professor, Molecular Microbiology, University of Manchester

Aggregation is known to play an important part in the immunogenicity of therapeutic proteins. I will describe recent experiments which compared the immunological responses to immunization of selected example proteins, in monomeric and aggregated forms, in a mouse model. In addition, we also examined the effect of the heat shock protein DnaK, a common HCP, and show that it can play a role in modulating the immune response to aggregates.

14:50 Formulate and Characterize More Biologic Formulations than Ever before

Sponsored by UNCHAINED LABS

Daniel Lund, Ph.D., Applications Scientist. Unchained Labs

Biologic formulations are hard to make and difficult to characterize. The process to buffer exchange and concentrate proteins can take days. Screening them for stability take days to weeks and figuring out if they will aggregate can take months. In this talk, we'll present a rapid, total solution for formulating proteins, characterizing them for stability, predicting whether they will aggregate and determining the pathway of aggregation.

15:20 Refreshment Break in the Exhibit Hall with Poster Viewing

16:05 Using Denaturant Solutions to Probe the Colloidal Stability of Partially Folded Proteins and the Link to Aggregation

Robin Curtis, Ph.D., Senior Lecturer, School of Chemical Engineering and Analytical Sciences, University of Manchester

16:35 Immunogenicity Risk of Protein Aggregates – Could Bedside Filtration Be of Help?

Gerhard Winter, Ph.D., Professor, Pharmaceutical Technology and Biopharmaceutics, University of Munich

Characterization of protein particles has become a regular request by the authorities and measures to reduce such contaminations are taken. But, it will remain impossible to guarantee for each single container the absence of particles. Why has bedside filtration not been applied more often to reduce the potential risk dramatically? We will present the status quo of bedside filtration of biopharmaceuticals and describe technical aspects like injection forces, particle shedding, particle removal, dead volumes.

17:05 End of Day

17:00 Dinner Short Course Registration

Recommended Dinner Short Course*

SC8: Protein Aggregation: Mechanism, Characterisation and Consequences

**Separate registration required, please see page 4 for details*

FRIDAY 4 NOVEMBER

08:00 Registration and Morning Coffee

MECHANISMS AND KINETICS OF AGGREGATION

08:30 Chairperson's Remarks

Hans Kiefer, Ph.D., Professor, Applied Biotechnology, Biberach University of Applied Sciences

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08:35 KEYNOTE PRESENTATION:
Impact of Non-Proteinaceous Particles on the Characterization and Formation of Protein Particles

Wim Jiskoot, Ph.D., Professor, Gorlaeus Laboratories, Division of Drug Delivery Technology, Leiden Academic Centre for Drug Research (LACDR)

Particulate impurities in protein formulations pose an analytical challenge and may compromise protein stability. In this presentation I will present a case study about the root cause of nanoparticulate (100–200 nm) impurities in protein formulations containing commonly used sugar excipients. These impurities interfere with the characterization of proteinaceous particles by dynamic light scattering and nanoparticle tracking analysis. Moreover, they compromise protein stability and potentially increase their immunogenicity.

09:05 Mechanisms of Protein Aggregation

Thomas Laue, Ph.D., Professor, Molecular, Cellular & Biomedical Sciences, University of New Hampshire

The proximity energy framework will be described as a useful way to think about high concentration solutions. Protein solvation, hydrophobic interactions and molecular crowding are incorporated into this framework. Protein charge contributes significantly to preventing aggregation and reducing viscosity. Charge cannot be calculated, so the importance and simplicity of measuring charge will be emphasized. Data presented showing how proximity energies impact protein-protein interactions in high concentration formulations as well as in serum.

09:35 Elucidation of Aggregation Mechanisms in Therapeutic Protein, and Prediction of Formulation Strategies

Paul Dalby, Ph.D., Professor, Biochemical Engineering, University College London

Various biophysical methods have investigated the aggregation kinetics, solution conformations, and conformational stabilities of several IgGs and Fab molecules. Structural changes in these molecules have been observed that correlate with their aggregation propensities. These studies have been complemented by molecular dynamics and docking simulations that then together reveal the potential features of protein structure that promote aggregation propensity, and also the potential mechanisms by which particular excipients increase protein stability.

10:05 Coffee Break in the Foyer with Poster Viewing

EVALUATING AGGREGATION PROPENSITY

10:35 Relationship between Aggregate Propensity and Biophysical Parameters of Proteins in Solution

Susumu Uchiyama, Ph.D., Associate Professor, Graduate School of Engineering, Osaka University

Aggregates formation of therapeutic proteins is one of the issues that should be solved. Here I will show how experimentally obtained biophysical parameters of proteins in solution, such as secondary virial coefficient and thermal unfolding temperature, are useful to predict aggregates formation during transport and storage. In addition, how chemical modification of protein changes its stability will be introduced. Finally total formulation developments of therapeutic proteins in solution are proposed.

11:05 Large Scale All-Atom Molecular Dynamics Analysis of Multi-Peptide Systems Reproduces Peptide Aggregation Propensity In Line with Experimental Observations

Yutaka Kuroda, Ph.D., Associate Professor, Life Science and Biotechnology, Tokyo University of Agriculture and Technology

We carried out all-atom molecular dynamics simulation for 18 systems containing ~3x104 water molecules and 27 tetra-peptides made from a single amino acid type and using a standard force-field without "artificial" hydrophobic forces. Surprisingly, hydrophobic peptides rapidly formed clusters whereas hydrophilic ones remained monomeric in line with experimental expectations. We believe that this study represents a step toward a molecular understanding of peptide/protein solubility, based on physico-chemical first principles.

DEVELOPING PARTICLE STANDARDS

11:35 Development and Applications of Protein-Like Reference Materials for Monitoring Protein Particles

Srivalli Telikepalli, Ph.D., Research Chemist, National Institute of Standards and Technology

NIST is developing subvisible and visible particle standards using ethylene tetrafluoroethylene polymer and SU-8 photoresist since these materials better mimic the morphology and optical properties of protein particles compared to the currently available particle standards. The development, stability, and challenges associated with working with these materials will be briefly described. Applications of the ETFE particles to standardize subvisible particle measurements and to standardize visual inspection processes will be discussed.

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Albumedix

12:05 When Standard Formulation Strategies Fails - Recombinant Albumin for Stabilization of Hard-to-Formulate Biotherapeutics

Phil Morton, Ph.D., Science Director, Bioprocess & Characterisation, Albumedix Ltd.

The expanding field of biotherapeutics gives promise for improvement of several treatment options. Many of the biopharmaceuticals found to be efficacious, however continue to face ex vivo instability challenges that are not readily solved by standard excipients. Recombinant human albumin, however, can potentially alleviate these shortcomings. The mechanisms by which albumin help stabilize biopharmaceuticals are multiple and dependent on the specific drug. Data is presented here that exemplifies these different mechanisms.

12:35 Problem-Solving Breakout Discussions with a Light Snack in the Foyer*

**See website for more details*

13:35 Session Break

PARTICLE ANALYSIS AND CHARACTERISATION – DETECTION, IDENTIFICATION, CHARACTERISATION AND CONTROL

14:00 Chairperson's Remarks

Thomas Laue, Ph.D., Professor, Molecular, Cellular & Biomedical Sciences, University of New Hampshire

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14:05 Comparisons between Particle Identification Techniques

Jonas Hoeg Thygesen, Ph.D., Research Scientist, R&D, Microanalysis Centre, Novo Nordisk Pharmatech A/S

MicroFlow Imaging (MFI), Raman and Fourier-Transform Infrared (FTIR) Spectroscopy, Electron- and Optical microscopy are strong and versatile tools for particle identification and characterization. This talk will provide specific cases to highlight advantages and challenges using the different techniques, and furthermore, illustrate how they may complement each other.

14:35 Microscopy-Based Particle Counting and Characterization in a High-Throughput Formulation Screening Platform

Christian Ried, Ph.D., Senior Scientist, Drug Product Development, AbbVie Deutschland GmbH & Co. KG

Protein particles formed from biologics during manufacture and storage might trigger unwanted effects like anti-drug antibody response in patients. Recently, we have set up an automated platform for high-throughput formulation screening of biologics. Here we present a method that allows for particle counting and characterization from microliter-sized samples as a final step in the screening process.

15:05 Mitigation of Aggregation during Elution from Protein A

John K. Kawooya, Ph.D., Director, Biologics Optimization, Amgen, Inc.

Bispecific protein engineering has produced many new "antibody-like" molecules that are not as stable as antibodies. Some of these molecules aggregate upon exposure to the strong acidic pH (2.5-3.7) encountered during elution from Protein Affinity columns. Presented here are strategies for mitigating aggregation by either protecting the molecules at low pH or by eluting the molecules at neutral pH (7.2) or mildly acidic pH (4.5-5.2).

15:35 Identification and Discriminant Analysis of Subvisible (Proteinaceous and Non-Proteinaceous) Particles

Zahir Akhunzada, Ph.D., Research Scientist, PPD, Bristol-Myers Squibb

This presentation discusses a method that successfully characterizes and distinguishes, both potentially proteinaceous and non-proteinaceous subvisible particles (SVPs) in protein formulations by using Microflow Imaging in conjunction with the MVAS software. Discriminant analysis approach will be discussed that will include measurements on seven morphological and light intensity parameters: Image Shape ratio, (C-circularity); Size; Pixel Intensity. The goal is to identify a mechanism that will discriminate a particle based on its parametric measurements.

16:05 QSAR Analysis of Additive Effects on the Aggregation of Monoclonal Antibodies in Downstream Processing

Hans Kiefer, Ph.D., Professor, Applied Biotechnology, Biberach University of Applied Sciences

We have established model experiments to induce aggregation of monoclonal antibodies through various stresses common in downstream processing. Aggregation rate constants of nucleation and growth were extracted from kinetic traces. In an additive screen using 150 compounds, molecular descriptors were correlated with rate constants and thermal stability changes using a quantitative structure activity relationship (QSAR) approach. Molecular properties of additives correlating with protective effects were extracted.

16:35 From *in silico* Simulations to Market: Improving Antibody CMC Protein Aggregation Properties by Rational Design

Sebastian Kube, Ph.D., Postoral Resesarch Associate, Boehringer Ingelheim Pharma GmbH & Co. KG

Early detection and mitigation of CMC risk factors such as protein aggregation propensity is vital for predictable and short timelines in the development of biologicals. We assembled a set of bioinformatics methods to assess candidate amino acid sequences for thermodynamic and colloidal stability and complementary biophysical methods to link a subset of residues to these properties. This knowledge serves as a basis for protein engineering to enhance developability.

17:05 End of Conference

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Basic Technologies in a Core Protein Expression Lab

Cambridge Healthtech Training SEMINARS
Comprehensive and Practical Training

Day 1: 31 October 13:40 – 18:25

Day 2: 1 November 08:30 – 18:45

Introduction to Expression Systems:

This seminar includes an introduction to heterologous protein expression and simple cloning technologies and covers the main systems: bacterial, insect and mammalian cells. In parallel, Mario discusses the basic considerations for protein purification and purification considerations for the different systems and downstream applications.

Instructors:

Tsafi Danieli, Ph.D., Director, BioGiv Excubator & Head, Protein Expression Facility, Wolfson Centre for Applied Structural Biology, Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem

Mario Lebendiker, Ph.D., Head, Protein Purification Facility, Wolfson Centre for Applied Structural Biology, Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem

Brief Description:

This seminar is designed to introduce basic technologies, strategies and considerations in recombinant protein production designed for core facility personnel. It will supply a basic toolbox for management of multiple and diverse projects.

Syllabus:

- Overview of recombinant proteins production: initiating a project, design and options for various downstream applications, requirements for customer/collaborator, and matching expectations
- Introduction to expression systems, covering the differences between the standard ones (*E. coli*, insect cells and mammalian cells) in protein quality, quantity and downstream applications, cost considerations, implementation time, required expertise and more
- Basic principles in affinity chromatography, ion exchange, hydrophobic exchange, size exclusion and mixed mode chromatography
- Protein purification strategies: input for purification protocol development, guidelines for protein purification, selection and combination of purification techniques
- Troubleshooting and case studies
- Balancing multiple projects: the challenge of "the few serving the many"

CLOSING PANEL DISCUSSION: Protein Production Core Facility Challenges: Methodologies, Strategies, and the Art of Managing Multiple Projects

There are many challenges in operating protein production core facilities. This seminar's panel of experts focuses on the following topics: Initiating projects, basic expression and purification systems, pros and cons for each system, screening platforms, troubleshooting and how much time should be spent on each system before moving to the next option. On top of "hands on" tips, we touch upon strategies on how to manage multiple "top priority" projects.

Moderator:

Tsafi Danieli, Ph.D., Director, BioGiv Excubator & Head, Protein Expression Facility, Wolfson Centre for Applied Structural Biology, Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem

Panelists:

Richard Altman, MS, Scientist, Protein Technologies, Amgen, Inc.
Nicola Burgess-Brown, Ph.D., Principal Investigator, Biotechnology, Structural Genomics Consortium (SGC), University of Oxford
Dominic Esposito, Ph.D., Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research, Leidos Biomedical Research, Inc.
Mario Lebendiker, Ph.D., Head, Protein Purification Facility, Wolfson Centre for Applied Structural Biology, Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem
Bjørn Voldborg, MSc, Director, CHO Cell Line Development, Novo Nordisk Foundation Center for Biosustainability (CFB), DTU Biosustain, Technical University of Denmark

Who should attend the training seminar?

The seminar is designed for researchers establishing a new core facility or entering an already established facility, students, postdocs, technicians and engineers wishing to expand their knowledge and basic technologies in recombinant protein production.

Each CHI Training Seminar offers 1.5 Days of instruction with start and stop times for each day shown above and on the Event-at-a-Glance published in the onsite Program & Event Guide. Training Seminars will include morning and afternoon refreshment breaks, as applicable, and lunch will be provided to all registered attendees on the full day of the class.

Each person registered specifically for the training seminar will be provided with a hard copy handbook for the seminar in which they are registered. A limited number of additional handbooks will be available for other delegates who wish to attend the seminar, but after these have been distributed no additional books will be available.

Though CHI encourages track hopping between conference programs, we ask that Training Seminars not be disturbed once they have begun. In the interest of maintaining the highest quality learning environment for Training Seminar attendees, and because Seminars are conducted differently than conference programming, we ask that attendees commit to attending the entire program, and NOT engaging in track hopping, as to not disturb the hands-on style instruction being offered to the other participants.

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9th Annual

Optimising Expression Platforms

Meeting the Demand for Recombinant Antibodies

Recommended Short Courses*

SC4: Transient Protein Expression: A Key Tool to Enable Rapid Protein Engineering

SC7: Protein Purification Strategies: Dealing with Proteins that are Prone to Aggregate

**Separate registration required, please see page 4 for details*

WEDNESDAY 2 NOVEMBER

07:45 Registration and Morning Coffee

ENGINEERING EXPRESSION PLATFORMS TO MEET THE DEMAND

08:30 Chairperson's Remarks

Bjørn Voldborg, MSc, Director, CHO Cell Line Development, Novo Nordisk Foundation Center for Biosustainability (CFB), DTU Biosustain, Technical University of Denmark

08:35 KEYNOTE PRESENTATION:
Animal Cells in Bioreactors for Production of High-Value Biologics – From Vaccines to Therapeutic Proteins, Lessons of the Past Applied Today and Tomorrow

Florian M. Wurm, Dr. rer. nat., Honorary Professor, Swiss Federal Institute of Technology Lausanne (EPFL); CEO, ExcellGene SA

The talk reviews the dramatic history of our industry -- 100 years -- towards high-value biologicals whose manufacturing requires a huge range of knowledge of fundamental and applied sciences in fields as diverse as molecular biology to fluid dynamics of water and gas. Reflecting and analysing the involved technologies in production provide excellent leads and opportunities for the future. CHO cells in bioreactors will be a central part of this discussion.

09:20 The Effect of Vector Design on the Expression of Bispecific Antibodies

Jason Saunders, MSc, Senior Scientist, Biologics Expression and Technology, Merck & Co., Inc.

09:50 Complementary Approaches for Protein Production in Insect and Mammalian Cell Lines

Konrad Büssow, Ph.D., Research Scientist, Structure and Function of Proteins, Helmholtz Centre for Infection Research

The benefits of the baculovirus system for the production of intracellular and secreted proteins are well known. The human HEK293 cell line represents a valuable alternative, especially for secreted proteins, and allows for virus-free transient transfection with plasmids. Recently, virus-free, plasmid-based transfection of insect cells has been optimised considerably. This system represents a useful alternative that combines advantages of the baculovirus system and transient transfection of HEK293 cells. Examples of proteins produced by transient transfection of HiFive insect cells will be presented, including intracellular and secreted production.

Sponsored by

10:20 Strep-Tactin XT - A Superior Next-Generation System for Purification of Proteins, Isolation of Cells & Assay Development

Dennis Niermeier, M.Sc., Scientist, IBA GmbH

The new third-generation Strep-tag® system is based on recently engineered Strep-Tactin®XT and Twin-Strep-tag®. Due to the affinity improved but still reversible binding of Strep-Tactin®XT to Twin-Strep-tag® in the low pM range, the system is superior to other affinity purification systems and now also suitable for assay development.

Sponsored by

10:35 Presentation to be Announced

10:50 Coffee Break in the Exhibit Hall with Poster Viewing

ENGINEERING GENES

11:30 Engineering the Baculovirus Genome to Improve Protein Production

Dominic Esposito, Ph.D., Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research, Leidos Biomedical Research, Inc.

The use of insect cell expression systems for the production of pharmaceutically relevant protein targets has dramatically increased over the last few years, with several products already approved by major regulatory agencies. In our laboratory, this system has been vital for production of post-translationally modified RAS proteins essential for cancer drug discovery. In using this system, we have developed a number of process and technology improvements which permit increased protein yield, protein quality, and virus stability. We discuss in detail the enhancements to the system and how they have been applied to high-level production of clinically relevant proteins, and examine ways in which synthetic biology and genome engineering can further enhance the utility of this system.

12:00 SINEUPs: A New Class of Antisense Long Non-Coding RNAs that Specifically Activate Translation of Targeted Proteins

Silvia Zucchelli, Ph.D., Assistant Professor, Health Sciences, University of Eastern Piedmont; CSO, TransSINE Technologies Inc.

SINEUPs represent a new functional class of natural and synthetic antisense long non-coding RNAs that upregulate translation of partially overlapping sense mRNAs through the activity of an inverted SINEB2 element. Given their modular structure, SINEUPs can be designed to increase protein synthesis of potentially any gene of interest. We propose SINEUPs as reagents for molecular biology experiments, in protein manufacturing as well as in therapy of haploinsufficiencies.

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12:30 Engineering of CHO Cell Lines for Enhanced Process Robustness

Sponsored by SELEXIS

Pierre-Alain Girod, Ph.D., CSO, Selexis

High-quality production cell lines secreting maximal levels of recombinant proteins require stable integration of the recombinant DNA, elevated gene transcription, optimized secretion machinery to handle increased protein secretion and folding loads and, ideally, being easily tracked during manufacturing. Using the data from our CHO-K1 genome and transcriptome, we have engineered our CHO-K1 to address these issues, particularly for difficult-to-express proteins, as well as to provide detailed genomic analysis packages for manufacturing cell lines.

13:00 A Stable Episomal Expression System to Streamline Mammalian Protein Production

Meelis Kadaja, Ph.D., MBA, Director, Business Development, Icosagen Cell Factory OÜ

We have found the way to stably maintain expression vectors in dividing mammalian cells as extrachromosomal units. This stable episomal expression system is scalable, and requires only 1ug of DNA to produce up to gram quantities of recombinant proteins with low endotoxin levels in few weeks. Our system enables to generate production cell banks in 10 days, and is also used in antibody discovery to express and screen antibodies.

13:30 Session Break

ENGINEERING HOSTS: CHO CELLS

14:00 Chairperson's Remarks

Nicola Burgess-Brown, Ph.D., Principal Investigator, Biotechnology, Structural Genomics Consortium (SGC), University of Oxford

14:05 CHO Cell Energetics: Understanding the Powerhouse of the Cell through Mitochondrial Deep Sequencing

Paul S. Kelly, Ph.D., Senior Postdoctoral Researcher, School of Biotechnology, National Institute for Cellular Biotechnology, Dublin City University

The predominant metabolic pathways, glycolysis and oxidative phosphorylation, have been linked to critical bioprocess relevant CHO cell phenotypes, growth and productivity. We have shown SEAP producing CHO cells engineered to be depleted of microRNA-23b exhibited a 3-fold increase in product yield associated with elevated mitochondrial activity. Given CHO cells' genetic instability, we sought to compare the mitochondrial genomic sequence of 22 CHO cell lines and provide a mitochondrial genome reference sequence from the hamster.

14:35 Precision Control of Recombinant Gene Expression for CHO Cell Synthetic Biology

Adam Brown, Ph.D., Research Fellow, Department of Chemical and Biological Engineering, University of Sheffield

To successfully apply the core concepts underpinning synthetic biology to CHO cell engineering, we must develop practical and robust enabling technologies. Fundamentally, we will require the ability to precisely control the relative stoichiometry of numerous functional components that are simultaneously introduced into the host cell factory. In order to enable this, we have developed a suite of complementary technologies that enable precise control of recombinant gene expression in CHO cells. Using synthetic promoters as an exemplar, the function of these tools in the context of CHO cell engineering will be described.

15:05 Inactivation of GDP-Fucose Transporter in CHO Cells: A New Strategy for Producing Fucose-Free Biobetter Antibody Therapeutics

*Zhiwei Song, Ph.D., Principal Scientist, Expression Engineering Group, Lead PI for GlycoSing Programme, Bioprocessing Technology Institute, A*STAR*

Removal of core fucose from IgG1 has been shown to significantly enhance its affinity to FcgRIII and thereby dramatically improves its antibody-dependent cellular cytotoxicity (ADCC). To address these industry-specific needs, we have inactivated the GDP-fucose transporter in CHO cells. The DHFR and GS genes have also been inactivated in these cells as selection markers. Using these cells, stable lines have been developed to produce fucose-free rituximab and fucose-free obinutuzumab (Gazyva).

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

ENGINEERING HOSTS: CHO CELLS (CONT.)

16:15 A Big Step Forward for Next-Generation CHO Clone Characterization and Selection

Oliver Popp, Dr. rer. nat., Senior Scientist, Pharma Research and Early Development, Large Molecule Research, Roche Innovation Center Munich, Roche Diagnostics GmbH

In-depth characterization of high-producer cell lines and bioprocesses is vital to ensure robust and consistent production of recombinant therapeutic proteins in high quantity and quality for clinical applications. For that, we established a novel hybrid approach for supporting comprehensive characterization of metabolic CHO clone performance. The proposed approach also provides a mechanistic link between observed clone phenotype, process setup, and feeding regimes, and thereby offers concrete starting points for subsequent process optimization.

16:45 FEATURED PRESENTATION: Engineering the CHO Cell

Bjørn Voldborg, MSc, Director, CHO Cell Line Development, Novo Nordisk Foundation Center for Biosustainability (CFB), DTU Biosustain, Technical University of Denmark

Using high-throughput (HT) technologies, the CHO Cell Line Engineering project at the Center for Biosustainability is genetically modifying CHO cells based on experimental and *in silico* generated data, to engineer CHO cell lines optimised for the production of therapeutic proteins. The HT cell line engineering pipeline as well as examples of the engineered improved cell lines will be described.

17:15 Cmax: A Heterotrophic Cell Platform for Improved Biologics Production

Nicky C. Caiazza, Ph.D., Principal Scientist, Metabolic Engineering and Synthetic Biology, Heterotrophic Cell Systems, Synthetic Genomics Inc.

We have developed a robustly fermentative heterotrophic system for efficient end-to-end biologics discovery, development and manufacturing. This platform has intrinsic advantages for biologics production and a suite of synthetic biology tools that has enabled high productivity (>1 g/l/d) mAb production with beneficial attributes for downstream processing. Here we show that these organisms can be engineered to secrete genuine, functional monoclonal antibody with favorable characteristics related to protein production and quality.

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17:45 Problem-Solving Breakout Discussions*
*See website for details.

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

19:15 End of Day

THURSDAY 3 NOVEMBER

08:00 Registration and Morning Coffee

CASE STUDIES: PROTEIN TO PRODUCT

08:30 Chairperson's Remarks
Henry C. Chiou, Ph.D., Associate Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific

08:35 Expression of IgG in Genetically Engineered *E. coli*
Na Ke, Ph.D., Research Scientist, Protein Expression and Modification Division, New England Biolabs
We have expressed for the first time in the cytoplasm of *E. coli* full-length human, rabbit and mouse antibodies, along with chimeric versions, including the commercial blockbuster Humira. The expression is further improved by the co-expression of a series of protein-folding helpers. Microbial expression of IgG offers an expanded potential for rapid screening, engineering and expression antibodies.

09:05 Meeting Demand: Optimisation of Our Transient Expression Platforms to Increase Throughput and Titre
Christina Gordon, Scientist, New Meds, UCB Pharma
Development of antibody therapeutics, from early stage research to preclinical and clinical development, requires ever-increasing amounts of reagents. To meet the challenge of furnishing a diverse and full pipeline, we utilise several different transient platforms. Through continuous optimisation, streamlining and automation of component parts of our panel of platforms (utilising both HEK293 and CHO host cells with a variety of transfection methods), we now have the capability to produce microgram-to-gram quantities of panels of purified antibodies and antibody fragments in as few as four weeks from receipt of plasmid DNA.

09:35 Server of Many Masters: The Challenges of a Slim Protein Expression Core Facility
Tsafi Danieli, Ph.D., Director, BioGiv Excubator & Head, Protein Expression Facility, Wolfson Centre for Applied Structural Biology, Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem
Running a small core facility that serves multiple academic groups with a wide range of disciplines is extremely challenging. Trying to do it with one technician, two postdocs and no automated platforms sounds like mission impossible. However, it is all about the surrounding! An academic environment and supporting ecosystem allowed our facility to turn the challenge into a new model that successfully accommodates not only academic groups but also early stage biotech startups.

10:05 Application of Streamlined Processes to Improve Process Productivity and Throughput
Sponsored by FUJIFILM Diosynth Biotechnologies
Nazanin Dadehbeigi, Ph.D., Principal Scientist, Programme Design Group, FUJIFILM Diosynth Biotechnologies

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

CASE STUDIES: PROTEIN TO PRODUCT (CONT.)

11:15 Efficient Production of Recombinant Human Monoclonal Antibodies from Single B Cells
Hugo Mouquet, Ph.D., Head, Laboratory of Humoral Response to Pathogens, Immunology, Institut Pasteur
The molecular dissection of anti-pathogen B-cell responses using modern technologies to efficiently generate and characterize antigen-specific human monoclonal antibodies has allowed breakthrough discoveries in antiviral responses to viruses such as Influenza virus and HIV-1. These recombinant antibodies represent unique "fingerprints" for each B-cell clone and when characterized at a molecular and functional level, provide crucial information to help developing therapeutic and vaccine strategies against a given pathogen.

11:45 FEATURED PRESENTATION: Expressing Challenging Proteins at the SGC
Nicola Burgess-Brown, Ph.D., Principal Investigator, Biotechnology, Structural Genomics Consortium (SGC), University of Oxford
The SGC has solved >1700 human protein structures and 6 novel integral membrane proteins. Although we have significantly contributed to structural biology and protein production for functional studies, there are many highly desired targets including protein-protein complexes and known drug targets that remain a challenge to obtain. We present our established expression systems using *E. coli* and BEVS, and new processes (BacMam and mutagenesis) to generate the most difficult-to-produce proteins.

12:15 Enjoy Lunch on Your Own

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

13:30 End of Optimising Expression Platforms

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2nd Annual

Protein Purification Technologies

Streamlining Processes to Achieve Quality

THURSDAY 3 NOVEMBER

12:30 Registration

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

PRODUCTIVITY STRATEGIES

13:30 Chairperson's Opening Remarks
Ana Cecília Afonso Roque, Ph.D., Assistant Professor, Chemistry, UCIBIO, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa

13:35 KEYNOTE PRESENTATION:
Biopharmaceuticals: Past, Present & Future
Frank Riske, Ph.D., Senior Consultant, BioProcess Technology Consultants (BPTC)

14:20 Molecular Properties of Antibodies and Their Derivatives Impacting Manufacturing
Stefan Schmidt, Ph.D., MBA, Vice President, Process Science & Production, Rentschler Biotechnology
Certain molecular properties and process conditions can lead to aggregation, truncation and chemical modifications complicating downstream processing. Particularly highly engineered molecules differing from the original antibody format require a careful evaluation of parameters like contact time, ligand density, elution pH, capacity, etc. to identify optimal settings for the initial capture step. Several examples and case studies illustrate the general approaches undertaken to deliver high-quality antibodies and derivatives taking into account their molecular properties.

14:50 Quality Control of Recombinant Proteins: Best Practice Recommendations
Mario Lebendiker, Ph.D., Head, Protein Purification Facilities, Wolfson Centre for Applied Structural Biology, The Hebrew University of Jerusalem
Around 200 specialists in protein production and in biophysical characterization of biomolecules, of the most important Core facilities in Europe and Israel, have formed a joint initiative to establish guidelines on recombinant protein quality.
The Production and Purification Partnership in Europe (P4EU) and the Association of Resources for Biophysical Research in Europe (ARBRE-MOBIEU) aim to develop a best practice/minimal standard for the quality control of recombinant proteins to ensure that the input material used in biophysical and biochemical research is of high quality, which, in turn, will result in optimized data quality. The prescribed tests must be both feasible by all protein production labs, and, at the same time, acceptable for biophysical or structural biology labs as admission criteria. A series of 'best-practice' methods is suggested for further characterization. To include an extended discussion with conference delegates.

15:20 Refreshment Break in the Exhibit Hall with Poster Viewing

ENHANCING PURIFICATION PROCESSES USING HIGH-THROUGHPUT TECHNIQUES

16:05 Development of an Automated Parallel System for Production of High-Quality Lead Candidate Antibodies – Keeping Pace with Researchers' Appetites
Lars Linden, Ph.D., Head, Protein Biochemistry, Bayer HealthCare
In early research, project teams profile multiple antibody candidates in functional and often cell-based assays. Within a growing portfolio, this leads to an increasing resource need for the production of mg amounts of high-quality antibodies. To meet this demand, transient transfection and expression were automated, a novel high-throughput 2-step chromatography system was set up, and an integrated automation concept for sample handling was developed.

16:35 Enhancing Operational Efficiency during Protein Purification
Martin Bader, Ph.D., Head, Biochemistry, Roche Pharmaceuticals
Purification of bispecific antibodies is often more labor-intensive due to complex impurity profiles. We have systematically analyzed and optimized individual process steps during preclinical protein supply. We have developed work flows that reduce operator time and combine critical pooling decisions with high-throughput analytics. In addition, generic steps are either automated or outsourced. In summary, we present a highly efficient purification platform for next-generation proteins.

17:05 End of Day

17:00 Dinner Short Course Registration

Recommended Dinner Short Course*

SC7: Protein Purification Strategies: Dealing with Proteins that are Prone to Aggregate
**Separate registration required, please see page 4 for details.*

FRIDAY 4 NOVEMBER

08:00 Registration and Morning Coffee

INCREASING SOLUBILITY AND PURIFYING MEMBRANE PROTEINS

08:30 Chairperson's Remarks
Stefan Schmidt, Ph.D., MBA, Vice President, Process Science & Production, Rentschler Biotechnology

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08:35 Continuous Aqueous Two-Phase Extraction of Proteins – Novel Process Windows by Increasing Protein Solubility

Christoph Brandenbusch, Ph.D., Group Leader, Department of Biochemical and Chemical Engineering, Laboratory of Thermodynamics, TU Dortmund University

Increasing product titers in pharmaceutical protein production led to a demand for novel workup strategies (e.g. protein extraction by Aqueous Two-Phase Systems). However, the effort and costs required in selecting appropriate ATPS and process windows hinder the industrial applicability. Hybrid modeling approaches enable the estimation of efficient phase formers and novel displacement agents. This allows for both a selective purification and stabilization of the protein in solution by increasing solubility.

09:05 Resolving Perplexing Purification Paradigms with CD-FAST: Calcium Dependent Fragment Assembly Separation Technology

David O'Connell, Ph.D., Lecturer & Director, Biomolecular & Biomedical Science, University College Dublin, and Founder, YourProteome

Membrane proteins and chaperone-assisted cytosolic proteins prove to be particularly perplexing when it comes to isolating them in sufficient quantity and purity for downstream assays. Most rationales involve multi-step strategies that consume valuable amounts of protein. The application of CD-FAST technology is a powerful innovation in the single step isolation of pure, functional proteins with recent advances in GPCR and aggregation-prone kinase purification and downstream assay reported here.

09:35 A Saposin-Based Nanoparticle System for Stabilization of Membrane Proteins

Jens Frauenfeld, Ph.D., CEO, Salipro Biotech AB

We present a saposin-lipoprotein nanoparticle system, which allows for the reconstitution of membrane proteins in a lipid environment. We demonstrate the applicability of the method on purified membrane proteins as well as by the direct solubilization and nanoparticle incorporation of membrane protein complexes from the virus membrane. The Salipro system allows for high-resolution cryo-EM of membrane proteins and is applicable for the development of novel drugs, vaccines and therapeutic antibodies.

10:05 Coffee Break in the Foyer with Poster Viewing

AFFINITY PURIFICATION

10:35 Versatile Affinity Ligands for Bioseparation Processes

Ana Cecília Afonso Roque, Ph.D., Assistant Professor, Chemistry, UCIBIO, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa

We employed biological and chemical combinatorial libraries supported by computational design tools to develop robust peptidomimetics based on different scaffold molecules. The scaffold molecules ranged from small synthetic ligands, to artificial β-hairpin peptides and small protein domains produced chemically. We studied the potential of these scaffold affinity reagents to find binding partners against several targets (e.g. recombinant proteins, phosphorylated peptides, and virus-like particles), and to develop affinity-based purification processes.

11:05 Affitins as a Novel Tailored Class of Robust Reagents for Affinity Chromatography Purification of Antibodies and Non-Immunoglobulin Proteins

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

This presentation reveals how Affitins can be used as ligands to design affinity columns for one-step purification of human immunoglobulin G (hIgG), with 95% purity and recovery of 100%. Affitin production in *E. coli* makes it possible to produce these affinity columns at low cost. Our results validate Affitins as a new class of tailored ligands for the affinity purification of potentially any proteins of interest including biopharmaceuticals.

11:35 A Novel IgG-Binding Purification Matrix for Mild Elution

Sophia Hober, Ph.D., Professor, Biotechnology, KTH-Royal Institute of Technology

Antibodies are widely used affinity molecules in many fields of biological science and the therapeutic field for monoclonal antibodies is constantly growing. The most common method for purification of antibodies is protein A affinity chromatography. It offers high-selectivity, and yields pure and concentrated antibodies. One of the major issues with protein A purification is the low pH that is essential to elute the bound antibody from the column. Here, we have addressed this by protein engineering of the IgG-binding domain from protein A.

12:05 Sponsored Presentation *(Opportunity Available)*

12:35 Problem-Solving Breakout Discussions with a Light Snack in the Foyer*

**See website for more details.*

13:35 Session Break

IMPROVING AND INNOVATING PURIFICATION PROCESSES

14:00 Chairperson's Remarks

Christoph Brandenbusch, Ph.D., Group Leader, Department of Biochemical and Chemical Engineering, Laboratory of Thermodynamics, TU Dortmund University

14:05 Peptides in Headlock: A Novel Nanobody-Derived Capture/Detection System

Ulrich Rothbauer, Ph.D., Professor, Pharmaceutical Biotechnology, University of Tübingen

Single-domain antibodies (nanobodies) have emerged as an attractive alternative to traditional antibodies and have become highly valuable tools for numerous bioanalytical and biotechnical applications. Here we present a novel nanobody-derived capture/detection system that enables a fast and efficient isolation of epitope-tagged proteins from prokaryotic and eukaryotic expression systems. The high-affinity-binding and modifiable peptide tag of this system renders it a versatile and robust tool to combine biochemical analysis with microscopic studies.

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14:35 Case Study: Human Kinase Crystallization, Phosphatase Co-Expression

Mario Lebendiker, Ph.D., Head, Protein Purification Facilities, Wolfson Centre for Applied Structural Biology, The Hebrew University of Jerusalem

We present a case study of production of a human Kinase co-expressed in *E.coli* cells together with phosphatase in order to get a homogeneous, non-phosphorilated, and crystallizable protein. The reproducible production of different batches in *E.coli* allow us to successfully crystallize our target with a great variety of ligands with possible therapeutic implications. We describe our expression and purification approach, bottlenecks, etc. Since this protein was crystallized in the past, this case study emphasizes the need to establish "minimal protein quality information" in publications in order to assure reproducibility of results.

15:05 Use of Succinylated Trypsin as a Manufacturing Aid

Nina Madsen, M.S., Scientist, Downstream Process Development, Bristol-Myers Squibb

We present a robust method for the charge modification of lysine residues on trypsin, by way of an acylation reaction between succinic anhydride and the lysine functional group. We then demonstrate the use of this modified enzyme as a tool in the downstream manufacture of a recombinant microbial product. Our protein is expressed in *E. coli* as a prohormone precursor and is enzymatically converted to the desired product using trypsin.

15:35 Development of a Robust Ultrafiltration/Diafiltration Step for Highly Concentrated Drug Substance Using High-Throughput Methods and Aggregation Modelling

Dejan Arzensek, Ph.D., Research Scientist, Downstream Process Development, Sandoz Biopharmaceuticals

The present study focused on evaluating critical parameters within the Ultrafiltration/Diafiltration (UF/DF) operation that lead to aggregation due mainly to the physical instability of therapeutic mAbs. Insight into the physical instability of the protein in solution was achieved by using a directed approach based on a more detailed biophysical characterization required to ensure successful process development. Aggregation and particle formation were monitored using multiple analytical techniques for UF/DF conditions tested.

16:05 A New Shaped Rocking Bioreactor for Insect and Mammalian Cells

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

Wave-rocking bioreactors have increasingly replaced traditional stainless steel stirred tank reactors for large-scale cultivation of insect or mammalian cells during the last decade. Disposable wave bags are available in many shapes and sizes from several commercial providers. In research laboratories, however, production in wave bags is much less established for cost reasons and still mainly performed in shaking flasks. We will discuss how we have developed a re-usable, fixed-shaped bioreactor, which can be used on the diverse rocking unit platforms that control temperature, aeration rate, rocking speed, and rocking angle.

16:35 End of Conference

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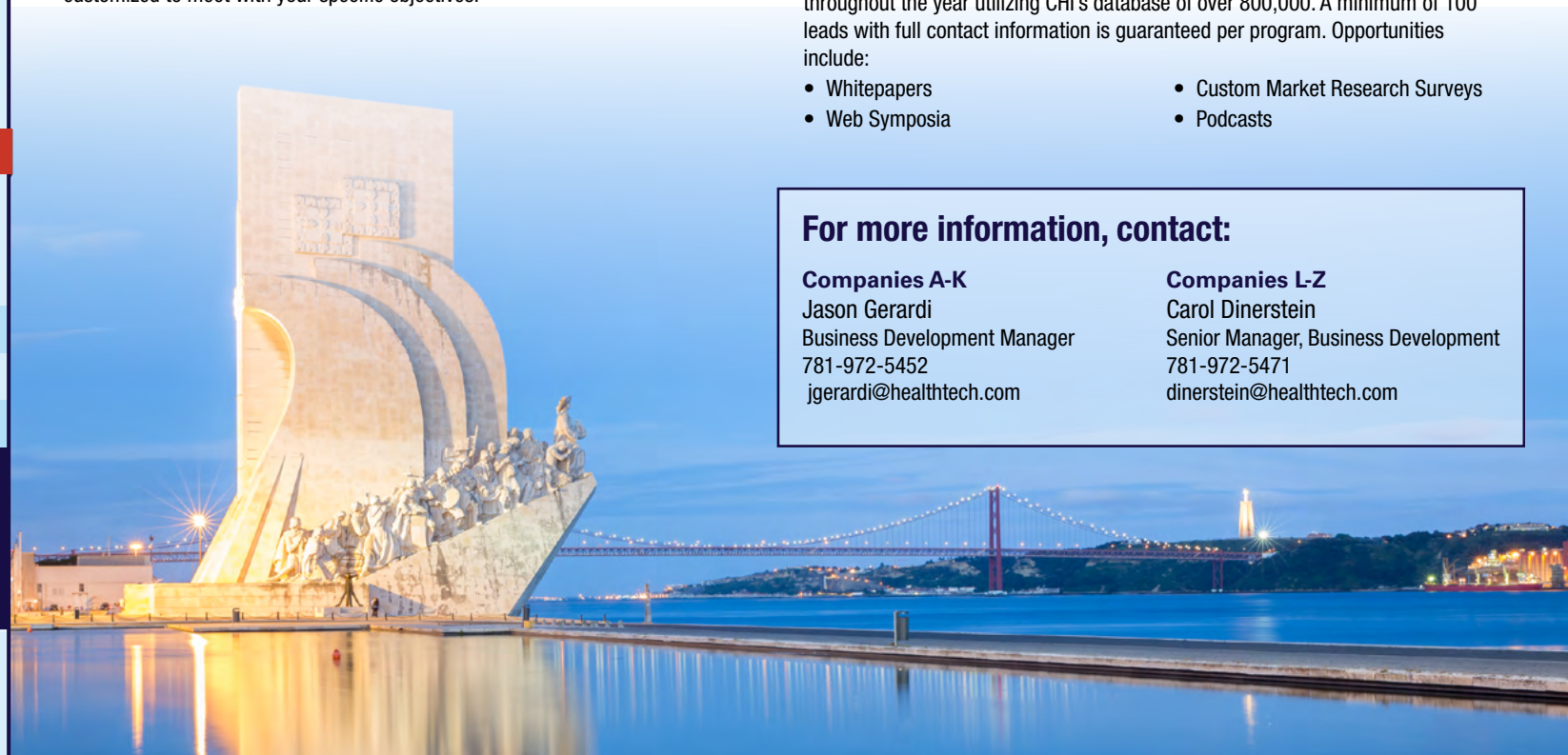

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Avenida Engenheiro Duarte Pacheco 15,
1070-100 Lisbon, Portugal
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