

Engineering

- Display of Biologics
- Engineering Antibodies
- Engineering Bispecifics

Oncology

- Antibody-Drug Conjugates
- Advancing Bispecifics
- Novel Targets for Cancer

Analytical

- Optimisation & Developability
- Analytical Characterisation
- Aggregation & Stability

Immunotherapy

- Tumour Microenvironment
- CAR T, TIL & TCR Therapy
- Agonist Immunotherapy Targets

Expression

- Systems Engineering
- Optimising Expression
- Purification Technologies

Bispecifics

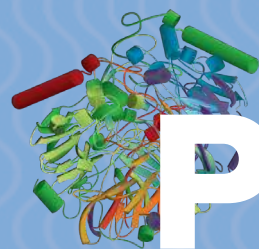
- Advancing Bispecifics
- Engineering Bispecifics

Training Seminars

- Deep Sequencing and Single Cell Analysis
- Intro to Bispecifics
- Genome Editing with CRISPR
- Biologics Formulation and Delivery

FINAL AGENDA

SAVE UP TO €200, REGISTER BY 11 OCTOBER



11th Annual

PEGS EUROPE

Protein and Antibody Engineering Summit

18-22 NOVEMBER 2019 ■ LISBON, PORTUGAL ■ LISBON CONGRESS CENTER

2019 PLENARY KEYNOTES



Bispecific, Soluble TCR as the Next Therapeutic Platform

Bahija Jallal, PhD
CEO and Director of the Board, Immunocore



Attacking Cancer Cell Surfaceomes with Recombinant Antibodies

James A. Wells, PhD
Professor, Departments of Pharmaceutical Chemistry and Cellular & Molecular Pharmacology, University of California, San Francisco

- Be part of a growing event – attendance has increased more than 50% since 2016
- Network with 1,300 colleagues at Europe's leading protein engineering event
- See unpublished data & case studies from leading researchers from industry & academia
- Learn from 260 speakers and 250 poster presenters

PEGSummitEurope.com

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MONDAY - TUESDAY (18 - 19 November)

 ENGINEERING
 ONCOLOGY
 ANALYTICAL
 IMMUNOTHERAPY
 EXPRESSION
 BISPECIFICS
Training SEMINARS <small>By Cambridge Healthtech Institute</small>

Pre-Conference Short Courses*	Plenary Keynote Session	Display of Biologics
		Antibody-Drug Conjugates
		Optimisation & Developability
		Tumour Microenvironment
		Systems Engineering
		Deep Sequencing and Single Cell Analysis
		Intro to Bispecifics

WEDNESDAY - THURSDAY (20 - 21 November)

Dinner Short Courses*	Engineering Antibodies
	Advancing Bispecifics
	Analytical Characterisation
	CAR T, TIL & TCR Therapy
	Optimising Expression
	Advancing Bispecifics
	Genome Editing with CRISPR
	Biologics Formulation and Delivery

THURSDAY - FRIDAY (21 - 22 November)

Engineering Bispecifics
Novel Targets for Cancer
Aggregation & Stability
Agonist Immunotherapy Targets
Purification Technologies
Engineering Bispecifics

* Separate registration required for short courses

“The best biologics technology meeting in Europe:
A must-attend conference for novel biologics.”

Rakesh D., PhD, VP, AstraZeneca





Moderator's Opening Remarks



Kerry Chester, PhD
Professor, Molecular Medicine, University
College London Cancer Institute

Bispecific, Soluble TCR as the Next Therapeutic Platform



Bahija Jallal, PhD
CEO and Director of the Board, Immunocore
Of the two adaptive immunity recognition motifs, only antibodies have been brought to patients. However, antibody therapeutics only recognize 10% of human proteome (surface-expressed). The other motif, T cell receptor (TCR), has potential to unlock 90% of the human proteome, but requires converting a low-affinity, specificity membrane receptor into a soluble therapeutic. IMCgp100, a soluble, TCR bispecific-targeting melanoma, is the most advanced soluble TCR therapeutic in development.

Attacking Cancer Cell Surfaceomes with Recombinant Antibodies



James A. Wells, PhD
Professor, Departments of Pharmaceutical
Chemistry and Cellular & Molecular
Pharmacology, University of California,
San Francisco
The cell surface proteome (surfaceome) is the primary hub for cells to communicate with the outside world. Oncogenes are known to cause huge changes in cells and we find this translates to significant remodeling of the surfaceome. We generate recombinant antibodies to detect and then attack these cells by toxifying the antibodies or recruiting immune cells to kill. I'll discuss the technologies for surface protein analysis, an industrialized platform for rapid antibody generation using phage display, and using these tool reagents for target validation.



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MONDAY 18 NOVEMBER

09:00 - 12:00 | MORNING

SC1: Advanced Introductory Course on Making Antibody Libraries in Phage and Yeast

Instructor:

Andrew R.M. Bradbury, MB BS, PhD, CSO, Specifica, Inc.

This course will provide an advanced introduction to antibody engineering. Students will learn about antibody background, including structure, genetics and the generation of diversity, as well as the creation of naïve antibody libraries in the phage and yeast display formats. This will include a description of phage and yeast display technologies, the creation of naïve libraries from natural and synthetic sources, and the use of next-generation sequencing. The seminar will be fully interactive with students provided ample opportunities to discuss technology with the instructor.

SC2: The Tumour Microenvironment and Response to Cancer Immunotherapy

Instructors:

Stephen Beers, PhD, Professor, Immunology and Immunotherapy, Centre for Cancer Immunology, Cancer Sciences Unit, University of Southampton

Björn Fréndeus, PhD, CSO, BioInvent International AB

The tumour microenvironment (TME) is a complex, dynamic environment containing tumour cells, extracellular matrix (ECM), cytokines, immune cells, and stromal cells. These cell populations interact and influence each other to help the tumour grow and suppress immune responses. As well as propagating tumour growth and spread, the TME may also influence the response to immunotherapy. In this short course we will discuss the nature of the TME and the multiple ways in which it promotes an immunosuppressive environment. Opportunities to alter the TME in order to more effectively deliver immunotherapy will also be discussed. Finally, we will present and discuss emerging therapeutic approaches and consider how they might be used to enhance patient outcomes.

SC3: Mutation and Selection Strategies beyond Affinity Optimisation

Instructors:

Orla Cunningham, PhD, Senior Director, BioMedicine Design, Pfizer

Jonny Finlay, PhD, CEO, Ultrahuman

In therapeutic antibody discovery, few lead molecules meet all the demands required of a truly manufacturable drug. Most lead candidates require some form of engineering and optimization. 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.

SC4: Surfactants in Biotherapeutics: Can't Live with Them, Can't Live without Them

Instructors:

Atanas Koulov, PhD, Head, Drug Product Analytical Development and Quality Control, Drug Product Services, Lonza Pharma and Biotech

Hanns-Christian Mahler, PhD, Head, Drug Product Services, Lonza Pharma and Biotech

Additional Instructor to be Announced

Surfactants are excipients critical to the stability of most biopharmaceutical parenteral formulations. They stabilize proteins in solutions by mitigating potential adsorption and interfacial stress-induced aggregation or precipitation encountered during many stages of production, shipment and use. The most commonly used surfactants are the non-ionic excipients, Polysorbate 20 and 80. However, the use of these surfactants can also lead to a number of liabilities related to stability (of the surfactant and of the active protein) as well as potential for pseudoallergenic reactions. Regulatory authorities are therefore also paying increasing attention to this critical excipient. This workshop will provide a complete perspective on the use and control of polysorbates in biotherapeutic products.

SC5: Use and Troubleshooting of Eukaryotic Expression Systems

Instructors:

Richard Altman, MS, Field Application Scientist, Protein Expression, Biosciences Division, Life Sciences Solutions Group, Thermo Fisher Scientific

Henry C. Chiou, PhD, Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific

Dominic Esposito, PhD, Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research

THURSDAY 21 NOVEMBER

17:30 - 20:30 | DINNER

SC6: Selection, Screening and Engineering for Affinity Reagents

Instructors:

Nathalie George, PhD, Investigator III, NIBR Biologics Center, Discovery Technologies, Novartis Pharma AG

Christoph Erkel, PhD, Associate Director, Discovery Alliances & Technologies, MorphoSys AG

Biologics such as recombinant antibodies and alternative binding scaffolds are routinely used in a wide variety of applications from basic research to clinical indications. This success has led to the development of a vast number of different selection, screening and engineering technologies for these molecules. This short course will give a comprehensive overview on different display technologies as well as screening approaches for the selection of specific binders. In addition, it will discuss engineering strategies including affinity maturation and how to implement these strategies. Classical antibodies and antibody fragments as well alternative binding scaffolds will be covered.

SC7: Protein Aggregation: Mechanism, Characterization and Consequences

Instructors:

Instructors:

Thomas Laue, PhD, Professor Emeritus, Molecular, Cellular and Biomedical Sciences, University of New Hampshire

Kevin Mattison, Principal Scientist, Malvern Panalytical, Inc.

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



SC8: Advanced Analytical Technologies for Developability and Early Formulation Assessments

Instructor:

Danny K. Chou, PharmD, PhD, President, Compassion BioSolution, LLC

For biopharmaceuticals, drug design, lead selection and formulation/manufacturing process development constitute significant areas of risk because of their decisive influence on product quality, biological activity and safety, as well as cost of goods. The purpose of this short course is to introduce how a range of advanced analytical technologies, along with the concept of Quality by Design (QbD) may be incorporated at the interface of drug discovery and development in order to both select drug candidates with the best inherent stability and deliver the most suitable formulation for these molecules. Part of the course will be focused on the practical tools (both conceptual tools and analytical tools) one can use to achieve this objective.

SC9: T Cell Therapies: Current Field, Challenges and Future Directions

Instructor:

Reno Debets, PhD, Associate Professor, Laboratory of Tumor Immunology, PI, Medical Oncology, Erasmus MC-Cancer Institute

The field of Adoptive T cell therapy (AT) is advancing rapidly and with the FDA approval of T cell products expressing CD19-specific Chimeric Antigen Receptor (CAR) to treat B cell leukemias (Kymriah and Yescarta), it has entered a new era. However, significant challenges remain and need to be addressed to keep the momentum. These include safety assessment of target antigen and corresponding CARs or T cell receptors (TCRs), optimisation of T cell fitness, and the search for combinatorial approaches to enable T cells to target solid tumors. In addition to the preclinical trajectory, it is important to roll out these therapies in the clinical setting, which includes steps such as the manufacture and testing of clinical grade vector, development of efficient and reliable manufacturing methods, and delivering the therapies to patients safely, effectively and at a cost that is considered reasonable. This workshop will explore these important issues as we look to transition AT from the laboratory into mainstream medicine.

SC10: Engineering of Bispecific Antibodies and Multi-Specific Non-Antibody Scaffolds

Part 1: Engineering of Bispecific Antibodies

Instructor:

Simon Brack, PhD, Director External Innovation DPDS, Janssen Pharmaceutical Companies of Johnson & Johnson

Over the last decade, the field of bispecific antibodies (BiAbs) has significantly matured. Today, BiAbs represent a clinically validated class of therapeutic molecule as several products have been approved for different therapeutic indications and many others BiAbs are in clinical trials. Protein engineers have been incredibly active and inventive, providing numerous solutions to the fundamental problem of how to effectively combine two antibody specificities into a single molecule. These efforts resulted in the vast array of formats that is currently available. Different BiAb formats have distinct characteristics, supporting the unique modes of action that are enabled by BiAb. Beyond biology and therapeutic activity, manufacturing and stability of these innovative molecules has been and remains an important factor that can limit progression of BiAb towards the clinic.

By attending this interactive workshop, you will learn about the various approaches used for the engineering of bispecific antibodies. Different technologies will be compared and examples for applications of bispecific antibodies in drug development will be presented. Opportunities and challenges in the field of bispecific antibodies will be discussed, highlighting pros and cons of different approaches.

Part 2: Non-Antibody Multi-Functional Scaffolds

Instructor:

Mathieu Cinier, PhD, Scientific Director, Afflogic

Non-antibody scaffolds represent a new class of therapeutic molecules that fill a molecular weight gap between antibodies and peptides. While sharing the high specificity and potency of antibodies, their low molecular weight and simple structure make them amenable to peptide-like properties such as high tissue penetration. They are also easy to assemble, providing a straightforward “plug and play” approach to combine active modules into a single molecule that displays the desired druglike properties. At this age of multi-functional therapeutic molecules, non-antibody scaffolds continue to rise with an increasing number in ongoing clinical phases, making them valuable assets in the landscape of next generation biologics. In this interactive workshop, you will be provided with an overview on existing non-antibody scaffold technologies. Challenges in their development will be discussed together with their pros and cons regarding antibody-based therapeutics. Applications and therapeutic needs that are targeted with non-antibody scaffolds will be also addressed, highlighting the diversity of formats currently in development. Eventually, take home messages will be given over the review of several case studies.

**Separate registration required.*



Cambridge Healthtech Institute Training Seminars offer real-life case studies, problems encountered, and solutions applied, along with extensive coverage of the academic theory and background. Each training seminar offers a mix of formal lecture and interactive discussions and activities to maximize the learning experience. These training seminars are led by experienced instructors who will focus on content applicable to your current research and provide important guidance for those new to their fields.

MONDAY, 18 NOVEMBER AND TUESDAY, 19 NOVEMBER

DAY 1

13:30 – 18:20.....Training Seminars in Session
18:20 – 19:30.....Welcome Reception

DAY 2

8:30 – 18:30.....Training Seminars in Session
12:45.....Lunch Provided

Refreshment breaks and exhibit hall viewing hours also provided.

TS6A: Antibody Deep Sequencing and Single Cell Analysis

Instructors:

Brandon DeKosky, PhD, Assistant Professor, Department of Chemical Engineering, Department of Pharmaceutical Chemistry, Kansas Vaccine Institute, The University of Kansas

Matías Gutierrez Gonzalez, PhD, Postdoctoral Researcher, Pharmaceutical Chemistry, The University of Kansas

In this training seminar, participants will learn about recently developed methods for Next-Generation Sequencing (NGS) and single-cell analysis of antibody repertoires. Part 1 will provide an introduction to antibody repertoires, including genetic background, generation of diversity, and sequencing technologies. Part 2 will incorporate an introduction and hands-on session on computational tools for analyzing antibody repertoire NGS data. We will focus on pre-processing, analysis, and visualization of data, along with presentation of existing bioinformatics pipelines available. Part 3 will focus on an overview of the development of newer methods in single-cell analysis of antibody immune responses. The course will be interactive with case studies, and participants will be able to download data and examples. Please bring your computer.

TS7A: Intro to Bispecifics: History, Engineering, and Applications

Instructors:

Regis Cebe, MSc, Scientific Technical Leader, Novartis Biologic Center, NIBR, Novartis Pharma AG, Switzerland

Rakesh Dixit, PhD, DABT, President & CEO, Bionavigen

Intro to Bispecifics will be organized as an informative and practical guide to get up to speed on critical aspects of bispecific antibody therapeutics. Topics will include historical successes, failures, and lessons learned. Specific practical instruction will span mechanisms of action, engineering, developability, regulatory considerations, and translational guidelines. Perspectives on ideal implementation of bispecifics as targeted and immunomodulatory approaches will be discussed.

WHAT IS A TRAINING SEMINAR?

Each 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 and symposia hopping between conference programs, we ask that Training Seminars not be disturbed once they

WEDNESDAY, 20 NOVEMBER AND THURSDAY, 21 NOVEMBER

DAY 1

8:30 – 17:45.....Training Seminars in Session
12:45.....Lunch Provided
17:45 – 18:45.....Networking Reception
18:45 – 19:45.....Problem Solving Breakout Discussions

DAY 2

8:30 – 12:45.....Training Seminars in Session

Refreshment breaks and exhibit hall viewing hours also provided.

TS6B: Genome Editing with CRISPR: Toward Novel Research, Translational and Clinical Applications

Instructor:

Serguei V. Kozlov, PhD, MBA, PMP, Principal Scientist/PM, Team Leader PTO, Center for Advanced Preclinical Research, Frederick National Laboratory for Cancer Research (NCI)

This rigorous day-and-a-half program compiled for specialists interested in applying genome editing technologies for both basic and translational research will comprehensively review the state-of-the-art information on gene editing strategies and applications in various areas, such as disease modelling, drug discovery, and development. Beginning from introductory level basic technology aspects, key molecular features, strengths, and shortcomings of CRISPR/Cas9 systems, the instructor will advance towards sharing in-depth knowledge related to virtually all facets of present-day genome editing applications, such as constructing of cell culture-based experimental platforms, engineering disease models for *in vivo* research supporting preclinical drug development workflows, rational design and functional screening of sgRNA libraries, application of CRISPR/Cas9 technology for diagnostic and therapeutic purposes, and many others.

TS7B: Rational Approaches to Biologics Formulation and Delivery

Instructor:

Christina Vessely, PhD, Senior Consultant, CMC, Analytical and Formulation Development, Biologics Consulting

This course is intended to give participants an understanding of the basic principles of biologics formulation development, with an emphasis on maintaining long-term product stability. Participants should expect to come away with a better understanding of biochemical and biophysical properties of proteins and peptides, and how excipients and other strategies can be used to mitigate degradation. Formulation development discussions will cover both liquid and lyophilized dosage forms. The focus of the session will be on maximizing efficiency during formulation development, with an eye on regulatory compliance throughout the product development lifecycle. As such, following the introduction to formulation development, we will cover more complex formulation development topics, including strategies for the formulation of low solubility APIs, advice for the selection of container/closure systems and drug delivery devices, as well as the studies that must be performed to demonstrate the compatibility of those materials with the product.

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.

Display of Biologics

Leading the Way for New Classes of Therapy

Recommended Short Course*

SC1: Advanced Introductory Course on Making Antibody Libraries in Phage and Yeast

*Separate registration required. See pages 6 & 7 for details.

MONDAY 18 NOVEMBER

12:00 Conference Registration

IMPROVEMENTS IN PHAGE DISPLAY FOR AUTOIMMUNE AND ONCOLOGY

13:30 Organiser's Welcome

Christina Lingham, Executive Director, Conferences & Fellow, Cambridge Healthtech Institute

13:35 Chairperson's Opening Remarks

Ahuva Nissim, PhD, Professor, Antibody and Therapeutic Engineering, William Harvey Research Institute, Queen Mary University of London

13:45 Using Phage Display and Computational Approach to Dissect Structural Determinants of Celiac Disease Autoantibodies

Daniele Sblattero, PhD, Professor, Dipartimento Scienze della Vita, Università degli Studi di Trieste

Characterization of antibody repertoires is essential for understanding disease mechanisms involving humoral Ag-specific auto-immunity. Here we describe the construction and selection of antibody fragment libraries from celiac disease (CD) patients. Selected antibodies to tissue transglutaminase (TG2), a hallmark of CD, show a striking bias in VH and VL gene usage with clear preferences in pairing. By applying computational analyses based on selected Abs, we were able to successfully design *in silico* a synthetic TG2-directed Abs.

14:15 A New Phage Display Vector Allowing Direct Screening in IgG Format

Pierre Martineau, PhD, Deputy Director, Functional Screening and Targeting in Cancer, Institut de Recherche en Cancérologie de Montpellier, Inserm, Université de Montpellier - ICM

Display methods are restricted to antibody fragments and based on binding activity. However, the preferred format for therapeutic applications is the IgG, whose binding properties are affected by reformatting but also engages the immune system by its Fc part. We thus developed a display vector and an engineered mammalian cell line that allow both phage display and direct generation of cells stably secreting a monoclonal human IgG for functional screening.

14:45 A Novel scFv Antibody Fragment to Misfolded Alpha Synuclein as a Potent Modulator of Neuroinflammation by *in vivo* Intranasal Delivery

Jacob George, MD, Founder, Cognyx

A scFv (CGX208) that was cloned from Fab phage display libraries binds preformed fibrils and short alpha synuclein(aSyn) oligomers. CGX208 exhibited avid binding to brain extracts from patients with synucleinopathies. Intranasal delivery of CGX208 results in a significant attenuation of

neuroinflammation driven by misfolded aSyn and is effective in ameliorating motoric dysfunction in different *in vivo* experimental Parkinson's Disease models. CGX208 may prove a novel promising agent to treat aSyn mediated neuroinflammation.

15:15 Streamlined Discovery and Production of Therapeutic Antibodies

Lauri Peil, Key Account and Technology Officer, Icosagen


We take advantage of the universal HybriFree antibody discovery engine to efficiently discover therapeutic antibodies by direct cloning from B cells of immunized rabbit, chicken, human, or dog. HybriFree method is further powered by our patented QMCF expression platform to produce high-quality recombinant protein antigens, and antibodies cost-effectively for preclinical research (including afucosylated antibodies for enhanced ADCC). Technologies and case studies will be presented and discussed.

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15:45 Networking Refreshment Break

PLENARY KEYNOTE SESSION

16:15 Moderator's Opening Remarks


 Kerry Chester, PhD, Professor, Molecular Medicine, University College London Cancer Institute

16:20 Bispecific, Soluble TCR as the Next Therapeutic Platform

 Bahija Jallal, PhD, CEO and Director of the Board, Immunocore

Of the two adaptive immunity recognition motifs, only antibodies have been brought to patients. However, antibody therapeutics only recognize 10% of human proteome (surface-expressed). The other motif, T cell receptor (TCR), has potential to unlock 90% of the human proteome, but requires converting a low-affinity, specificity membrane receptor into a soluble therapeutic. IMCgp100, a soluble, TCR bispecific-targeting melanoma, is the most advanced soluble TCR therapeutic in development.

17:20 Attacking Cancer Cell Surfaceomes with Recombinant Antibodies

 James A. Wells, PhD, Professor, Departments of Pharmaceutical Chemistry and Cellular & Molecular Pharmacology, University of California, San Francisco

The cell surface proteome (surfaceome) is the primary hub for cells to communicate with the outside world. Oncogenes are known to cause huge changes in cells and we find this translates to significant remodeling of the surfaceome. We generate recombinant antibodies to detect and then attack these cells by toxifying the antibodies or recruiting immune cells to kill. I'll discuss the technologies for surface protein analysis, an industrialized platform for rapid antibody generation using phage display, and using these tool reagents for target validation.

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

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19:30 End of Day



Display of Biologics

TUESDAY 19 NOVEMBER
07:45 Registration and Morning Coffee
08:30 Chairperson's Remarks
David Lowe, PhD, Senior Director, R&D, Antibody Discovery and Protein Engineering, AstraZeneca
08:35 KEYNOTE PRESENTATION: Antibodies with Affinity Switches

Stefan Dübel, PhD, Professor & Chair, Technische Universität Braunschweig, Institute of Biochemistry, Biotechnology and Bioinformatics

Using cyclic mutants of human calmodulin as an allosteric effector module, antigen-binding affinity of various antibodies could be regulated. This allosteric effect was demonstrated for five different scFv fragments under physiological conditions without the need of pH or ion concentration changes. Antibodies could be both switched on or off, and the switch worked with the antibodies bound to living cells. Therefore, this approach may provide a universal strategy to obtain affinity-switchable antibodies without the need for individual paratope engineering, and to use these to fine-tune any immunomodulatory effect.

GENOME EDITING FOR ANTIBODY ENGINEERING

09:05 High-Throughput Antibody Engineering in Mammalian Cells by Homology-Directed Mutagenesis
Sai Reddy, PhD, Associate Professor, Department of Biosystems Science & Engineering, Laboratory for Systems and Synthetic Immunology, ETH Zurich

We have recently established a technique known as homology-directed mutagenesis (HDM), which is able to generate mutagenesis libraries directly in mammalian cells using CRISPR-Cas9. In HDM, we introduce genetic diversity into the genome of antibody-expressing cells by using site-specific or random mutagenesis DNA donor templates, which are integrated after Cas9 targeted double-stranded breaks. HDM enables several of the most essential methods of antibody engineering to be performed directly in mammalian cells expressing full-length IgG. This includes generation and screening of synthetic libraries for antibody discovery and affinity maturation.

09:35 Problem-Solving Breakout Discussions*
**See website for details.*
10:30 Coffee Break in the Exhibit Hall with Poster Viewing

NEW APPROACHES TO ANTIBODY LIBRARY GENERATION

Chairperson's Remarks
David Lowe, PhD, Senior Director, R&D, Antibody Discovery and Protein Engineering, AstraZeneca
11:15 SAMURAI (Solid-Phase Assisted Mutagenesis by Uracil Restriction for Accurate Integration) – A Method for Generation of High-Quality Antibody Libraries
Johan Rockberg, PhD, Assistant Professor, Protein Science, KTH Royal Institute of Technology

Mutagenesis libraries are essential for combinatorial protein engineering. Despite improvements in gene synthesis and directed mutagenesis, current methodologies still have limitations regarding the synthesis of complete antibody single-chain variable fragment (scFv) genes and simultaneous diversification of all six CDRs. Here, we present the generation and use of mutagenesis libraries for antibody affinity maturation, using a cell-free solid-phase technique for annealing of single-strand mutagenic oligonucleotides.

11:45 Generation of Neutralising Antibodies against Tenascin-C: Targeting Early Changes in the Synovial Microenvironment as a New Class of Immunotherapy?
Peter Slavny, PhD, Project Leader, IONTAS Ltd.

Tenascin-C is a matrix molecule that drives chronic inflammation in models of rheumatoid arthritis (RA) via activation of Toll-like receptor 4. Here, we will discuss the generation, optimization, and characterisation of neutralising antibodies, recognising the fibrinogen-like globe (FBG) of tenascin-C. These potentially constitute a new drug class that could offer early, disease-specific immune modulation in RA, without engendering global immune suppression.

12:15 Targeting Membrane Proteins Using Isogenica's Synthetic VHH Libraries

 Sponsored by

Guy Hermans, PhD, CSO, Isogenica Ltd

Isogenica's llamDA™ library is a highly diverse, fully synthetic single domain VHH library.

We will illustrate some of the unique benefits of VHH technology over conventional antibodies and demonstrate how the unbiased diversity and lack of tolerance enables rapid and resource efficient isolation of VHH to membrane proteins.

Examples will include the use of the library in 'whole cell' panning projects, as well as in selections using purified membrane proteins complexes.

12:45 Luncheon Presentation I: Streamlining the Biologics Development Process with the ExpiCHO Expression System

 Sponsored by

Chao Yan Liu, Associate Director, Cell Biology of the Life Sciences Solutions Group, Thermo Fisher Scientific

The ExpiCHO™ transient expression system offers a turnkey solution for generating high-titer recombinant proteins for therapeutic drug development, reagent generation, as well as an alternative platform for proteins that express poorly in 293-based systems. Here, we present data on the optimized expression of antibody and non-antibody proteins in the ExpiCHO Expression System as well as solutions for generating stable ExpiCHO cells lines for GMP manufacturing.

13:15 Luncheon Presentation II: Synthetic DNA Technologies Enable Antibody Discovery and Optimization

 Sponsored by

Aaron Sato, PhD, CSO, Biopharma, Twist Bioscience

Utilizing its proprietary DNA writing technology to create oligo pools, genes, and synthetic libraries, Twist Pharma, a division of Twist Bioscience, provides the biotechnology industry with an end-to-end antibody discovery solution. This solution includes (1) a panel of high-diversity synthetic antibody libraries, (2) a proprietary human anti-GPCR antibody phage display library focused on this validated target class, and (3) a Twist Antibody Optimization (TAO) platform for antibody affinity and developability optimization.

13:45 Dessert Break in the Exhibit Hall with Poster Viewing


Display of Biologics

NEXT GENERATION PLATFORMS FOR TARGET DISCOVERY

14:15 Chairperson's Remarks

Ana Barbás, PhD, Coordinator, Bayer Satellite Laboratory at iBET, iBET and Bayer Portugal SA

14:20 Synthetic Antibody Discovery against Native Antigens by CRISPR/Cas9-Induced CDR Variability

João Gonçalves, PharmD, PhD, Tenured Associate Professor, Faculdade de Farmácia Universidade Lisboa; Group Leader/Principal Investigator, Research Institute for Medicines/Instituto de Investigação do Medicamento (iMed.Ulisboa)

Despite the significant advances of antibodies as therapeutic agents, there is still much room for improvement concerning the discovery of these macromolecules. Here, we present a new synthetic cell-based strategy that takes advantage of eukaryotic cell biology to produce highly diverse antibody libraries, and simultaneously link them to a high-throughput selection mechanism, replicating B-cell diversification mechanisms. The interference of site-specific recognition by CRISPR/Cas9 with error-prone DNA repair mechanisms was explored for the generation of diversity, in a cell population containing a gene for a light chain antibody fragment. This targeted variability strategy can be integrated with an intracellular selection mechanism. We successfully obtained lead candidates against several therapeutic targets both as small-domain antibodies and fully human IgG.

14:50 From Nanobodies to Megabodies for Applications in Cryo-EM

Jan Steyaert, PhD, Francqui Research Professor at the Vrije Universiteit Brussel (VUB); Director, VIB-VUB Center for Structural Biology, VIB

Nanobodies (Nbs) are highly popular and versatile tools for structural biology. Here we report the development of megabodies, whereby Nbs are rigidly grafted into selected protein scaffolds to increase their molecular weight while retaining the full antigen-binding specificity. The megabody design principles are applicable to other scaffolds without size limitations and expand cryo-EM analysis to proteins that are small and/or display preferential orientation in ice, two major factors that limit the resolution of reconstructed density maps.

15:20 Next Generation Platforms for Antibody Discovery

Andrew R.M. Bradbury, MB BS, PhD, CSO, Specifica, Inc.

Antibody display libraries have served as a rich source of therapeutic antibodies. However, antibody leads selected from display libraries usually require downstream affinity and developability optimization, extending lead development timelines and costs. Specifica has established a unique antibody discovery display platform based on natural antibody sequences in which subnanomolar antibodies, requiring minimal optimization, are routinely selected.

15:50 High Quality Antibodies for Therapeutic Applications

Vera Molkenthin, PhD, Chief Scientist, AbCheck

AbCheck discovers and optimizes human antibodies for therapeutic applications leveraging several proprietary platforms, including *in vitro* and *in vivo* technologies. AbCheck delivers high-quality leads with subnanomolar affinities and good stabilities, which are compatible with different antibody designs, including bispecifics.

16:20 Refreshment Break in the Exhibit Hall with Poster Viewing

17:00 Discovery of Potent Human Therapeutic Antibodies Using Phage and Yeast Display Technologies

Thomas Bouquin, PhD, Head, Biologics Research France, Centre de Recherche de Vitry/Alfortville, Sanofi

This speech will present our strategy and process for the discovery of highly potent therapeutic human antibodies targeting soluble or membrane-anchored targets by means of phage display technologies, including naïve scFv, synthetic Fab, and immune libraries. Yeast display-based antibody engineering aiming at increasing antibody affinity or species cross-reactivity will also be presented.

17:30 Novel Strategies for the Generation of Yeast Surface Display and Phage Display Antibody Libraries

Stefan Zielonka, PhD, Associate Director, Protein Engineering & Antibody Technologies, Discovery Technologies, Global Research and Development, Merck Healthcare KGaA

Yeast Surface Display and Phage Display are promising platform technologies for antibody engineering. Still, generation of antibody libraries is a cumbersome process involving multiple steps. During this talk, a focused approach for the construction of antibody libraries using type IIs restriction enzymes will be presented. This method seems to be valid for the generation of diversities with adequate qualities.

18:00 Single-Cell Technologies for Interpreting Antibody Function on a Repertoire Scale

Brandon DeKosky, PhD, Assistant Professor, Department of Chemical Engineering, Department of Pharmaceutical Chemistry, Kansas Vaccine Institute, The University of Kansas

Recently developed technologies in paired heavy:light sequencing, native antibody library display, and computational analysis of NGS datasets have opened up new possibilities for discovering and annotating antibodies from large populations of single B cells. We will discuss the development and application of these technologies to pair native human antibody sequences with their functional targets and to identify new antibodies with desired functional properties.

18:30 Using Phage Display to Select soloMERS that Target Cryptic Epitopes

Caroline Barelle, PhD, MBA, CEO, Elasmogen Ltd.

SoloMERS are small, incredibly robust, single-chain binding domains. Elasmogen has exploited phage display to isolate these domains both from immunized and large diverse synthetic libraries against multiple therapeutic targets. This talk will focus on the propensity of these domains to bind cryptic epitopes and the advantages gained from combining these into multi-functional and multi-valent formats.

19:00 End of Display of Biologics



Engineering Antibodies

New Explorations in Antibody Engineering & Design

WEDNESDAY 20 NOVEMBER

07:45 Registration and Morning Coffee

NEW MODALITIES AND PLATFORMS

08:30 Chairperson's Opening Remarks

Janice M. Reichert, PhD, Executive Director, The Antibody Society, and Editor-in-Chief, mAbs

08:35 TriTAC: A Tri-Specific T Cell Engaging Platform for the Treatment of Solid Tumors

Bryan D. Lemon, PhD, Senior Director, Protein Science, Harpoon Therapeutics, Inc.

T cell engagers are protein therapeutics that tether T cells to surface antigens on tumor cells, leading to activation of those T cells and destruction of the tumor. The TriTAC (tri-specific T cell activating construct) technology is designed to optimize the therapeutic window by addressing half-life and stability limitations of pioneering T cell engagers (e.g., bispecific T cell engagers, or BiTEs). HPN424 first entered the clinic in 2018 and is under development for the treatment of metastatic castration-resistant prostate cancer.

09:05 The Making of a Biparatopic Molecule

Fernando Garces, PhD, Senior Scientist, Biologics Optimization, Amgen

Multispecific molecules show great promise as a vehicle to boost pharmacokinetic properties such as therapeutic efficacy and controlled toxicity. Biparatopic antibodies, bispecific molecules that recognize two unique and non-overlapping epitopes on the same antigen/target, have been shown to facilitate receptor internalization, promote superior antagonistic effect, among others. Here, we describe the making of a biparatopic molecule that recognizes two distinct domains on our target receptor. Using a structural-guided approach we have designed, generated and demonstrated that these novel bispecific formats can efficiently bind to both epitopes on the same molecule whereas cross-binding is restricted by the insertion of selected linkers.

09:35 RNAntibody® – A Potent mRNA Technology for Antibody Therapies

Johannes Lutz, PhD, Senior Scientist, CureVac

The delivery of genetic information has emerged as a promising alternative to overcome drawbacks associated with the use of recombinant proteins in protein therapies. Recently, we demonstrated that a single injection of antibody-encoding mRNA rapidly leads to high neutralizing antibody titers in animals, sufficient to provide fast protection against lethal rabies infection or botulinum intoxication. Additionally, we demonstrated that our RNAntibody technology is able to generate therapeutically effective amounts of antibodies in two different mouse models for malignant diseases.

10:05 An Integrated Approach to Managing Immunogenicity Risk and Optimum Protein Design

Jeremy Fry, PhD, Director of Sales, Prolimmune, Ltd.

Integrated platforms can be used to mitigate immunogenicity risk and characterize immune responses during the drug design and development stages. Prolimmune offers mutational activity mapping for optimal protein design, DC-T/T cell proliferation assays for biologic lead selection/optimization, a Mass Spectrometry assay for characterization of antigen presentation; HLA-peptide binding assays to characterize individual epitopes & undiluted whole blood cytokine storm assays.

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

11:15 Targeted Thorium Conjugates (TTCs): A New Modality for the Treatment of Cancer Utilizing Alpha Particle-Based Radiotherapy

Alan Cuthbertson, PhD, Head of Thorium R&D, TCR, Bayer AS

This talk will cover many preclinical aspects of cancer therapy using tumor antigen specific antibodies for the delivery of alpha particle radiation to tumors. The core elements of targeted alpha therapy will be explained along with a selection of data from *in vitro* and *in vivo* models demonstrating the potential of this versatile platform.

11:45 The Contorsbody, a Format for Agonism: Design, Structure, Function

Guy Georges, PhD, Expert Scientist, Large Molecule Research, Roche Innovation Center Munich

The contorsbody is a novel Ab format designed to achieve receptor dimerization. A hybrid structure combining X-ray diffraction and cryo electron microscopy data reveals a special architecture for this format. Depending on receptor and epitope, regular IgG antagonist antibody (ligand blocker or dimerization blocker) can be switched into full agonist when transformed into mono-specific bivalent contorsbody. Bispecific contorsbodies can be obtained via the "Knob into Hole" technology so that receptor hetero-dimerization or hetero-clustering can be achieved.

12:15 Preclinical Development of ELN/22, a Novel "Super-Neutralising" Solomer™ Specific for Human TNF-Alpha

Obinna Ubah, PhD, Senior Research Scientist, Biologics Drug Discovery and Protein Engineering, Elasmogen Limited Aberdeen

TNF α is implicated in a host of chronic autoimmune inflammatory diseases. Therapeutic targeting and subsequent neutralisation of TNF α has demonstrated positive clinical outcomes, however a significant percentage of these patients fail to respond or have their disease satisfactorily controlled with many patients discontinuing treatment due to life-threatening side effects. The ELN/22 drug candidate is an empirically designed novel biologic with a unique mechanism of TNF α neutralisation and delivers a superior efficacy in an *in vivo* model of polyarthritis. In addition, the ELN/22 has been designed to reduce the risk of ADA and serious side effects development.



Engineering Antibodies

12:45 Industrializing IO Therapeutic Discovery Platforms: Multispecifics, Engineered TCRs and CARs

Jana Hersch, Scientific Consultant, Biologics, Genedata

Novel classes of bio-molecules are currently evaluated for their use in cancer immunotherapy. Bi- and multi-specific antibodies, Ab-cytokine fusion proteins, non-Ig scaffolds, chimeric antigen receptors (CARs), engineered TCRs and TCR-based bispecific constructs promise significant advantages. However, these highly engineered molecules pose new challenges in design, engineering, cloning, expression, purification, and analytics. We present an infrastructure that addresses these challenges and enables the industrialization of these various novel therapeutic platforms.

13:15 Luncheon Presentation I: Integrated mAb Pipeline from Virtual Machine Learning to Transposon Mediated Cell Line Development

Claes Gustafsson, Co-Founder and CEO, ATUM (formerly DNA2.0)

Monoclonal antibodies in their many divergent formats have revolutionized medicine and today represents >\$100B/year in pharmaceutical sales. ATUM has built an integrated pipeline from generation of antigens via affinity maturation, developability, engineering and humanization all the way through scale up and stable cell line generation. The presentation will include case studies highlighting the process, each step uses technological breakthroughs in synthetic biology, machine learning, LIMS data integration, robotics and engineered transposases to ensure maximum efficiency.

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13:45 Luncheon Presentation II: Quality. Speed. Value. Therapeutic Antibody Discovery in Challenging Projects Using AlivaMab Mouse and AlivaMab Discovery Services

Larry L. Green, PhD, CEO, Ablexis and AlivaMab Discovery Services

AlivaMab Mouse delivers superior molecular diversity and greater numbers of high-affinity, high-potency therapeutic antibody candidates with faster timelines than other platforms. AlivaMab Discovery Services uses its proprietary processes to overcome the challenges of modern antibody drug discovery with industry-leading timelines. Case studies in the rapid generation of therapeutic quality antibodies with challenging discovery plans including against several GPCRs will be presented.

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14:15 Session Break

DEVELOPING SUCCESSFUL ANTIBODY PRODUCTS

14:30 Chairperson's Remarks

Fernando Garces, PhD, Senior Scientist, Biologics Optimization, Amgen

14:35 FEATURED PRESENTATION: Antibodies to Watch in 2020

Janice M. Reichert, PhD, Executive Director, The Antibody Society, and Editor-in-Chief, mAbs

The "Antibodies to Watch" talks and papers focus on antibody therapeutics in late-stage clinical studies, as well as those in regulatory review and recently approved in the United States and European Union. In this presentation, Dr. Reichert will provide an overview of approvals granted to antibody therapeutics in these regions in 2019, and predict which antibody therapeutics may be approved or move to regulatory review in 2020.

15:05 KEYNOTE PRESENTATION: Explorations in Antibody Product Discovery



Janine Schuurman, PhD, Corporate Vice President Research & Innovation, Antibody Research & Technology, Genmab

The basis for successful product discovery is a conceptual product idea which integrates scientific information on the biology of the disease and the target (or targets), and a thorough understanding of antibody format opportunities. Nevertheless, empirical screening of different target and antibody format combinations is critical, and often adaptations to initial assumptions are required before a novel product fulfilling the anticipated product criteria is discovered: the antibody fine specificity, combined with the format chosen, can have a huge and not always predictable impact on the functional characteristics of novel antibody product. Examples will be shared and discussed.

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

ANTIBODIES AGAINST MEMBRANE PROTEINS

16:15 Pipeline Update on GPCR and Ion Channel Antibodies

Catherine Hutchings, PhD, Independent Consultant

G protein-coupled receptors (GPCRs) and ion channels represent some of the most important drug target classes across a wide range of therapeutic areas. An update on antibody-based therapeutics in the pipeline will be provided outlining the breadth and diversity of the target landscape, as well as progress in clinical development. This presentation will also include a summary overview of antigen formats that have been successfully combined with different platforms to address the challenges inherently encountered with complex membrane protein targets.

16:45 Strategies to Isolate and Engineer Functional Antibodies against GPCR and Ion Channel Targets

Trevor Wilkinson, PhD, Associate Director, Antibody Discovery and Protein Engineering, AstraZeneca

G-protein-coupled receptors (GPCR) and Ion Channels represent challenging target classes for the isolation and optimization of therapeutic antibodies. In this presentation we review the technical challenges inherent in generating target antigens suitable for antibody isolation and strategies to overcome these challenges. Progress in this area will be illustrated by case studies demonstrating how we have applied phage display and immunization strategies to isolate and optimize functional, antagonistic monoclonal antibodies targeting GPCRs and ion channels.

17:15 ibody AD-214: A Novel Therapy for Fibrosis

Michael Foley, PhD, CSO, AdAlta Pty Ltd.

AD-214 is a single domain i-body with affinity for CXCR4, a GPCR which is known to be upregulated in a number of cancers and recently has been implicated in fibrosis. We have shown that AD-214 can block the recruitment of fibrocytes into the lungs of mice with bleomycin induced pulmonary fibrosis and that the anti CXCR4 i-bodies have anti-inflammatory and anti-fibrotic effects in several different animal models of fibrosis.

17:45 Networking Reception in the Exhibit Hall with Poster Viewing

18:45 Problem-Solving Breakout Discussions*

*See website for details.

19:45 End of Day



Engineering Antibodies

THURSDAY 21 NOVEMBER

08:00 Registration and Morning Coffee

DEEP SEQUENCING AND B CELL CLONING APPROACHES FOR ANTIBODY DISCOVERY & OPTIMISATION

08:30 Chairperson's Remarks

Jonny Finlay, PhD, CEO, UltraHuman

08:35 Deep Sequencing of Natural Antibody Repertoires for Antibody Discovery and Optimization and Elucidation of Repertoire Properties

Isidro Hotzel, PhD, Senior Scientist, Antibody Engineering, Genentech

Hybridoma and B cell cloning remain the main technologies for antibody discovery based on mining of natural immune repertoires. Deep sequencing technologies are now used to enhance repertoire sampling of these technologies for rapid identification of optimized antibody leads and *de novo* discovery. The application of deep sequencing to repertoire mining coupled to high throughput characterization of antibody panels also provides a broader view of how natural immune repertoires are structured.

09:05 Commonality Despite Exceptional Diversity in the Baseline Human Antibody Repertoire

Bryan Briney, PhD, Assistant Professor, Immunology & Microbiology, Scripps Research Institute

09:35 A Comprehensive Screening Platform to Identify the Next Generation Targeted Cancer Immunotherapy Targets

Stefanie Urlinger, PhD, Vice President, Antibody Development, iOmx Therapeutics AG

We have developed a systematic, high-throughput genetic screening approach that enables the identification and comprehensive validation of novel immune checkpoint targets in human cancer cells. Inhibition of these targets by a broad range of methods, such as CRISPR/Cas9 mediated gene knockouts, tool compounds or monoclonal antibodies, results in immune activation and enhanced T cell-mediated tumor cell killing in diverse tumor models. To date, we have validated various novel immune checkpoint targets that drive unique and previously undescribed immune evasion biologies – paving the way for innovative future cancer immunotherapies.

10:05 Talk Title to be Announced

Sherie Duncan, PhD, Manager Partners & Programs, AbCellera

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

NOVEL ENGINEERING APPROACHES FOR ANTIBODY DEVELOPMENT

11:15 Antibody Polyspecificity as a Critical Development Risk in Therapeutic Antibody Development

Jonny Finlay, PhD, CEO, UltraHuman

UltraHuman Eight has shown for the first time that antibody polyspecificity can be a direct cause of unpredictable side effects in the clinic. Novel insights into identification of off-target binding events and their remediation to create ideal, low-risk clinical leads will be presented.

11:45 Advancing Therapeutic Protein Development Using a Novel O-Glycan-Based Conjugation Approach

Monika Papworth, PhD, Senior Scientist, Antibody Discovery and Protein Engineering, AstraZeneca

Our technology represents an amalgamation of genome editing, cell line metabolic engineering and the application of a novel peptide-based tag to efficiently generate site-specific, homogeneously-labelled recombinant secretory proteins containing modified O-glycans. We demonstrate the facile addition of genetically-encoded O-glycosylation motifs and the robust incorporation of functionalised O-glycans to recombinant proteins using a UDP-galactose-4-epimerase (GALE) knockout, serum-free, cell expression system. This technology represents an elegant, controllable approach to generate bespoke, consistently labelled recombinant proteins 'On Demand'.

12:15 Luncheon Presentation I: Computational Immuno-Engineering Therapeutics against Hard Targets: Cracking into GPCR Antagonists & Blood-Brain Barrier

Sarah Ives, Principal Scientist & Director, Contract Research, Distributed Bio

Immune checkpoint inhibitors make attractive yet challenging targets for antibody discovery, where a therapeutic-ready monoclonal antibody can take years to be discovered and subsequently engineered. Here we describe a computational antibody library design that was optimized for both sequence diversity and engineering fitness through the analysis of thousands of human antibody repertoires. The technology enables routine discovery against previously challenging targets including GPCRs, pMHC complexes, and rare epitopes.

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12:45 Luncheon Presentation II: Synthetic Biology Capabilities of the BioXp™ 3200 System

Lindsey Wolf, Product Manager, Catalog Reagents, SGI DNA Inc.

The BioXp™ 3200 is a benchtop platform that enables researchers to rapidly synthesize high-quality DNA Libraries, Tiles and Clones in an automated fashion by simply uploading sequence files to a customer portal. The platform dramatically improves workflow productivity for a variety of applications such as protein production, antibody library generation and cell engineering giving more control over genomic workflows. This talk will focus on some of our recent developments for new capabilities on the BioXp.

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13:15 Dessert Break in the Exhibit Hall with Poster Viewing

14:00 End of Engineering Antibodies

17:00 Dinner Short Course Registration*

17:30 – 20:30 Dinner Short Courses

Recommended Short Course*

SC6: Selection, Screening and Engineering for Affinity Reagents

**Separate registration required. See pages 6 & 7 for details.*



Engineering Bispecifics

Next-Generation Approaches for Discovery, Screening and Optimising Bispecifics

THURSDAY 21 NOVEMBER

13:00 Registration

13:15 Dessert Break in the Exhibit Hall with Poster Viewing

INSIGHTS INTO EFFECTIVE BISPECIFIC MECHANISMS

14:00 Chairperson's Opening Remarks

Mark Chiu, PhD, Associate Director, BioTherapeutics Analytical Development, Janssen Research & Development LLC

14:05 KEYNOTE PRESENTATION: Turning Receptors Off and On with Bispecific Agents: Mechanistic Insights from Biophysics and Biochemistry



Andreas Plückthun, PhD, Professor & Director, Biochemistry, University of Zurich

Seemingly similar bispecific molecules, binding to the same receptors, can show very different biological behavior with dramatic consequences for their therapeutic suitability. Thus, bispecific agents may affect in opposite ways interaction with neighboring receptors, downstream signaling, internalization and subsequent degradation. A series of advanced biophysical methods have been developed to shed light on these phenomena, laying out blueprints for designing effective therapeutics.

14:35 Lisbon Wasn't Built in a Day – Alternative Scaffolds Gain Momentum

H. Kaspar Binz, PhD, Binz Biotech Consulting

The advent of alternatives to antibodies has been observed with large skepticism by the mAb community. It was while turning the academic ideas into businesses that the differentiating strengths of novel scaffolds crystallized. With safety doubts dispelled with clinical data, we now start to see alternatives to antibodies deliver differentiated drugs addressing unmet medical need in novel ways.

15:05 TCER® Platform: Targeting Of Tumor-Specific HLA Ligands Using T Cell Receptor Bispecifics

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Sebastian Bunk, PhD, Immunology, Immatics Biotechnologies GmbH

Bispecific T cell-engaging receptors (TCER) are soluble fusion proteins consisting of an affinity-matured T cell receptor targeting human leucocyte antigen-bound peptides and an antibody for recruitment of T cells and half-life prolongation. The design of the potent TCER molecules allows redirection of human T cells towards peptide-HLA targets showing highly selective expression in tumor tissue as validated by our target discovery engine, XPRESIDENT®. We present data supporting proof-of-concept of this novel class of T cell engagers.

15:35 Networking Refreshment Break

NEW PLATFORMS FOR DISCOVERY, PRODUCTION, AND IDENTIFICATION OF SYNERGISTIC TARGET PAIRS

16:00 A Simple IgG-like Discovery Platform for a Complex IgG-like (1+1) Format

Régis Cebe, MSc, Scientific Technical Leader, Novartis Biologic Centre, Novartis Institute of Biomedical Research

A variety of bispecific antibody formats are being developed at Novartis. The IgG-like (1+1) format is often preferred when maximal tolerability is in focus. Over the past years, we have been developing a technology platform that enables efficient discovery, engineering, and production of such bispecific format. Based on illustrative case studies, the power of this platform in advancing therapeutic bispecific projects will be highlighted.

16:30 A New Platform for the Identification of Synergistic Bispecific Combinations

Ulrich Brinkmann, PhD, Expert Scientist, Large Molecule Research, Roche Pharma Research & Early Development, Roche

Bi- and multispecific antibodies enable the exploration of new biological concepts and treatment strategies. Within Roche such next generation biologics have found broad application prospects in various disease areas. The presentation will focus on how format matters when designing multispecific onco-immunological antibodies and how this affects its biological activity, and a novel large-scale combinatorial platform to rapidly generate bispecific antibodies of different format and with different binders.

17:00 End of Day

17:00 Dinner Short Course Registration*

17:30 – 20:30 Dinner Short Courses

Recommended Short Course*

SC10: Engineering of Bispecific Antibodies and Multi-Specific Non-Antibody Scaffolds

*Separate registration required. See pages 6 & 7 for details.



Engineering Bispecifics

FRIDAY 22 NOVEMBER

08:00 Registration and Morning Coffee

ENGINEERING TO OVERCOME VIRAL RESISTANCE, TO CROSS THE BLOOD BRAIN BARRIER, AND FOR AUTOIMMUNE DISEASE

08:30 Chairperson's Remarks*H. Kaspar Binz, PhD, Binz Biotech Consulting***08:35 Multi-Specific Agent to Overcome Potential Resistance to Influenza***Mark Chiu, PhD, Associate Director, BioTherapeutics Analytical Development, Janssen Research & Development LLC*

A multi-specific agent was designed to target multiple epitopes on pan influenza strains. The engineering to prepare the relevant therapeutic product profile involving viral neutralization, immune effector function, and optimal pharmacokinetic profile will be presented.

09:05 Brain Penetrant Bispecific Agonist Antibodies to Neurotrophin Receptors TrkB and TrkC*Frank S. Walsh, PhD, CEO, Ossianix, Inc.*

Neurotrophins are attractive therapeutic targets for neurodegenerative disease, but their utility has been restricted by an inability to deliver therapeutic levels of the natural ligands, such as BDNF and NT3, to the CNS. We have used agonist antibodies to the receptors TrkB and TrkC and made them brain penetrant using VNARs to the transferrin receptor. The bispecific antibodies retain agonist activity *in vitro* and *in vivo*.

09:35 Preclinical Development of Xmab27564, a Long-Acting IL2-Fc Fusion Protein, as a Novel Treg-Selective Therapy for Autoimmune Diseases*Suzanne Schubert, PhD, Lead Scientist, Cell Biology, Xencor, Inc.*

Regulatory T cells are critical for maintaining immune homeostasis, and their deregulation is associated with autoimmunity. Low-dose IL-2 is used therapeutically to expand Tregs, but suffers from rapid clearance and a narrow therapeutic index. To solve these problems, we developed Xmab27564, an IL2-Fc fusion protein with reduced potency and longer persistence. Xmab27564 selectively expands Tregs in human PBMCs in mice and monkeys, supporting its clinical development in autoimmune diseases.

10:05 Networking Coffee Break

HIGH THROUGHPUT SCREENING APPROACHES FOR BISPECIFICS

10:35 Bispecific Target Discovery by High-Throughput Functional Screening*Pallavi Bhatta, PhD, Principal Scientist, Bispecific Target Discovery, UCB*

To exploit the potential of bispecific antibodies to discover new target pairs and invoke novel biology, we have developed technology that enables unbiased functional screening with large, combinatorial panels of bispecific antibodies. Our novel mix-and-match bispecific format allows grid-screening of thousands of bispecifics to hundreds of antigen combinations in high-throughput, disease-relevant assays. We will describe the discovery of several 'obligate' bispecifics across multiple disease areas, including autoimmunity, fibrosis, and oncology.

11:05 NestLink Technology to Determine Key Pharmacokinetic Parameters of Hundreds of Bispecifics Simultaneously*Pascal Egloff, PhD, Platform Leader, Medical Microbiology, University of Zurich*

NestLink enables the simultaneous characterization of thousands of different binding proteins without the need to handle individual clones at any stage of the process. The technology was previously applied *in vitro* for the efficient identification of high-affinity binders against integral membrane proteins in the cellular context. In this talk, I will show that NestLink can be applied *in vivo* as well, such as to simultaneously determine pharmacokinetic parameters of more than one hundred individual bispecific binding proteins in a single model organism.

11:35 Next-Generation CLD Platform for Advanced Bispecific Antibodies Expression*Severine Fagete, Director, Cell Line Services, Selexis SA*

Despite technologies that have advanced the forced heterodimerization of bi-specific antibodies (bsAb) and innovative purification procedures that remove homodimer by-products, new solutions that improve the bsAb production during the cell line development step are still needed. Here, we present a breakthrough cell line development platform using a single-cell system to express any bsAb format. Scalability and stability issue will be discussed and a case study of rescued bsAb program originally poorly expressing will be presented.

12:05 Problem-Solving Breakout Discussions with a Light Snack***See website for more details.*

FOCUS ON T CELL ACTIVATION, SPECIFICITY, PK, AFFINITY, AND MAXIMIZING THE THERAPEUTIC INDEX

13:00 Chairperson's Remarks*Annelise Vuidepot, PhD, Vice President, Pipeline Research, Immunocore***13:05 Specificity of Bispecific T Cell Receptors (TCR) and Antibodies Targeting Peptide-HLA***Annelise Vuidepot, PhD, Vice President, Pipeline Research, Immunocore*

Maintaining peptide selectivity is essential for the development of therapeutic agents targeting peptide-HLA complexes on cancer cells. Using multiple approaches, we assessed the selectivity of two novel classes of T cell redirecting pHLA-targeting bispecifics based on TCR-mimic antibodies or high-affinity TCRs. We show that peptide selectivity is associated with a broad and balanced energetic binding observed predominantly in TCR-pHLA interactions, whereas higher levels of cross-reactivity are associated with more focused 'hotspot' binding.

13:35 Dual Agonist Bispecific Antibody Targeting OX40 and CD137 Mediates Anti-Tumour Immunity and Synergises with PD-1/PD-L1 Blockade to Improve Survival in a Syngeneic Mouse Model*Francisca Wollerton, PhD, Director, Antibody Engineering, F-star*

CD137 (4-1BB) and OX40 are key mediators of costimulatory signals and they play important roles in driving anti-tumour immunity, but combination of CPI with costimulatory agonists has not delivered significant clinical benefit. The activity of Fcγ receptor-dependent agonists may be limited by suboptimal costimulation of T cells and inadequate clustering via Fcγ receptors. We have developed FS120, a dual agonist bispecific antibody that drives potent activation of T cells via co-engagement of CD137 and OX40 and independent of Fcγ receptor binding.

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Engineering Bispecifics

14:05 Optimization of Preclinical Safety and Efficacy of Anti-HER2/CD3

Teemu Junttila, PhD, Senior Scientist, Translational Oncology, Genentech, Inc.

Systemic cytokine release and on-target/off-tumor toxicity on normal tissues are the main adverse effects limiting the applicability of T cell-redirecting bispecific antibodies. We have investigated how affinity to HER2 and CD3 impacts anti-tumor efficacy, distribution, and pre-clinical safety of anti-HER2/CD3 TDB and describe that affinity has a major impact on tolerability. Our studies suggest that fine-tuning the affinities to both the antigen and CD3 is likely critical to maximize therapeutic index in clinical use.

14:35 Concept to Clinic: Development of Fc-containing XmAb Bispecific Antibodies for Immunotherapy

Umesh Muchal, PhD, Director, Molecular Biology & Protein Sciences, Xencor, Inc.

We present a robust and modular heterodimeric Fc platform, engineered for efficient development of bispecific antibodies and Fc fusion therapeutics. These XmAb bispecific molecules are effective, stable, and easy to manufacture, and allow for the design of potent and/or tunable molecules with enhanced therapeutic index and safety profile. Several tumor-targeting CD3 bi-specifics and dual checkpoint-blocking molecules developed using this platform are in early clinical testing.

15:05 Engineering Mono- and Multi-Valent Inhibitors on a Modular Scaffold

Aurora Diamante, Scientist, Pharmacology, University of Cambridge

We have exploited simple, ultrastable, modular architecture of consensus-designed tetratricopeptide repeat proteins (CTPRs) to build a platform capable of displaying single and multiple functions with diverse geometrical arrangements. Our results point to the tremendous potential of the CTPR platform to exploit the 100,000+ SLiMs in the human proteome and build synthetic protein binders with multi-valent and multi-specific capabilities arrayed with precise pre-programmed geometries.

15:35 End of Engineering Bispecifics

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Next-Generation Antibody-Drug Conjugates

Engineering Strategies & Success

Recommended Short Course*

SC2: The Tumour Microenvironment and Response to Cancer Immunotherapy

*Separate registration required. See pages 6 & 7 for details.

MONDAY 18 NOVEMBER

12:00 Conference Registration

FIGHTING CANCER WITH ADCs

13:30 Organiser's Welcome

Mary Ruberry, Senior Biomedical Conference Director, Cambridge Healthtech Institute

13:35 Chairperson's Opening Remarks

James Baker, PhD, Associate Professor, Chemistry, University College London

13:45 FEATURED PRESENTATION: NBE-002, an Anthracycline-Based Immune-Stimulatory Antibody-Drug Conjugate (iADC) Targeting ROR1 for the Treatment of Triple-Negative Breast Cancer



Roger Beerli, PhD, CSO, NBE-Therapeutics AG

Presenting the profound *in vivo* anti-tumor efficacy of NBE's lead iADC program, NBE-002, in preclinical, patient-derived triple-negative breast cancer models over a wide range of ROR1 expression levels, as well as the potent immune-oncology function of NBE's iADC platform.

14:15 MGC018: A Duocarmycin-Based ADC Targeting B7-H3

Deryk Loo, PhD, Director, Targeted Therapeutics and Site Operations, MacroGenics, Inc.

MGC018 is an ADC comprised of the cleavable linker-duocarmycin payload, valine-citrulline-seco DUocarmycin hydroxyBenzamide Azaindole (DUBA), conjugated to a humanized anti-B7-H3 antibody through interchain disulfides. MGC018 demonstrated antitumor activity *in vivo* toward B7-H3-expressing tumor xenografts at clinically relevant doses. MGC018 was tolerated in cynomolgus monkeys at exposure levels exceeding those required for antitumor activity. Our findings support clinical development of MGC018 to evaluate its potential as a therapeutic for B7-H3-expressing solid cancers.

14:45 Amanitin-Based Antibody-Drug Conjugates as New Therapeutic Modalities for Cancer Therapy

George Badescu, PhD, Vice President, Scientific Affairs, Heidelberg Pharma AG

Antigen-Targeted Amanitin-Conjugates (ATACs) represent a new class of ADCs using the payload Amanitin. This payload introduces a novel mode of action into oncology therapy, the inhibition of RNA polymerase II. The technology platform includes Amanitin supply, site-specific conjugation, demonstrated safety profile and biomarker. HDP-101 is the first ATAC directed against BCMA entering Phase I trials in 2020

15:15 POSTER SPOTLIGHT

From Site-Selective Bioconjugation of Cysteines or Tryptophans to General Targeting of Aromatic Residues: Novel Chemistry for Bioconjugation, Structural Proteomics and Interactomics

Václav Matoušek, PhD, CEO, CF Plus Chemicals

15:45 Networking Refreshment Break

PLENARY KEYNOTE SESSION

16:15 Moderator's Opening Remarks



Kerry Chester, PhD, Professor, Molecular Medicine, University College London Cancer Institute

16:20 Bispecific, Soluble TCR as the Next Therapeutic Platform



Bahija Jallal, PhD, CEO and Director of the Board, Immunocore

Of the two adaptive immunity recognition motifs, only antibodies have been brought to patients. However, antibody therapeutics only recognize 10% of human proteome (surface-expressed). The other motif, T cell receptor (TCR), has potential to unlock 90% of the human proteome, but requires converting a low-affinity, specificity membrane receptor into a soluble therapeutic. IMCgp100, a soluble, TCR bispecific-targeting melanoma, is the most advanced soluble TCR therapeutic in development.

17:20 Attacking Cancer Cell Surfaceomes with Recombinant Antibodies



James A. Wells, PhD, Professor, Departments of Pharmaceutical Chemistry and Cellular & Molecular Pharmacology, University of California, San Francisco

The cell surface proteome (surfaceome) is the primary hub for cells to communicate with the outside world. Oncogenes are known to cause huge changes in cells and we find this translates to significant remodeling of the surfaceome. We generate recombinant antibodies to detect and then attack these cells by toxifying the antibodies or recruiting immune cells to kill. I'll discuss the technologies for surface protein analysis, an industrialized platform for rapid antibody generation using phage display, and using these tool reagents for target validation.

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

19:30 End of Day

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Next-Generation Antibody-Drug Conjugates

TUESDAY 19 NOVEMBER
07:45 Registration and Morning Coffee

ACHIEVING ADC SUCCESS FROM BENCH TO CLINIC – AND INTO MANUFACTURING

08:30 Chairperson's Remarks

Pedro MP Gois, PhD, Assistant Professor with Habilitation and Group Leader, Pharmaceutical Chemistry and Therapeutics, Universidade de Lisboa

08:35 KEYNOTE PRESENTATION: How to Build a Diversified Portfolio of Pyrrolobenzodiazepine-Based Antibody-Drug Conjugates



Patrick van Berkel, PhD, Senior Vice President, R&D, ADC Therapeutics, Ltd.

Pyrrolobenzodiazepine (PBD) dimers represent a promising new class of toxins for the development of antibody-drug conjugates (ADCs) and many PBD-based ADCs are currently in various stages of clinical development. This keynote will highlight some experiences when developing PBD-based ADCs from bench to clinic, with an emphasis on target, linker and toxin selection.

09:05 Effective Management of ADC Development and Clinical Manufacturing Including Outsourcing – A Big Pharma Perspective

Ulrich Rümenapp, PhD, Head, Launch Preparation and Coordination, Bayer AG

CMC development and manufacturing of ADCs has its special challenges. It is key for companies to establish a comprehensive plan for development including clinical supplies and towards BLA/MAA submission and licensure. This often involves outsourcing to CDMOs with the need for tech transfers. The presentation will review the benefits and challenges, best practices, and how to avoid pitfalls when developing, manufacturing and outsourcing the production of ADCs.

09:35 Problem-Solving Breakout Discussions*

*See website for details.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

ENGINEERING NEXT-GEN ADCs

11:15 ADCs Targeting CD163: A Platform for Modulating Macrophage Activity in Cancer and Inflammation – Preclinical Proof-of-Concept

Jonas Heilskov Graversen, PhD, Associate Professor, Molecular Medicine, University of Southern Denmark

We have utilized the macrophage specific internalization receptor CD163 as an ADC target for modulating macrophage activity in cancer and inflammation. We have obtained PoC data in mice, rats and pigs inflammatory models of sepsis and NASH, showing a 50-fold reduced effective dose of dexamethasone when targeted to macrophages. In a murine melanoma model, we observe increased tumor infiltration of effector T cells and T cell dependent tumor regression by eradicating CD163+ tumor associated macrophages.

11:45 Drug Conjugates Based on Engineered Affibody Molecules

Torbjörn Gräslund, PhD, Professor, Protein Science, KTH Royal Institute of Technology

Affibody molecules are small and robust alternative scaffold affinity proteins. We have recently investigated drug conjugates consisting of engineered affibody molecules with specific affinity for the HER2 receptor, coupled to the tubulin polymerization inhibitor DM1. Affibody molecules allow for site-specific drug attachment and easy control over DAR. We found that the drug conjugates were potent agents that prolonged survival of mice with human tumor xenografts.

12:15 POSTER SPOTLIGHT:

Isolation and Characterization of Light Chain Misassembled Bispecific Antibody Variants by Hydrophobic Interaction Chromatography and Knowledge Use for Production Cell Line Optimization

Thomas von Hirschheydt, Dr. rer. nat., Principal Scientist and Technical Development Leader, Roche Diagnostics GmbH

12:45 Luncheon Presentation I: Next Generation Phage Antibody Libraries for Drug Discovery: Enhanced Affinity & Developability Straight from Selections

Sponsored by


André Teixeira, PhD, Scientist, Specifica Inc.

To make good antibodies and antibody drug conjugates (ADC) it is important to start with antibodies with ideal developability profiles. In this work, we present a new antibody display library architecture designed to yield high affinity (pM or low nM range measured using SPR/Carterra), and highly developable antibodies straight from the initial selection campaign. The combination of natural diversity with clinically proven scaffolds enables the rapid discovery of good leads for ADC and antibody therapy.

13:15 Luncheon Presentation II: De-Risking ADC Development through Design and Developability Assessment

Sponsored by


Mark Frigerio, PhD, Vice President, Design and Development, Abzena

13:45 Dessert Break in the Exhibit Hall with Poster Viewing

INNOVATING BIOCONJUGATION AND LINKER TECHNOLOGIES

14:15 Chairperson's Remarks

George Badescu, PhD, Vice President, Scientific Affairs, Heidelberg Pharma AG

14:20 Site-Selective, Serum Stable ADCs by Disulfide Bridging and Cysteine Conjugation

James Baker, PhD, Associate Professor, Chemistry, University College London

This talk will describe the development and optimisation of the Next Generation Maleimide and Pyridazinedione reagent classes for the construction of ADCs. It will include a discussion of their use for the rapid formation of robustly stable ADCs by either rebridging the native disulfide bonds or conjugating to Thiomabs™ respectively. Insights into the construction of multispecifics using these reagents will also be made, along with recently discovered new conjugation platforms.

14:50 Exploring Boron Reagents for the Assembly of Functional Bioconjugates

Pedro MP Gois, PhD, Assistant Professor with Habilitation and Group Leader, Pharmaceutical Chemistry, Universidade de Lisboa



Next-Generation Antibody-Drug Conjugates

and Therapeutics, Universidade de Lisboa

Targeting drug conjugates, emerged as a powerful class of chemotherapeutic agents that are capable of sparing healthy tissues by liberating the cytotoxic payload only upon specific antigen recognition. A considerable body of work in this field highlighted that targeting drug conjugates therapeutic efficacy, correlates well with the conjugate homogeneity and activation of the drug at the diseased site. Therefore, the linker technology used to connect both functions contributes decisively to the therapeutic usefulness of these constructs. In this communication will be presented the use of boron-based complexes as functional linkers in the design of cancer cell targeting conjugates.

15:20 Developing Differentiated Next-Generation ADC Therapeutics

Robert Lutz, PhD, CSO, Iksuda Therapeutics

Improved ADC stability through novel PermaLink bioconjugation technology paves the way for use of novel payloads. A pipeline of differentiated next-generation ADC candidates is in preclinical development with the lead ADC candidate, IKS01, showing markedly improved efficacy compared to clinically-validated benchmark ADC in solid tumor models. Initiation of a Phase I clinical trial for IKS01 is expected to initiate in late 2020.

15:50 Clinical-Stage GlycoConnect Technology Enables ADCs with Superior Therapeutic Index

Floris van Delft, PhD, CSO, SynAffix BV, and Special Professor, Bioconjugate Chemistry, Organic Chemistry, Wageningen University

GlycoConnect™ is a site-specific antibody conjugation technology that does not require prior genetic modification, by applying the native glycan as a privileged attachment site for cytotoxic payloads. Combined with the polar HydraSpace™ technology, ADCs are readily generated from any IgG isotype in a straightforward two-stage procedure. GlycoConnect™ and HydraSpace™ technologies may be readily combined with a payload selected from Synaffix' toxSYN™ platform, covering multiple mode of actions, leading to ADCs with an expanded therapeutic index.

16:20 Refreshment Break in the Exhibit Hall with Poster Viewing

NOVEL TECHNOLOGIES

17:00 Conjugating Payloads to Native Antibodies Without the Need of Any Prior Antibody Engineering in One or Two Steps

Philipp Spycher, PhD, CEO and Co-Founder, Araris Biotech AG, and PSI Founder Fellow, Center for Radiopharmaceutical Sciences (CRS), Paul Scherrer Institute

We will introduce a new linker antibody-conjugation technology that enables site-specific payload attachment to native antibodies 'off-the-shelf' without engineering, i.e. neither the antibody nor the glycosylation needs to be engineered. We will provide a comprehensive set of data demonstrating that the ADCs generated with our new linker technology retain their binding properties, are stable and highly cytotoxic to target over-expressing cell-lines and show superior *in vivo* performance versus reference, state-of-the art ADCs.

17:30 DARPin Drug Conjugates (DDC): Combining the Potency of Antibody-Drug Conjugates and the Flexible DARPin Architecture

Christian Reichen, PhD, Senior Scientist Lead Generation, Molecular Partners AG

The use of the robust DARPin® technology enables the exploration of new therapeutic design space and the establishment of drugs acting on multiple disease pathways. We have generated site-specific DARPin drug conjugates (DDCs) using an anti-EGFR DARPin as a model system to explore the potential of DARPin molecules to deliver potent cytotoxic drugs. We describe here the potency and selectivity of anti-EGFR DDCs and discuss the flexibility of the DARPin platform to generate DDCs to multiple target classes.

18:00 Tailoring Antibody Fragment Drug Conjugates for Solid Tumours

Mahendra Deonarain, PhD, CEO and CSO, Antikor Biopharma Ltd.

Antikor's Fragment Drug Conjugate (FDC) platform small-format antibody-drug conjugates with superior penetrating and clearance properties high payload capacity for more potent action PK, tolerability and tumour cure efficacy data in HER2 and a 2nd undisclosed gastric cancer target.

18:30 End of Next-Generation Antibody-Drug Conjugates



Advancing Bispecifics and Combination Therapy to the Clinic

Refinements for Improved Safety and Efficacy

WEDNESDAY 20 NOVEMBER
07:45 Registration and Morning Coffee

BISPECIFICS FOR T CELL ENGAGEMENT DEMONSTRATING SUPERIOR PROPERTIES

08:30 Chairperson's Opening Remarks
Paul W.H.I. Parren, PhD, Executive Vice President, Head, R&D, Lava Therapeutics B.V.
08:35 Progress with Bispecific V γ 9V δ 2-T Cell Engagers
Paul W.H.I. Parren, PhD, Executive Vice President, Head, R&D, Lava Therapeutics B.V.

V γ 9V δ 2-T cells constitute the largest $\gamma\delta$ -T cell subset in human peripheral blood and are powerful anti-tumor immune effector cells that can be identified in many different tumor types. Our V γ 9V δ 2-T cell engager platform brings important advantages over existing (CD3-based) T cell engagers. Recent preclinical development data including potency, mechanism of action, activity with patient-derived tumor cells, and safety will be discussed.

09:05 Preclinical Combinations of T Cell Bispecifics Targeting Solid Tumors and Hematological Malignancies
Marina Bacac, PhD, Head, Cancer Immunotherapy Department 2 (CIT-2), Roche Innovation Center Zurich

We give an overview of preclinical activity of CEA-TCB and CD20-TCB, two clinical stage T cell bispecific antibodies based on the "2:1" IgG format. In addition, we present combination strategies of these two TCBs with checkpoint inhibitors and novel targeted costimulatory molecules.

09:35 A Novel Mucin 16 Bispecific T Cell Engaging Antibody for the Treatment of Ovarian Cancer
Alison Crawford, PhD, Senior Staff Scientist, Oncology and Angiogenesis, Regeneron Pharmaceuticals, Inc.

REGN4018 binds both Mucin 16 (MUC16) and CD3. REGN4018 induced T cell killing of MUC16-expressing tumor cells *in vitro* in the presence of CA-125. REGN4018 potently inhibited tumor growth in a xenogeneic mouse model, as well as in immuno-competent mice genetically engineered to express human CD3 and human MUC16. Toxicology studies in cynomolgus monkeys revealed no overt toxicity, supporting clinical evaluation of REGN4018 in patients with advanced ovarian cancer.

10:05 Renmab™ Mouse: A Leading Platform for Fully Human Antibody Generation
Chaoshe Guo, Vice President, PhD, Global Head, Business Development, Biocytogen

Biocytogen has recently developed RenMab Mouse, a fully human antibody mouse with its entire variable regions replaced by human Ig heavy chain and light chain. The RenMab™ model has also demonstrated a similar immune response to the wildtype strain as it carries the full human antibody repertoire. Combined with existing inventory of single, double or triple target humanized mouse models, Biocytogen is poised to provide an one-stop solution from target validation to IND application.

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10:35 Coffee Break in the Exhibit Hall with Poster Viewing
11:15 KEYNOTE PRESENTATION: Bispecific Antibodies: Discovery, Development, and Next Generation

Tomoyuki Igawa, PhD, CEO, Head, Research, Global Biologics Leader, Chugai Pharmabody Research Pte. Ltd.

Emicizumab, a humanized anti-FIXa/FX bispecific antibody for hemophilia A, is the first bispecific IgG antibody which was approved by the FDA. Now, many T cell-redirecting bispecific IgG antibodies are being developed. In my presentation, I will talk about the discovery and development of these bispecific IgG antibodies, and how novel antibody engineering can further improve the properties of these molecules.

11:45 Discovery and Optimization of a Novel T Cell Bispecific for the Treatment of Solid Tumors
Adam Root, MSc, Senior Principal Scientist, BioMedicine Design, Pfizer Inc.
12:15 Targeting Cancer with BiTE® Antibody Constructs
Roman Kischel, MD, Director, Research, Amgen Research (Munich) GmbH

The presentation will discuss the structure and mode of action of BiTE antibody constructs, provide an update on the development of the BiTE antibody platform, and showcase early clinical data for a novel BiTE antibody construct targeting myeloma.

12:45 The Journey to 'the' Antibody: Tailoring for Success
María González Pajuelo, CSO, FairJourney Biologics

To maximize the possibility to select "the" antibody, at FJB we have taken antibody discovery to an unprecedented level by creating a versatile toolbox that allows the selection by phage display of antibody fragments of different species from large naïve and immune repertoires. Ultimately, these fragments can be engineered and converted to mono- and bi-specific formats that are produced in CHO cells.

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13:15 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own
14:15 Session Break

INNOVATIVE APPROACHES YIELDING PRODUCTS HEADING FOR THE CLINIC

14:30 Chairperson's Remarks
Adam Root, MSc, Senior Principal Scientist, BioMedicine Design, Pfizer Inc.
14:35 Developing Bi- & Multi-Specific Immune-Modulatory Biologics to Address Unmet Needs
Tariq Ghayur, PhD, Distinguished Research Fellow, AbbVie Bioresearch Center

This will examine the technical challenges of making bi-/multi-specific biologics that have been (or can be) solved, and address the key challenges, namely to design molecules that match the disease biology and meet clinical needs. We are developing methods and tool molecules to understand the biology of the various aspects of cancer, ranging from the immunity cycle to the design of therapeutic molecules. Examples of these efforts will be discussed.



Advancing Bispecifics and Combination Therapy to the Clinic

15:05 Benefits of Chicken-Derived Antibodies for Combination Immunotherapy

Klaus Koefoed, PhD, MSc, Director, Antibody Technology, Symphogen A/S

Development of novel antibodies and more powerful therapeutic combinations for immunotherapy is an intense area of focus. However, difficult and/or conserved targets, finding antibodies with unique functionality, and generating early PoC pose challenges to the development of novel antibody therapeutics. Symphogen's approach to discovery and development of potent antibody combinations for cancer immunotherapy using different species, including chicken, will be presented. Examples from our clinical pipeline will be shown.

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

16:15 DuoHexaBody-CD37, a Novel CD37-Targeting Bispecific Antibody with a Hexamerization-Enhancing Mutation, Demonstrating Superior Preclinical Activity Against Malignant B Cells *in vitro*, *ex vivo*, and *in vivo*

Esther Breij, PhD, Senior Director, Translational Research, Genmab B.V.

DuoHexaBody™-CD37 is a bispecific antibody with a hexamerization-enhancing mutation that targets two different epitopes on CD37. DuoHexaBody-CD37 was designed to induce highly potent cytotoxicity of B cells in a variety of B cell malignancies through enhanced complement-dependent cytotoxicity (CDC) and other Fc-mediated effector functions. Here we will present studies on the rational design, mechanism of action, and pre-clinical efficacy of DuoHexaBody-CD37.

16:45 Towards RNA-Based Cancer Immunotherapy: Advances in the Development of mRNA Encoded Therapeutic Antibodies

Ursula Ellinghaus, PhD, Scientist, Bispecific Antibodies, BioNTech RNA Pharmaceuticals GmbH

BioNTech's RiboMAB® platform, based on *in vitro*-transcribed non-immunogenic mRNA encoding for a variety of antibodies, is circumventing the production challenges and manufacturing cost of protein-based monoclonal antibodies. Systemic administration of RiboMABs formulated in LNPs results in sustained antibody levels and elimination of advanced tumors in mice as efficient as the corresponding purified antibody. Given the feasibility and safety of RiboMABs, we created an exciting platform technology for cancer immunotherapy.

17:15 Anticalin Proteins and Their Application in Respiratory Disease

Christine Rothe, PhD, Vice President, Discovery & Alliance Management, Pieris Pharmaceuticals GmbH

Anticalin® proteins are based on human lipocalins and can be formulated as inhalable biologics, allowing local delivery to the lung. This was demonstrated with AZD1402/PRS-060, an IL-4Ra antagonist that Pieris is developing in collaboration with AstraZeneca for the treatment of moderate-to-severe asthma. A first-in-human study has revealed a promising clinical profile. The ability to generate bi- and multi-specific Anticalin proteins offers the potential to address more than one target in a disease pathway and thus improve efficacy and/or broaden the patient population for a range of respiratory diseases.

17:45 Networking Reception in the Exhibit Hall with Poster Viewing

18:45 Problem-Solving Breakout Discussions*

*See website for details.

19:45 End of Day

THURSDAY 21 NOVEMBER

08:00 Registration and Morning Coffee

CHECKPOINT BLOCKADE IN COMBINATION WITH ANTAGONISTS/AGONISTS

08:30 Chairperson's Remarks

Tariq Ghayur, PhD, Distinguished Research Fellow, AbbVie Bioresearch Center

08:35 PD-1 x LAG-3 (MGD013) and PD-1 x CTLA-4 (MGD019): Two Clinical-Stage DART® Molecules Designed to Simultaneously Block Two Checkpoint Pathways

Alexey Berezchnoy, PhD, Scientist, Cell Biology & Immunology, MacroGenics, Inc.

Tumor-infiltrating lymphocytes frequently co-express multiple immune checkpoint receptors, whose co-blockade provides additional benefits in immunotherapy. Here we applied a bispecific platform to increase stringency and specificity of immune checkpoint co-blockade. Two clinical-stage bispecific DART molecules, PD-1 x CTLA-4 (MGD019) and PD-1 x LAG-3 (MGD013), will be discussed in this presentation, including format selection, preclinical pharmacology, IND-enabling studies, and clinical trial design.

09:05 A Novel, Monovalent Tri-Specific Antibody-Based Molecule that Simultaneously Modulates PD-L1 and 4-1BB Exhibits Potent Anti-Tumoral Activity *in vivo*

Stefan Warmuth, PhD, Head, CMC, Therapeutic Program Lead, Numab Therapeutics AG

Targeting PD-L1 and 4-1BB with multi-specific antibodies holds the promise of increased potency, while improving the safety profile compared to combination therapy. Numab develops a molecule that potently blocks PD-L1/PD-1 signaling and elicits further T cell activation through its costimulatory domain solely in the proximity of cells that overexpress PD-L1. Preclinical data show efficacy on tumor growth in combination with an enhanced intratumoral CD8+ T cell activation when compared to the combination of the PD-L1 and 4-1BB modalities.

09:35 Development of a Novel Bi-Functional Fusion Protein Platform (Agonist Redirected Checkpoint or ARC) for Cancer Immunotherapy

George Fromm, PhD, Vice President, Research & Development, Shattuck Labs, Inc.

The ARC platform was developed to solve the challenge of incorporating immune-checkpoint blocking functional domains and tumor necrosis factor (TNF) superfamily agonists (OX40, CD40, 4-1BB, etc.) into single therapeutics. This was achieved by engineering hexameric TNF ligands, which uniquely activate TNF receptors compared to mono- or di-valent antibody-based approaches. The ARC platform has provided a means to unlock this family of costimulatory molecules, which is currently being evaluated in a clinical study.



Advancing Bispecifics and Combination Therapy to the Clinic

10:05 Next-Generation Reporter Technologies for Immunotherapy Discovery and Potency Testing

Jamison Grailer, Senior Research Scientist, Research & Development, Promega Corporation

Immunotherapy strategies, including immune checkpoint monoclonal antibodies (mAbs), bispecific molecules, and chimeric antigen receptor T (CAR T) cells, are promising new approaches for treating cancer, autoimmunity, and other diseases. A major challenge in immunotherapy drug development is access to quantitative and reproducible functional assays for screening (e.g. TCR screening), measurement of target cell-specific killing, and potency testing. Here we will present a variety of next-generation reporter technologies to address these needs in the context of mAb-mediated ADCC, bispecific molecules, and TCR-mediated cell therapies.

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

SCREENING AND IDENTIFICATION OF BISPECIFIC COMBINATIONS / FOCUS ON CYTOKINE RELEASE

11:15 Unbiased Functional Screening Unlocks Novel Biology For Targeted and I-O Bispecific Antibodies

Pieter Fokko van Loo, PhD, Director, Oncology-Immunology, Merus

Our technology platform leverages the natural human IgG1 format; enabling high throughput functional screening to discover drug candidates with excellent anti-tumour properties. The discovery of two clinical stage pipeline candidates will be discussed that highlight the power of this functional screening approach: MCLA-117, a CLEC12AxCD3 T cell engaging antibody for acute myeloid leukemia and MCLA-145, CD137xPD-L1 bispecific antibody that recruits and supercharges tumor infiltrating lymphocytes.

11:45 An International Collaborative Study to Establish a 1st Reference Panel for Cytokine Release Assays

Sandrine Vessillier, PhD, Principal Scientist, Head, Immunotoxicology Cellular Immunology, Biotherapeutics, National Institute for Biological Standards and Control, UK

Cytokine release assays (CRAs) are key for hazard ID of immunotherapeutics, such as cytokine release syndrome (CRS). To gain a better understanding of the comparability between different CRA formats, NIBSC recently produced a panel of lyophilised recombinant antibodies known to induce CRS of different intensities and three isotype-matched negative controls. The relative potency of these antibodies to stimulate cytokine release was evaluated in an international collaborative study.

12:15 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

13:15 Dessert Break in the Exhibit Hall with Poster Viewing

14:00 End of Advancing Bispecifics and Combination Therapy to the Clinic

17:00 Dinner Short Course Registration*

17:30 – 20:30 Dinner Short Courses

Recommended Short Course*

SC10: Engineering of Bispecific Antibodies and Multi-Specific Non-Antibody Scaffolds

*Separate registration required. See pages 6 & 7 for details.



Novel Targets for Cancer and Emerging Therapeutic Areas

Exploring Unconventional Approaches for Clinical Success

THURSDAY 21 NOVEMBER

13:00 Registration

13:15 Dessert Break in the Exhibit Hall with Poster Viewing

CHALLENGES AHEAD FOR CANCER IMMUNOTHERAPY/IMMUNE PHENOTYPES

14:00 Chairpersons' Opening Remarks

Daniel Chen, MD, PhD, Chief Medical Officer, IGM Biosciences

Pablo Umaña, PhD, Head, Cancer Immunotherapy Discovery, Roche Innovation Center Zurich (Roche Glycart AG)

14:05 A New Era in Cancer Therapeutics: Biologic Problems and Engineering Solutions

Daniel Chen, MD, PhD, Chief Medical Officer, IGM Biosciences

The opportunity for therapeutics that turn on or off a singular target has largely been explored. However, advancements in our understanding of cancer, immune biology, and protein/cellular engineering approaches begin to define what seemed like science fiction only a few years ago. The objectives and challenges for next-generation therapy and spatial temporal coordination of modulating different biologies and cell types within emerging cancer immunotherapy will be explored.

14:35 Novel Antibody Engineering to Improve Therapeutic Index of Antibody Targeting Solid Tumors

Kanako Tatsumi, PhD, Researcher, Discovery Biologics, Chugai Pharmaceutical Co. Ltd.

One of the remaining issues of antibody therapeutics is on-target off-tumor toxicity induced by binding to target antigens expressed in normal tissues. To overcome this issue, we have established a novel antibody engineering technology to enable antibody to bind the antigen selectively at tumor site, but not at normal tissues.

15:05 OmniChicken Facilitated Discovery of High Affinity Antibodies Against the Myeloid Checkpoint Receptor SIRP α

Janet Sim, PhD, Vice President, Protein Science, ALX Oncology

Targeting the CD47/SIRP α pathway is an exciting new approach that shows promise in the clinic. As SIRP α expression is more restricted, it may offer differential safety and efficacy profile than CD47-targeted therapies. In this study, OmniChicken was used to identify a panel of high affinity monoclonal antibodies that are cross-reactive to human, monkey and rodent SIRP α . Importantly, these antibodies bind to all human SIRP α variants, a critical attribute for global patient population. Selected anti-SIRP α antibodies enhance the antitumor activity of checkpoint inhibitors and have favorable safety profiles. Altogether, these data support development of anti-SIRP α therapy, and provide opportunities to study similarities and differences for targeting CD47 and SIRP α .

Sponsored by



15:20 Sponsored Presentation (*Opportunity Available*)

15:35 Networking Refreshment Break

16:00 Avidity-Based Binding to HER2 Results in Selective Killing of HER2 Over-Expressing Cells by Anti-HER2/CD3

Teemu Junttila, PhD, Senior Scientist, Translational Oncology, Genentech, Inc.

A primary barrier to the success of T cell-recruiting bispecific antibodies in the treatment of solid tumors is the lack of tumor-specific targets, resulting in on-target off-tumor adverse effects from T cell autoreactivity to target-expressing organs. To overcome this, we developed an anti-HER2/CD3 T cell-dependent bispecific (TDB) antibody that selectively targets HER2-overexpressing tumor cells with high potency, while sparing cells that express low amounts of HER2 found in normal human tissues. Selectivity is based on the avidity of two low-affinity anti-HER2 Fab arms to high target density on HER2-overexpressing cells. The increased selectivity to HER2-overexpressing cells is expected to mitigate the risk of adverse effects and increase the therapeutic index.

16:30 Tumor-Targeted 4-1BB Co-Stimulation to Boost T Cell Activity for Cancer Immunotherapy

Claudia Ferrara Koller, PhD, Group Leader, Roche Innovation Center Zurich

Endogenous costimulatory molecules on T cells, such as 4-1BB (CD137), can be leveraged for cancer immunotherapy. To overcome issues of first generation 4-1BB agonistic antibodies, we engineered proteins simultaneously targeting 4-1BB and a tumor-stroma or tumor antigen (TA): FAP-4-1BBL (RG7826) and CD19-4-1BBL. In the presence of a T cell receptor (TCR) signal (endogenous or provided by a T cell bispecific antibody), they provide potent T cell costimulation strictly dependent on tumor target-mediated hyper-clustering without systemic activation by Fc γ R-binding.

17:00 End of Day

17:00 Dinner Short Course Registration*

17:30 – 20:30 Dinner Short Courses

Recommended Short Course*

SC9: T Cell Therapies: Current Field, Challenges and Future Directions

**Separate registration required. See pages 6 & 7 for details.*





Novel Targets for Cancer and Emerging Therapeutic Areas

FRIDAY 22 NOVEMBER

08:00 Registration and Morning Coffee

NEXT GENERATION APPROACHES (ANTIBODY-BASED)

08:30 Chairperson's Remarks

Daniel Chen, MD, PhD, Chief Medical Officer, Research & Development, IGM Biosciences

08:35 Agonist and Bispecific IgM: Nature's Approach to Highly Avid, Multivalent Antibodies

Bruce Keyt, PhD, CSO, IGM Biosciences

Death receptor 5 (DR5) is widely expressed on tumor cells and directly induces apoptosis. Agonistic IgG anti-DR5 has preclinical efficacy, but not clinical efficacy. Multivalent IgM anti-DR5 induces receptor clustering and rapid tumor cell apoptosis. *In vitro*, anti-DR5 IgM was 1,000-fold more potent compared to anti-DR5 IgG. *In vivo*, anti-DR5 IgM eradicated colorectal tumors and extended survival with leukemic models. We are developing IgM anti-DR5 for treatment of solid and hematologic tumors.

09:05 Insights into the Mechanism of Action of ImmTAC® Molecules in Melanoma Patients

Marco Lepore, PhD, Group Leader, Immunocore LLC

Immune mobilising monoclonal TCRs Against Cancer (ImmTAC) molecules are soluble bispecific T cell engagers which use high affinity TCRs fused to an anti-CD3 scFv to redirect polyclonal T cells toward tumor cells. ImmTAC molecules target tumour antigen-derived peptides naturally presented by HLA molecules on the surface of cancer cells and induce multiple cytolytic and pro-inflammatory T cell responses. Here we will discuss key immunological aspects of ImmTAC mechanism of action and therapeutic activity in advanced melanoma patients.

09:35 Bintrafusp Alfa (M7824): A New Class of Next Generation Immune-Oncology Agent Targeting PDL-1 and TGF-Beta

Michael R. Streit, PhD, Executive Director, Cancer Epigenetics, GlaxoSmithKline

10:05 Networking Coffee Break

EMERGING TARGETS & APPROACHES

10:30 Chairperson's Remarks

Kerry Chester, PhD, Professor, Molecular Medicine, University College London Cancer Institute

10:35 Rare Arginase 2 Specific Inhibitory Antibodies Restore T Cell Proliferation *in vitro* and Have a Novel Allosteric Mechanism of Inhibition

Maria Groves, PhD, Associate Director, R&D Antibody Discovery and Protein Engineering, AstraZeneca; Head, Cancer Research UK AstraZeneca Alliance Laboratory

Dysregulated expression of Arginase 2 (ARG2) within tumours has recently been proposed to result

in significant levels of ARG2 in the extracellular matrix, generating an immunosuppressive niche that deactivates the immune system. Here we report the identification, characterisation and affinity maturation of rare antibodies, typified by CMAL1158, which completely inhibit ARG2 activity but not ARG1 and restore T-cell proliferation *in vitro*. We have solved the crystal structure of CMAL1158 and its parent, CMAL0187. CMAL1158 contacts a region of ARG2 away from the enzyme active site and induces major conformational changes in several regions of ARG2, which lead to subtle but important conformational changes at the active site. A comparison with the parent CMAL0187:ARG2 crystal structure reveals that CMAL1158 has a significant epitope shift and a modified 'angle' of binding that creates a better enzyme inhibition profile. Inhibiting extracellular ARG2 with CMAL1158 could represent an exciting new strategy for stimulating the hosts immune system to fight tumours that release this immunosuppressive enzyme

11:05 What Intratumoral Tregs Eat Makes Them Strong, but Vulnerable: A New Metabolic Intervention for Cancer Immunotherapy

Ping-Chih Ho, PhD, Assistant Professor, Oncology, University of Lausanne

Targeting intratumoral Tregs is a desirable strategy to reprogram the tumor microenvironment for cancer immunotherapy. However, the systemic impairment and destruction of Tregs caused by current strategies limit its application in cancer treatment. Here, I will discuss how intratumoral Tregs support their survival and suppressive functions in the tumor microenvironment via metabolic adaptation and how targeting this metabolic machinery can lead to selective destruction of intratumoral Tregs.

11:35 Tertiary Lymphoid Structures and Tumor-Specific B Cell Response in Gastrointestinal Cancer

Hans Schlöber, MD, Principal Investigator, Cologne Translational Immunology, Center for Molecular Medicine Cologne

Tumor-infiltrating lymphocytes (TILs) are correlated to prognosis of several kinds of cancer. Most studies focused on T cells, while the role of tumor-associated B cells (TABs) has only recently gained more attention. TABs are highly differentiated and frequently organize in tertiary lymphoid structures. Tumor-specific B cell response as well as composition and spatial distribution of TABs in gastrointestinal cancer will be discussed in the context of emerging immunotherapies.

12:05 Problem-Solving Breakout Discussions with a Light Snack*

*See website for more details.

DISCOVERING DISEASE-ASSOCIATED EPITOPES AND PATIENT-DERIVED APPROACHES

13:30 Chairperson's Remarks

Daniel Emerling, PhD, Senior Vice President, Research, Atreca, Inc.

13:05 Using Phage Display of Antibodies as a Discovery Tool to Identify Disease-Related Targets

Peter Kristensen, PhD, Head of Section of Biotechnology, Associate Professor, Department of Chemistry and Bioscience, Aalborg University





Novel Targets for Cancer and Emerging Therapeutic Areas

Large repertoires of recombinant antibodies displayed on filamentous bacteriophage can be applied as a discovery tool to identify new disease-related targets. As selection of recombinant antibodies can be performed on single cells in heterogeneous population or tissue sections, the ability to identify posttranslational modified targets, or targets where localization is changed, is improved. Here a few examples will be given as to how recombinant antibody technology is used as a discovery tool in cancer.

13:35 Microsphere Affinity Proteomics: High Throughput Deconvolution of Antibody Libraries

Fridtjof Lund-Johansen, MD, PhD, Senior Scientist, Department of Immunology, Oslo University Hospital, Norway

Microsphere Affinity Proteomics (MAP) is a versatile platform to study antibody-antigen interactions by flow cytometry. MAP antibody arrays provide means to probe 4,300 antibodies for binding of proteins from complex samples, such as cell and tissue lysates, while MAP arrays with 12,000 full-length human proteins open new possibilities for assessing antibody specificity and detection of autoantibody targets.

14:05 Targeting Disease-Specific Inflammatory Stimuli: Novel Immunotherapies to Prevent or Reinforce Autoimmunity

Kim Midwood, PhD, Professor, Kennedy Institute of Rheumatology, University of Oxford

Whilst immune defense against cancer is a key determinant of tumor elimination, mistargeted inflammation directed against healthy tissue underpins autoimmune disease pathogenesis. Investigating how regulatory

control over endogenous triggers of inflammation goes awry in rheumatoid arthritis, and how tumors exploit these mechanisms to evade immune surveillance, has led to the development of new therapies designed to prevent autoimmune joint destruction in arthritis and to re-educate anti-tumoral immunity.

14:35 Functional Anti-Tumor Antibodies from Cancer Patients

Daniel Emerling, PhD, Senior Vice President, Research, Atreca, Inc.

By analyzing monoclonal antibodies derived from plasmablast IgG sequences of non-progressing cancer patients, we have identified more than 1,400 antibodies that bind to non-autologous human tumor tissue. These data, along with binding data from both human and mouse tumor cell lines, suggest that these antibodies target public tumor antigens. Among these antibodies, we have antibodies that show anti-tumor functional activity *in vitro* and that show activity in mouse tumor models. Our research on mechanism of action reveals potential for novel immuno-oncology targets and treatments.

15:05 End of Novel Targets for Cancer and Emerging Therapeutic Areas



Optimisation & Developability

New Methods & Models for Prediction and Assessment

MONDAY 18 NOVEMBER

Recommended Short Course*

SC3: Mutation and Selection Strategies Beyond Affinity Optimisation

*Separate registration required. See page 6 & 7 for details.

12:00 Conference Registration

DEVELOPABILITY SCREENING FOR COMPLEX MOLECULES

13:30 Organiser's Welcome

Mimi Langley, MBA, Senior Conference Director, Cambridge Healthtech Institute

13:35 Chairperson's Opening Remarks

Lars Linden, PhD, Director & Head, Protein Biochemistry, Bayer Healthcare AG

13:45 KEYNOTE PRESENTATION: Developability Assessment to Enable Candidate Selection of Therapeutic Proteins



Steffen Hartmann, PhD, Head, Characterization, Formulation and Bioinformatics, Novartis Pharma AG

14:15 Developability of Hexabody®-Based IgG Antibodies: The Impact of Formulation on Colloidal and Conformational Stability

Muriel van Kampen, PhD, Senior Scientist, Genmab

The HexaBody format is a novel platform for the potentiation of therapeutic antibodies by enhancement of antigen-dependent hexamer formation at the cell surface, which may drive subsequent target receptor activation or complement activation. The biophysical characteristics and stability of HexaBody-based model compounds in different formulations will be discussed, probed by a variety of analytical techniques.

14:45 An Integrated Approach for Optimization and Developability Assessment of Peptides Intended for Multiple-Dose Pen Devices

Andreas Evers, PhD, Senior Scientist, Synthetic Molecular Design, Integrated Drug Discovery, Sanofi

Physicochemical properties of peptides need to be compatible with the manufacturing process and formulation requirements to ensure developability toward the commercial drug product. This aspect is often disregarded and only evaluated late in discovery, imposing a high risk for delays in development, increased costs, and finally for the project in general. In the presentation, a general roadmap is proposed to optimize physicochemical properties towards developability of peptide drugs by combining experimental and *in silico* profiling to provide stable peptide formulations at the end of discovery.

15:15 Probing proteins in small volumes

Tuomas Knowles Professor Department of Chemistry University of Cambridge

Probing protein-protein interactions in small volumes using microfluidics. Measurements that are challenging on bulk scales become more accessible on microfluidic scales. In particular, the absence of convective mixing allows PPI's to be probed under native conditions in solution through monitoring changes in diffusivity as they interact. We show the applicability of this approach to different classes of interacting protein systems. Finally, we outline our efforts to bring this technology to market in an easy-to-use platform.

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15:45 Networking Refreshment Break

PLENARY KEYNOTE SESSION

16:15 Moderator's Opening Remarks



Kerry Chester, PhD, Professor, Molecular Medicine, University College London Cancer Institute

16:20 Bispecific, Soluble TCR as the Next Therapeutic Platform



Bahija Jallal, PhD, CEO and Director of the Board, Immunocore

Of the two adaptive immunity recognition motifs, only antibodies have been brought to patients. However, antibody therapeutics only recognize 10% of human proteome (surface-expressed). The other motif, T cell receptor (TCR), has potential to unlock 90% of the human proteome, but requires converting a low-affinity, specificity membrane receptor into a soluble therapeutic. IMCgp100, a soluble, TCR bispecific-targeting melanoma, is the most advanced soluble TCR therapeutic in development.

17:20 Attacking Cancer Cell Surfaceomes with Recombinant Antibodies



James A. Wells, PhD, Professor, Departments of Pharmaceutical Chemistry and Cellular & Molecular Pharmacology, University of California, San Francisco

The cell surface proteome (surfaceome) is the primary hub for cells to communicate with the outside world. Oncogenes are known to cause huge changes in cells and we find this translates to significant remodeling of the surfaceome. We generate recombinant antibodies to detect and then attack these cells by toxifying the antibodies or recruiting immune cells to kill. I'll discuss the technologies for surface protein analysis, an industrialized platform for rapid antibody generation using phage display, and using these tool reagents for target validation.

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

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19:30 End of Day



Optimisation & Developability

TUESDAY 19 NOVEMBER
07:45 Registration and Morning Coffee

METHODS AND MODELS FOR DEVELOPABILITY ASSESSMENT

08:30 Chairperson's Remarks

Charlotte Deane, PhD, Professor of Structural Bioinformatics & Head of Department, Department of Statistics, University of Oxford

08:35 Physicochemical Predictors of Antibody Solution Behavior

Jonathan Kingsbury, PhD, Head, Developability and Preformulation, Biologics Development, Sanofi

The development of successful high-concentration biologic drugs requires that the therapeutic protein have properties amenable to achieving the target product profile. Selection of molecules that are resistant to unfavorable solution behaviors, such as high viscosity and poor colloidal stability is enabled by developability assessment. A framework for developability is presented, which is centered on assessing the fit to the required dosage form and to the established manufacturing platform. The measurement of molecular and dilute solution properties predictive of high concentration behaviors will be discussed within the context of the underlying solution phenomena and illustrated with examples.

09:05 Developability Assessment to Select Candidates for Clinical Development

Anup Arumugan, PhD, Principal Scientist, Antibody Analytics, Roche

We have developed a highly versatile next generation biologics platform with a number of candidates in clinical development. During lead identification and optimization of candidates, we typically rank molecules based on their potential for successful future development. Such developability assessments provide important information about potential liabilities, e.g., chemical degradation of amino acids or unfavorable CMC properties. We have recently expanded our developability concept to systematically combine in-silico analysis, including pharmacokinetics analysis with biophysical and functional testing. In summary, this concept provides a more holistic picture of a candidate's fitness for future development.

09:35 Problem-Solving Breakout Discussions*

*See website for details.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing
11:15 Biophysical Screening of Unwanted Protein Interactions

Nikolai Lorenzen, PhD, Specialist, Biophysics and Formulation, Novo Nordisk A/S

Stickiness is a critical parameter to measure during developability assessment of antibodies, as it can lead to non-specific interactions, reversible self-association, and aggregation. I will give examples on how we at Novo Nordisk screen for such unwanted protein interactions and how we collaborate with leading academic groups to develop new sophisticated biophysical screening assays.

11:45 Re-Examination of the Hydrophobic Effect at Antibody-Antigen Interfaces

Jim Warwicker, PhD, Reader, School of Chemistry, University of Manchester

Prediction of developability requires a molecular level understanding of the behaviour of therapeutic proteins. We find that interactions at antibody CDRs challenge current empirical models for the hydrophobic effect. Improvements can be made with introduction of shape-dependence, and this coupling of modern protein science with traditional protein engineering concepts will lead to better predictive models for the biologics community.

12:15 Get the Whole Story on Protein Stability and Aggregation with Uncle

Kevin Lance, PhD, Product Manager, Unchained Labs

Novel protein therapeutics mean that examining thermal stability and non-specific interactions is ever more important in choosing the best formulations for maintaining protein stability and avoiding aggregation. Uncle's unique combination of static light scattering, dynamic light scattering, and full-spectrum fluorescence tells the full story of your protein's conformational and colloidal stability from one small sample.

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12:45 Luncheon Presentation I: Keeping Kinetics Real: A New Level of Performance and Flexibility in Drug Discovery

Fabio Spiga, Senior Application Scientist, Application Team Leader Switzerland, Creoptix AG

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13:15 LUNCHEON PRESENTATION II: Choose the New Gold Standard in Protein Stability Characterization

Peter A. Fung, PhD, NanoTemper Technologies

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TEMPER**

13:45 Dessert Break in the Exhibit Hall with Poster Viewing

DEEP LEARNING AND IN SILICO SCREENING FOR ANTIBODY OPTIMISATION

14:15 Chairperson's Remarks

Jim Warwicker, PhD, Reader, School of Chemistry, University of Manchester

14:20 Toward in silico Lead Discovery

Lars Linden, PhD, Director & Head, Protein Biochemistry, Bayer Healthcare AG

- How will artificial intelligence and machine learning change and impact the way big pharma performs antibody lead discovery and optimization processes in the future?
- What is already there and what is needed on the journey to *in silico* drug discovery?

14:50 Deep Learning Enables Therapeutic Antibody Optimization in Mammalian Cells

Derek Mason, MSc, PhD Candidate, Department for Biosystems Science & Engineering (D-BSSE), ETH Zurich

Deep learning, as part of a family of tools related to machine learning, is an emerging field of information and computer science that uses large data to identify complex relationships. Here, I will describe how we are moving beyond experimental screening by applying deep learning to augment multi-parameter optimization of therapeutic antibodies in mammalian cells.



Optimisation & Developability

15:20 Using Structural Information to Aid *in silico* Therapeutic Design from Next Generation Sequencing Repertoires of Antibodies

Charlotte Deane, PhD, Professor of Structural Bioinformatics & Head of Department, Department of Statistics, University of Oxford

We have built the freely available Observed Antibody Space database of over a billion antibody sequences. Using this data, I will show how predicted structural information can enrich data from next-generation sequencing experiments. In particular, TAP, our novel therapeutic antibody profiler that provides five computational developability guidelines.

15:50 Antibody Protein Sequencing with Mass Spectrometry

Anthony Stajduhar, Manager, Business Development, Rapid Novor, Inc.

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

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16:05 Affinity Maturation and Optimisation of Trastuzumab using RAMP

Richard Buick, Chief Technical Officer, Fusion Antibodies, plc.

We have used RAMP (Rational Affinity Maturation Platform) to generate an improved version of trastuzumab. The resulting antibody is >3-fold higher affinity and performs equivalently in several analytical assays with no reduction in specificity.

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16:20 Refreshment Break in the Exhibit Hall with Poster Viewing

ASSESSING CQAs AND OPTIMISING BIOPHYSICAL CHARACTERISTICS

17:00 SELECTED POSTER PRESENTATION: Customized Glycosylation of Therapeutics via a Novel Production Platform

Stefan Herwig, PhD, Group Leader, Mass Spectrometry, LimmaTech Biologics AG

LimmaTech Biologics utilizes its glycosylation expertise to develop a novel glycoengineering platform for better therapeutics. Scouting of Kinetoplastida led to the identification of a unicellular eukaryote with surprisingly unique N-glycosylation features. We engineered the organism to produce improved therapeutic proteins characterized by custom and homogenous N-glycosylation. Our glycoengineering platform bears the promise of cheaper and faster production. At the same time, it avoids potentially disadvantageous features of mammalian cell production such as glycan microheterogeneity and variable site occupancy. Several proof of concept studies, including EPO and an anti-CD20 antibody, confirm

the potential of this novel glycoengineering platform. Next, we will perform mode of action studies of optimized candidate therapeutics to show advantageous glycoengineering effects.

17:30 Begin with Quality in Mind: Identifying CQAs from Early Stage of Product Lifecycle

Archana Shah, Investigator, Analytical and Product Characterisation, Biopharm Process Research, GlaxoSmithKline United Kingdom

Identification of Critical Quality Attributes (CQAs) is an imperative step in the development of biopharmaceuticals. The presentation will focus on strategies used to identify CQAs from Discovery stage to Marketing Application. It will give an insight into how early developability screens could be used to get thorough understanding of the product and potential quality attributes affecting the safety and efficacy. Use of structure function studies and risk ranking tool to assess the criticality of quality attributes will also be outlined.

18:00 Importance of Vernier Zone Residues in Antibody Engineering Approaches

Sibel Kalyoncu, PhD, Research Group Leader, Antibody Engineering Lab, Izmir Biomedicine and Genome Center, Turkey

Vernier zone residues locate in framework regions of antibodies affecting conformations of CDR loops and they are underrepresented in the literature. In this talk, an antibody engineering approach based on vernier zone has been applied to improve biophysical characteristics of an anti-VEGF antibody fragment. According to our preliminary results, solubility and, surprisingly, affinity increased with rationally designed mutation(s) on vernier zone residues. My talk will show one of important ways to improve certain biophysical and affinity characteristics of antibodies.

18:30 End of Optimisation & Developability



Analytical Characterisation of Biotherapeutics

Harnessing Technologies to Speed Innovation

WEDNESDAY 20 NOVEMBER

07:45 Registration and Morning Coffee

STANDARDS AND REGULATORY CONSIDERATIONS FOR ADVANCED THERAPEUTICS AND BIOSIMILARS

08:30 Chairperson's Opening Remarks

Jonathan Bones, PhD, Principal Investigator, CCL, National Institute for Bioprocessing Research and Training

08:35 KEYNOTE PRESENTATION: An International Collaboration: Towards the Standardisation of Gene Therapy



Yuan Zhao, PhD, Principal Scientist, Leader, Gene Therapy Section, Advanced Therapy Division, NIBSC, Medicines & Healthcare Products Regulatory Agency

Potential safety risks, limited efficacy, or ethical conflicts may present challenges in the success of developing GTMP. Manufacturing hurdles, including changes in production sites and manufacturing processes, pose challenges to developers regarding reproducibility and comparability of results for gene therapy. Introduction of an International Standard for gene therapy is especially important, given the usually orphan nature of the diseases to be treated with gene therapy, hampering the comparison of cross-trial and cross-manufacturing results. This presentation will discuss challenges and regulatory perspectives in quality control and standardization of gene therapy and an international effort in developing the 1st WHO International Standard for gene therapy products.

09:05 USP Standards and Best Practices for Advanced Therapies

Fouad Atouf, PhD, Vice President, Global Biologics, U.S. Pharmacopeia

The development of advanced therapy medicinal products offers great opportunities for therapeutic innovation; some challenges remain to be resolved for successful development and entry of these products to the healthcare market. Some of the challenges relate to the lack of consistency in quality of raw materials and the lack of harmonized analytical methods across the industry. The United States Pharmacopeia (USP) is committed to working with regulators and developers of advanced therapies on the standardization of analytical methods to assess the quality of these products throughout their lifecycle. This presentation will provide an overview of best practices and standardized procedures and associated physical reference materials in support of this important segment of the industry.

09:35 Mapping Analytical Methods for Quality Assessment of Biotherapeutics and Biosimilars; Quality Attributes and Regulatory Considerations Perspectives

Maha Hegazy, PhD, Professor, Analytical Chemistry, Cairo University

The FDA, EMA, and ICH have drawn attention to a number of structural features that have to be assessed to confirm consistent batch production and ensuring control of the manufacturing process for regulatory acceptance. Significant differences between batches need to be investigated, thus integrated advanced analytical methods with new tools of design of experiments (DOE) and data analysis are needed

to generate maximum information for quality assessment of biotherapeutics and comparability of biosimilars to the reference product. Mapping analytical methods for multiple quality attributes is also required to ensure the method's ability to detect relevant differences between samples.

10:05 Bispecific Binding Kinetics Analysed with a Two-Colour switchSENSE® Biosensor

Ulrich Rant, PhD, CEO, Dynamic Biosensors GmbH

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

NEW TOOLS AND APPROACHES

11:15 Anisotropy Resolved Multi-Dimensional Emission Spectroscopy (ARMES): A Multivariate Approach to Intrinsic Protein Emission Analysis

Alan G. Ryder, PhD, Professor, Nanoscale Biophotonics Laboratory, National University of Ireland Galway

Fluorescence anisotropy can be related to protein structure, size, and aggregation profile. When implemented using multi-dimensional measurements of intrinsic protein emission and combined with multivariate analysis, one can extract potentially very useful diagnostic information. Here we show how these 4D measurements can be applied to the study of protein structure changes, PEGylation reactions, and for bioreactor monitoring.

11:45 Aptamers and Enzyme Cascades as New Tools for Analytical Characterization of Biopharmaceuticals

Urs Lohrig, PhD, Lab Head, Physico-Chemical Characterisation, Novartis

Probing higher order structure of biopharmaceuticals is the domain of instrumental analytics like CD, FT-IR, NMR and X-ray crystallography. Here, we present two simple approaches to supplement the analytical toolbox: Aptamer technology and an Analytical Cascade of Enzymes (ACE) – both probing molecular structures. Aptamers offer an adoptable, not immunogenic-driven selection process and long-term supply of critical reagent in contrast to polyclonal antibodies. ACE detects structural differences in mAbs at a 1% level – a range inaccessible by most instrumental methods.

12:15 Characterization from Developability to BLA

Jean-Michel Menet, PhD, Head, Characterization, Biologics Development/BioAnalytics, Sanofi

Characterization toolbox is evolving along the development phase of therapeutic proteins (i.e., from developability studies to the filing of the BLA) and to suit protein modality (e.g., IgG1 to multispecific). Examples applied to monospecific and multispecific antibodies will be given showing toolbox used for early phase projects and for late phase projects. Approaches under development for CQA-driven CMC development will also be presented: high order structure technologies such as HDX-MS and NMR, native MS, MAM.



Analytical Characterisation of Biotherapeutics

12:45 How Merck is Going to Simplify the Paradigm of Mass Spectrometry: from Characterization Tool to Routine QC Method

Angelo Palmese, PhD, Head of Characterization & Innovative Analytics, Analytical Development, Biotech, Merck Serono S.p.A

13:15 Automated Multi Attribute Method Analyses for Process Development and Characterization of mAbs

Martin Hoffmann, PhD, Senior Scientist R&D – Bioanalytics, Frankfurt – Bioprocess Analytics, Sanofi-Aventis Deutschland GmbH

We present a mass spectrometry based approach to simultaneously monitor critical quality attributes (CQA) of therapeutic monoclonal antibodies (mAbs) - which has been termed multi-attribute method (MAM). With MAM we are supporting the process development of mAbs. For CQA quantification, mAbs samples were digested on an automated liquid handling robot and analyzed by HPLC separation in combination with high resolution mass spectrometric detection.

13:45 Luncheon Presentation II (Sponsorship Opportunity Available)

14:15 Session Break

HCP QUANTITATION

14:30 Chairperson's Remarks

Fouad Atouf, PhD, Vice President, Global Biologics, U.S. Pharmacopeia

14:35 Quantitation of HCP by Mass Spectrometry as a Method to Control the Quality of Biopharmaceuticals

Annick Gervais, PhD, Director, Analytical Development, Biologicals, UCB Pharma SA

15:05 Monitoring of Clearance of Lipase Host Cell Proteins in mAb Manufacturing Using a LC-MRM Quantitation Method

Rachel Chen, PhD, Scientist II, Analytical Development, Biogen

Successful removal of host cell proteins (HCPs) is very important for biopharmaceutical product development to ensure product quality and safety. Recently, it has been demonstrated that certain lipases may be the cause for enzymatic degradation of polysorbate 20 and 80, which are common surfactants used in protein formulations. An LC-MS/MS method was developed to achieve sub ppm quantitation level of three lipases. The method has been applied to monitor the clearance of lipases for various mAbs under different downstream processes.

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

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NATIVE MS AND MAM

16:15 The Transition to Native MS in a Biopharmaceutical Development Lab – Lessons Learned and the Road Ahead

Dan Bach Kristensen, PhD, Principal Scientist, Symphogen

In recent years, native MS has gained significant popularity as a tool for intact mass analysis of large biomolecules. Key strengths include the ability to interface a variety of chromatographic techniques with the MS, and the excellent quality of the spectral data. At Symphogen, native MS is established as the method of choice for intact mass analysis, and here learnings from the transition to native MS and thoughts on future applications will be presented.

16:45 Probing Biopharmaceutical Microheterogeneity Using Native LC-MS

Jonathan Bones, PhD, Principal Investigator, CCL, National Institute for Bioprocessing Research and Training

Hyphenation of charge variant analysis using pH gradient cation-exchange chromatography to high-resolution Orbitrap mass spectrometry under native conditions (CVA-MS) has recently been described. Here we demonstrate the power of CVA-MS for profiling microheterogeneity of biopharmaceutical product quality attributes on both drug substance and drug product. We will also discuss how high-resolution native LC-MS can be applied for automated process monitoring when combined with automation solutions to create a data generation engine to support Manufacturing 4.0.

17:15 A Reliable and Automated Workflow for LC-MS MAM Analysis of Biopharmaceuticals – From High Throughput Sample Preparation to Data Evaluation

Patrick Sascha Merkle, PhD, Postdoc, Analytical Development & Characterization, Novartis Pharma AG

The LC-MS multi-attribute method (MAM) has emerged as a promising approach for the characterization and relative quantification of critical quality attributes on biopharmaceutical molecules. Here, we present our peptide-level LC-MS MAM workflow that relies on high-throughput sample preparation, high-resolution MS acquisition, and automated data evaluation in the Genedata Refiner MS software. We envisage that the simplicity and state of automation of the presented LC-MS MAM workflow may allow its routine use in a non-expert laboratory.

17:45 Networking Reception in the Exhibit Hall with Poster Viewing

18:45 Problem-Solving Breakout Discussions*

*See website for details.

19:45 End of Day



Analytical Characterisation of Biotherapeutics

THURSDAY 21 NOVEMBER

08:00 Registration and Morning Coffee

CHARACTERIZING COMPLEX MODALITIES

08:30 Chairperson's Remarks

Annick Gervais, PhD, Director, Analytical Development, Biologicals, UCB Pharma SA

08:35 Analytical Characterization of a Complex Product: Lentiviral Vector

Julia Deuel, MSc, Senior Scientist, Analytical Characterization, bluebird Bio

Traditional molecular biology techniques can provide in-depth understanding of lentiviral vector activity and structure, but are often low-throughput and highly variable, contributing disproportionately to COGs, delays in batch release, and potential batch failures if assays cannot be repeated. Presented here are techniques for characterization of lentiviral vectors with a focus on elucidation of vector structure for evaluation of lot consistency and lentiviral vector comparability following manufacturing changes. These include modifications to commonly used techniques along with new technologies to provide a broad evaluation of lentiviral vector characteristics and impurities.

09:05 Strategy to Establish Clinically Relevant Specifications at Launch

Monika Meier, PhD, Manager, Development Analytics, Roche Diagnostics GmbH

09:35 Potent Bispecifics, Overcoming Analytical Challenges Enroute Preparation for FIH

Sachin Dubey, PhD, Deputy Director/Head, Formulation, Analytical and Drug Production Development, Glenmark Pharmaceuticals SA

There are around 130 ongoing clinical trials with different bispecifics formats (including Glenmark's proprietary BEAT molecules); they are potent and are dosed at extremely low levels (low ng/mL concentration). Preparing for FIH at such low concentration is a significant challenge from the analytical standpoint – quantification is challenging, release testing has to be adapted, and prevention against surface adsorption has to be ensured. Product characterization, de-risking manufacturing, and in-use stability for IV infusion are required to be carefully designed and executed with additional controls. Glenmark has three bispecifics in clinical development and experiences gained during their development will be discussed.

10:05 A Platform Approach to Manage Developability and Manufacturability Risks of Biologics Molecules

Jana Hersch, Scientific Consultant, Biologics, Genedata

We present a workflow system that enables systematic developability and manufacturability assessments, using both *in silico* and high throughput analytical confirmatory methods, over the entire biologics R&D process from initial discovery all the way to final candidate selection. We show use cases for mAbs and other complex multi/bispecific formats and discuss building predictive developability models utilizing this system. We also present the underlying molecule and task management needed for analytical organizations to accomplish this.

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

11:15 Kinetic Mechanism of Controlled Fab-Arm Exchange for the Formation of Bispecific Immunoglobulin G1 Antibodies

Mark Chiu, PhD, Associate Director, BioTherapeutics Analytical Development, Janssen Research & Development, LLC

A combination of FRET, non-reducing SDS-PAGE, and strategic mutation of the Ab hinge region was employed to characterize the cFAE process. Fluorescence correlation spectroscopy (FCS) was used to determine the affinity of parental (homodimer) and bispecific (heterodimer) interactions within the CH3 domain to further clarify the thermodynamic basis for bsAb formation. The result is a rate constant mechanism with the dissociation of the K409R parental Ab into half-Ab controlling the overall rate of the reaction.

11:45 Rapid Release of Autologous Cell Therapy Products to Patients: A Road Less Travelled

Kuldip Sra, PhD, Senior Director, Technical Operations, CRISPR Therapeutics

For autologous cell therapy products, each patient is a product batch. Manufacturing is a very tedious and manual process. Urgency to release the product quickly to the patient is very high. The presentation will cover the implementation of rapid analytical methods to release the final product in a desired timeframe to patients.

12:15 Luncheon Presentation I: Beyond Aggregation: a Wealth of Applications of High-Throughput DLS/SLS for Biologics and NanoDDS

Sponsored by

*Christian Sieg, PhD, Analytical Service, Wyatt Technology*

The DynaPro[®] Plate Reader III is used extensively throughout the biopharmaceutical industry to screen protein-based therapeutics for developability and optimal formulation conditions. While detection of aggregation is the most familiar application of this instrument, it is in fact far more versatile. This seminar will discuss advanced applications to biologics including solubility, aggregation kinetics, conformational and colloidal stability and optimizing crystallization conditions. Further, native reversible self-association of IgGs associated with high viscosity is addressed.

12:45 Quantifying Protein Aggregation and Subvisible Particle Size and Concentration with Nanoparticle Tracking Analysis

Sponsored by

*Jeff Bodycomb, Product Line Manager, HORIBA*

Quantifying protein aggregate and subvisible particle size and concentration in formulations remains a continuing challenge. These particles are too small to be imaged by optical microscopy; fractionation techniques change solution conditions and thereby aggregation; and the size distribution is too polydisperse for classical, single laser NTA. These issues can be addressed with multi-laser NTA, which simultaneously uses three lasers with different wavelengths to collect data on all of the particles in the suspension.

13:15 Dessert Break in the Exhibit Hall with Poster Viewing

14:00 End of Analytical Characterisation of Biotherapeutics

17:00 Dinner Short Course Registration*

17:30 – 20:30 Dinner Short Courses

Recommended Short Course*

SC8: Advanced Analytical Technologies for Developability and Early Formulation Assessments**Separate registration required. See pages 6 & 7 for details.*

Protein Aggregation & Stability

Advances in Particle Analytics and Prediction

THURSDAY 21 NOVEMBER

13:00 Registration

13:15 Dessert Break in the Exhibit Hall with Poster Viewing

PREVENTING AND MITIGATING AGGREGATION – FROM CONTAINER SPECIFICATIONS TO NEW DEVICE DESIGN

14:00 Chairperson's Opening Remarks

Thomas Laue, PhD, Professor Emeritus, Biochemistry and Molecular Biology; Director, Biomolecular Interaction Technologies Center (BITC), University of New Hampshire

14:05 KEYNOTE PRESENTATION: Closing the Analytical 0.1-to-2 Micron-Size Gap: Why, When, and How?



Wim Jiskoot, PhD, Professor, BioTherapeutics, Leiden University

Protein aggregates and other particulate impurities are critical quality attributes of biopharmaceutical drug products. Routine analytical methods, such as size-exclusion chromatography and light obscuration, are blind for aggregates and particles in the size range between about 0.1 and 2 micrometers. In this presentation, I will explain why it is important to characterize and quantify such "gap range" species, present trends in the development of analytical tools that cover this range, and discuss how these tools could be applied in product development.

14:35 FEATURED PRESENTATION: Final Container Specifications for Subvisible Particulate Matter in Therapeutic Protein Injections

Ewa Marszal, PhD, Regulatory Review Scientist, Division of Plasma Protein Therapeutics, Office of Tissues and Advanced Therapies, CBER, FDA

While ICH Q6B guidance recommends setting specifications based on data from preclinical and clinical trials and from lots used for demonstration of manufacturing consistency and product stability, the manufacturers tend to set specifications for subvisible particulate matter in biologics using as an analytical method light obscuration and the USP <787> and <788> limits. However, these limits were not developed for proteinaceous particulate matter and they are not supported with safety data. In this presentation, I will remind the history of the USP limits for subvisible particulate matter and will argue that other methods and product-specific limits will provide a better assurance of product safety, efficacy, and manufacturing consistency.

15:05 Are Particulates Hiding in Your Formulation?

Rick Gordon, Vice President, Sales, Halo Labs

See how the HORIZON system from Halo Labs uses Backgrounded Membrane Imaging (BMI) to measure subvisible particles, including translucent protein aggregates to help predict protein drug stability during early stage formulation development. The measurement is fully automated (up to 96 samples) and uses 1/10th the volume of other techniques.

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15:20 Developability Assessment and Property Prediction by pH-Dependent Conformational Sampling

Nels Thorsteinson, PhD, Scientific Services Manager, Biologics, Chemical Computing Group

mAb candidates identified from high-throughput screening or binding affinity optimization often present liabilities for developability, such as aggregation-prone regions or poor solution behavior. In this work, we developed a method for modeling proteins and performing pH-dependent conformational sampling, which can enhance property calculations such as hydrophobic patches, charge and pI. A retrospective data analysis demonstrates that these 3D descriptors, averaged over conformational sampling and stochastic titration, can accurately predict pI values, screen candidates and enrich libraries with favorable developability properties for a range of biotherapeutics. The clinical landscape of antibodies is also analyzed and its property profile and insights thereof are presented

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15:35 Networking Refreshment Break

16:00 New Design of a Blast Freezer Thawer to Minimize Freeze-Thaw Associated Protein Aggregation

Karoline Bechtold-Peters, PhD, Senior Strategy and Technology Leader, Biologics Technical Development & Manufacturing, Novartis Pharma AG

Freezing and thawing biologics drug substance is an important process step that can lead to protein destabilization and aggregation due to various, phenomena such as freeze concentration and interaction at the large ice-liquid interface. We found that the commercially available blast or shock freezers for DS bottles are not ideal because they are not working in a sufficiently homogeneous and powerful mode and are also not suitable for thawing. We have developed and further optimized an improved device to quickly freeze and thaw sensitive therapeutic proteins. The design and process results will be presented in the talk.

16:30 How Industry Handles Aggregate and Particle Issues – What Happens to Your Product Once It's Out of Your Control?

Christina Vessely, PhD, RAC, Senior Consultant, Analytical and Formulation Development, Biologics Consulting

Protein aggregates, as well as other particulate matter, have been definitively linked to immunogenicity and adverse outcomes in patients. As formulation and analytical scientists, we work very hard to ensure that the products we are sending out to clinics are of sufficient quality to maintain safety to patients. But what happens when those materials are no longer in our control? The purpose of this presentation is to inform sponsors as to what can occur between the time that you put your product into a vial and the time it is actually dosed to patients, as well as how to mitigate the potential issues thereby maintaining patient safety and product quality/efficacy.



Protein Aggregation & Stability

17:00 End of Day

17:00 Dinner Short Course Registration*

17:30 – 20:30 Dinner Short Courses

Recommended Short Course*

SC7: Protein Aggregation: Mechanism, Characterization and Consequences

*Separate registration required. See pages 6 & 7 for details.

FRIDAY 22 NOVEMBER

08:00 Registration and Morning Coffee

PREDICTION OF STABILITY AND DEGRADATION/AGGREGATION PROPENSITY

08:30 Chairperson's Remarks

Karoline Bechtold-Peters, PhD, Senior Strategy and Technology Leader, Biologics Technical Development & Manufacturing, Novartis Pharma AG

08:35 Progress in High Throughput Biophysical Characterization Approaches to Predict Long-Term Physical Stability of Protein Drugs in Pharmaceutical Formulations

Gerhard Winter, PhD, Professor, Department of Pharmacy, Pharmaceutical Technology and Biopharmaceutics, Ludwig-Maximilians-Universität

Finding the most suitable conditions which allow to minimize protein degradation during long-term storage is still a challenging task. We discuss the application of DSC 2, DSF 4, MST 8, ICD 3,5,6 and a new technique called TOPC 7, and the usefulness of determining the apparent protein-melting temperatures to select protein formulations with high physical stability. Finally, we show how the assessment of the aggregation of partially folded species during refolding can provide additional information for the selection of protein formulations with high physical stability during storage. The talk will conclude with general suggestions on how to select solution conditions that impede aggregation.

09:05 Different Grades of Polysorbate for Biopharmaceutical Products – Comparison of Their Degradation Propensity and Evaluation of Their Functional Properties

Klaus Wuchner, PhD, Scientific Director, DPDS/BioTD-Analytical Development, Janssen R&D, Cilag AG

Polysorbate 20 (PS20) and polysorbate 80 (PS80) grades compliant with major pharmacopeias (EP, USP, JP) are the most widely used surfactants in biopharmaceutical products. Chinese pharmacopoeia (ChP) requires an oleic acid content of $\geq 98.0\%$. However, still little is known about the stability and functional properties of these "higher" purity-grade PS in biopharmaceutical formulations. This talk will provide some insight into degradation behavior of different PS grades, present novel markers for oxidation, and compare the functional properties with respect to stabilizing protein against interfacial stress.

09:35 Thermodynamic Prediction of the Concentration-Dependence of Protein Solutions

Thomas Laue, PhD, Professor Emeritus, Biochemistry and Molecular Biology; Director, Biomolecular Interaction Technologies Center (BITC), University of New Hampshire

Prediction of the high-concentration behavior of biotherapeutics is of interest to their development and formulation. Approximations of solution thermodynamics are shown that allow a first-order prediction of protein behavior at high-concentrations. Though not exact, the predictions provide a useful guide to how protein and solvent characteristics impact solution behavior.

10:05 Networking Coffee Break

10:35 A Mechanistic Approach for the Assessment of Protein Aggregation Propensity in Therapeutic Proteins: Practical Application in Biopharmaceutical Drug Candidate Selection and Pre-Formulation Development

Danny K. Chou, PharmD, PhD, President, Compassion BioSolution, LLC

In recent years, our understanding of the fundamental mechanisms of protein aggregation has increased significantly. To identify the most stable and manufacturable drug candidates and develop the most robust formulation for such molecules, the logical approach is to take advantage of the current knowledge and make it the foundation of a stability assessment/formulation development plan. This presentation will show how one can implement such an approach to successfully evaluate stability of protein pharmaceuticals and develop a suitable formulation in a rapid manner.

11:05 Understanding Protein Aggregation via Computational Means

Sandeep Kumar, PhD, Senior Research Fellow, Biotherapeutics, Boehringer-Ingelheim Pharmaceuticals

- Protein folding & aggregation
- Aggregation process
- Aggregation prone regions in thermophiles, human proteome and biotherapeutics
- Benefits of aggregation mitigation
- Prediction of change in aggregation rate upon mutation
- Overall trends

11:35 Prediction and Measurement in Viscosity

Virginie Le Brun, Lonza Pharma & Biotech

12:05 Problem-Solving Breakout Discussions with a Light Snack*

*See website for more details.



Protein Aggregation & Stability

ADVANCED STRATEGIES & TECHNOLOGIES IN PARTICLE ANALYTICS

13:00 Chairperson's Remarks

Anacelia Rios Quiroz, PhD, Scientist, Group Leader, Particle Lab, Pharma Technical Development Biologics Europe, Hoffmann-La Roche

13:05 Chemometrics and Advanced Data Analytics for Particle Analysis

Jonas Hoeg Thygesen, PhD, Area Specialist, R&D Microanalysis, Novo Nordisk Pharmatech A/S

Regulatory agencies call for identification and characterization of any intrinsic, inherent, or extrinsic particles present in pharmaceuticals. Of the many tools in the analytical toolbox for particulate/foreign material identification, the methods of Fourier-Transform Infrared (FTIR) microscopy and Energy Dispersive X-ray Spectroscopy (EDS) have developed into industry standard workhorses. This presentation will highlight how chemometrics and advanced data analytics may be used to gain more insight from such analytical data collected during particle analysis.

13:35 Monitoring and Characterizing Aggregation Variants in Co-Formulated Biologic Products: Utilizing 2D Chromatography to Assess Aggregation

Mark Anthony Haverick, Associate Principal Scientist, Biologics Analytical R&D, MSD

Co-formulated drug products are currently being developed through the combination of multiple mAbs in a single vial. Coformulation of mAbs enables simplified dosing, better production and easier handling. Monitoring aggregation in co-formulated mAbs poses several challenges due to the similar size and shape of the individual mAbs. This requires a more sophisticated "analytical toolkit" to characterize the aggregation. During this presentation, we discuss the analytical control strategy for characterization of aggregation in co-formulated drug products, and the importance of understanding method performance for purity. Additionally, we will also discuss the application of two-dimensional liquid chromatography to understand aggregation and improve product knowledge.

14:05 sFIDA: A General Method for Detection and Quantitation of Protein Aggregates with Single-Particle Sensitivity for Quality Control of Biologics

Oliver Bannach, PhD, Senior Scientist, Structural Biochemistry, Institute of Complex Systems, Forschungszentrum Juelich

We have developed sFIDA as a general tool for detection and quantitation of protein aggregates with single-particle sensitivity and total insensitivity to non-aggregated protein. Thus, it allows the determination of the concentration and sizes of protein aggregate particles in any medium without pre-treatment. The method is fully automated and adaptable to any specific protein. We will demonstrate the technology and give some examples for its successful application.

14:35 Solution NMR Assessments of Therapeutic Protein Behavior

Mark McCoy, PhD, Principal Scientist, Discovery Chemistry – Screening, Target and Compound Profiling, MSD

Solution NMR spectroscopy provides detailed assessments of therapeutic peptide and protein behavior. Structural fingerprints capture solution structure, conformation, and probe for site-specific interactions at atomic resolution. Additionally, diffusion and dynamic profiling methods are used to understand self-association, assembly, aggregation, and the impact of sequence and formulation on molecular motions and interactions. Examples will be drawn from discovery and development applications that include higher-order structure characterization, developability assessments, formulation, and co-formulation studies.

15:05 Characterization of Subvisible Particles: Old Challenges and Newest Improvements

Anacelia Rios Quiroz, PhD, Scientist, Group Leader, Particle Lab, Pharma Technical Development Biologics Europe, Hoffmann-La Roche

The talk will give an overview on commercially-available counting methodologies for detection of sub visible particles (SbVP). This species, ubiquitously present in protein formulations, had been in focus due to immunogenicity and quality attributes of biotechnological products. Thus, the analytical toolbox to characterize them undergoes constant renewals and innovations. Their applicability towards the assessment of a meaningful array for particle-counting characterization will be discussed, including examples of their use in the frame of immunogenicity studies.

15:35 End of Protein Aggregation & Stability



Modulating the Tumour Microenvironment

Enhancing Effector Activity and Suppressing Inhibitory Factors

Recommended Short Course*

SC2: The Tumour Microenvironment and Response to Cancer Immunotherapy

*Separate registration required. See pages 6 & 7 for details.

MONDAY 18 NOVEMBER

12:00 Conference Registration

THE KEY TO THERAPEUTIC SUCCESS

13:30 Organiser's Welcome

Nicole Lyscom, PhD, Senior Conference Director, Cambridge Healthtech Institute

13:35 Chairperson's Opening Remarks

Dario Neri, PhD, Professor, Chemistry and Applied Biosciences, Swiss Federal Institute of Technology (ETH Zürich)

13:45 Using Antibodies to Target the Tumour Microenvironment - Good Intentions Can Often Lead to Unintended Consequences

Stephen Beers, PhD, Professor, Immunology and Immunotherapy, Centre for Cancer Immunology, Cancer Sciences Unit, University of Southampton

Despite the impact of monoclonal antibodies (mAb) in oncology, patient responses remain variable, therefore new mAb and strategies are required. Although the number of mAb reaching the clinic continues to rise, new targets are scarce and frequently fail. A key issue facing antibody drug development is understanding why promising candidates do not translate to clinical success. Here, we will show how mAb format can be critical to efficacy and how this could be particularly important when seeking to develop mAb to target the tumour microenvironment.

14:15 Fc-Dependent Expansion of Distinct Memory Populations Defines the Antitumor Efficacy of Checkpoint Immunotherapy

Sylvia Vincent, PhD, Scientist, Immuno-modulatory Drug Discovery, Agenus, Inc

We describe a novel mechanism by which distinct immune checkpoint antibodies require selective Fc-FcγR co-engagement between antigen-presenting cells (APCs) and T cells for the expansion of memory T cell subpopulations. We demonstrate that the Fc-dependent expansion of these memory populations is important for antitumor responses and is consistent between mice and man.

14:45 Targeted Cytokine Sweeping Activity Using New Bispecific Formats

Marie-Alix Poul, PhD, Professor, Immunology, Biology-Life Science, University of Montpellier, IRCM

We have designed a new functional type of bispecific antibody combining binding to a tumor-specific recycling cell surface receptor and to soluble pro-tumoral factors. This bispecific format mediates the targeted sweeping of tumor-microenvironment soluble factors by the cancer cells themselves. Three bispecific antibody formats have been designed with 2, 3, or 4 antigen-binding sites and their sweeping efficiency and cancer cell growth inhibitory properties have been compared in cancer models.

15:15 Flexible Antibody Discovery Solutions to Unlock Your Research, Diagnostic and Therapeutic Goals

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Jayne Hammersley, Principal Scientist, Abcam, PLC

Abcam's comprehensive approach to developing custom antibodies leverages three antibody discovery platforms in combination with comprehensive assay cascades. Here we describe our RabMAB peripheral B cell platform, in the context of T cell targets CTLA-4, PD-1 and PDL-1, delivering optimized IHC reagents to support your research and diagnostic goals.

15:30 Sponsored Presentation (*Opportunity Available*)

15:45 Networking Refreshment Break

PLENARY KEYNOTE SESSION

16:15 Moderator's Opening Remarks



Kerry Chester, PhD, Professor, Molecular Medicine, University College London Cancer Institute

16:20 Bispecific, Soluble TCR as the Next Therapeutic Platform



Bahija Jallal, PhD, CEO and Director of the Board, Immunocore

Of the two adaptive immunity recognition motifs, only antibodies have been brought to patients. However, antibody therapeutics only recognize 10% of human proteome (surface-expressed). The other motif, T cell receptor (TCR), has potential to unlock 90% of the human proteome, but requires converting a low-affinity, specificity membrane receptor into a soluble therapeutic. IMCgp100, a soluble, TCR bispecific-targeting melanoma, is the most advanced soluble TCR therapeutic in development.

17:20 Attacking Cancer Cell Surfaceomes with Recombinant Antibodies



James A. Wells, PhD, Professor, Departments of Pharmaceutical Chemistry and Cellular & Molecular Pharmacology, University of California, San Francisco

The cell surface proteome (surfaceome) is the primary hub for cells to communicate with the outside world. Oncogenes are known to cause huge changes in cells and we find this translates to significant remodeling of the surfaceome. We generate recombinant antibodies to detect and then attack these cells by toxicifying the antibodies or recruiting immune cells to kill. I'll discuss the technologies for surface protein analysis, an industrialized platform for rapid antibody generation using phage display, and using these tool reagents for target validation.

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

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19:30 End of Day



Modulating the Tumour Microenvironment

TUESDAY 19 NOVEMBER

07:45 Registration and Morning Coffee

TARGETING IMMUNE CHECKPOINTS

08:30 Chairperson's Remarks

Stephen Beers, PhD, Professor, Immunology and Immunotherapy, Centre for Cancer Immunology, Cancer Sciences Unit, University of Southampton

08:35 Targeting the Antibody Checkpoints to Enhance Cancer Immunotherapy—Focus on FcγRII

Björn Frendeus, PhD, CSO, BiInvent International AB

Immunotherapy with therapeutic antibodies has increased survival for patients with hematologic and solid cancers. Still, most patients fail to respond to therapy or acquire resistance. Understanding and overcoming mechanisms of resistance to antibody drugs, in particular those common to antibody drugs as a class, holds promise to improve cancer immunotherapy. This talk will discuss how activating and inhibitory Fc gamma receptors (FcγR)—the “antibody checkpoints”—regulate antibody-induced antitumor immunity, and in particular, how targeted blockade of the sole-known inhibitory FcγRIIB may help overcome resistance and boost activity of clinically validated and emerging anti-cancer antibodies.

09:05 The Development of KY1043, a Highly-Differentiated PD-L1-Based IL-2Ra-Biased Immunocytokine

Matthew McCourt, BSc, Vice President, Immuno-Oncology Discovery, Kymab Ltd.

Kymab is developing KY1043, an immunocytokine that combines an attenuated IL-2 molecule with our proprietary PD L1-blocking antibody. KY1043 is designed to remove checkpoint inhibition by preventing PD-1 signalling, deliver localized immune activation at the tumour site, and activate immunological memory against the tumour. In preclinical studies, KY1043 has been shown to eradicate tumours and lead to long-term survival, while avoiding the serious adverse events typically associated with systemic delivery of IL-2.

09:35 Problem-Solving Breakout Discussions*

*See website for details.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

KEYNOTE PRESENTATIONS: CHALLENGES AND BENEFITS OF IMMUNOCYTOKINES

11:15 Development of Novel Immunocytokines for Cancer Immunotherapy



Christian Klein, PhD, Head, Oncology Programs, Head, Cancer Immunotherapy Discovery, Roche Pharmaceutical Research and Early Development (pRED), Roche Innovation Center Zurich

High-dose IL-2 is approved for patients with metastatic melanoma and renal cell cancer, but is associated with significant toxicity. This presentation will give an overview of the engineering and development of IL-2 variant-based immunocytokines, like FAP-IL2v and novel generation immunocytokines, as well as of the combination of these agents for combination cancer immunotherapy.

11:45 Novel Formats for Antibody-Cytokine Fusion Proteins: Impact on Performance



Dario Neri, PhD, Professor, Chemistry and Applied Biosciences, Swiss Federal Institute of Technology (ETH Zürich)

Antibody-cytokine fusions allow the selective delivery of immunomodulatory stimuli to the site of disease, helping spare normal organs. In this lecture, I will show the impact of the format and architecture of antibody-cytokine fusions on therapeutic performance, both clinically and preclinically.

12:15 Vps34 Inhibitors Increase the Efficacy of Anti-PD1/PD-L1 Immunotherapy by Modulation of the Tumor Inflammatory Landscape

Angelo De Milito, PhD, Director, Tumor Biology and Therapeutics, Sprint Bioscience

New combination strategies are needed to increase therapeutic efficacy of anti-PD-1/PD-L1-based immunotherapy. Defective autophagy has been associated with a proinflammatory response regulating innate immunity. We found that genetic and pharmacological inhibition of the lipid-kinase Vps34 reduce tumor growth and increase the infiltration of immune cells, including NK, CD8+ and CD4+ T effector cells in melanoma and colon carcinoma murine tumors. Treatment with small molecule Vps34 inhibitors (Vps34i) induces an inflamed tumor microenvironment, characterized by the upregulation of pro-inflammatory cytokines and significantly improved the efficacy of anti-PD-L1/anti-PD1 therapy.

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

13:45 Dessert Break in the Exhibit Hall with Poster Viewing

TARGETING RESISTANCE: MACROPHAGES, MYELOID-DERIVED SUPPRESSOR CELLS AND CHECKPOINTS

14:15 Chairperson's Remarks

Björn Frendeus, PhD, CSO, BiInvent International AB



Modulating the Tumour Microenvironment

14:50 Selectively Inhibiting CD47 in the Tumor Microenvironment

Nicolas Fischer, PhD, Head, R&D, Novimmune

Restricting inhibition of the CD47-SIRPα signaling axis to the microenvironment using a bispecific antibody approach enables a better safety and pharmacokinetic profile when compared to monospecific approaches. This mode of action has been validated preclinically against different tumor-associated antigens covering both hematological and solid tumors. The latest development of this selective targeting approach, as well as a clinical update on the most advanced program, will be provided.

15:20 Targeting Tumor-Associated Macrophages to Improve Cancer Immunotherapy

Minhong Yan, PhD, Principal Scientist, Molecular Oncology, Genentech, Inc.

In homeostasis, apoptosis is immunologically quiescent because dying cells are disposed rapidly by tissue macrophages. As a potential way to evade immunosurveillance, tumor-associated macrophages (TAMs) may leverage the same clearance mechanism to avoid innate immune sensing of dying tumor cells. We showed that disabling the dying cell clearance transforms the tumor microenvironment towards an immunogenic milieu, which in turn, enhances the antitumor effect of the PD-1/PD-L1 blockade.

15:50 Efficacy in Syngeneic Models using a PD-L1 Affimer Antagonist in Combination with a Small Molecule Inducer of the Innate Immune System

Amrik Basran, PhD, CSO, Avacta Life Sciences

Affimer therapeutics are based on the human protein Stefin A, a small (12 kDa) intracellular protease inhibitor. Using phage display, we have generated high affinity antagonists to important check-point inhibitors, such as PD-L1. Our PD-L1 antagonist (AVA04 Fc) in combination with a small molecule inducer of the innate immune system (PT-100), demonstrated efficacy, tumour regression in several individuals, as well as immunity to rechallenge with the original mouse tumour cell line.

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16:20 Refreshment Break in the Exhibit Hall with Poster Viewing

REPROGRAMMING THE MICROENVIRONMENT/THE INNATE IMMUNE SYSTEM/GLYCO-IMMUNE CHECKPOINTS

17:00 Reprogramming Immunosuppressive Microenvironments with Multifunctional Biologics

David Mills, PhD, Director, Oncology, Therapeutics Research, Zymeworks

Although checkpoint blockade has revolutionized cancer treatment, some patient subsets remain resistant. The broader success of immunotherapy likely requires combinatorial approaches and targeting alternative mechanisms. In particular, suppressive myeloid cell accumulation reduces effector lymphocyte fitness, predicts immunotherapy resistance, and is negatively prognostic. We have undertaken a novel approach to reinvigorate anti-tumor immunity, and will discuss characterization of multifunctional, bispecific antibodies that antagonize suppressive myeloid cell activities and costimulate T cell differentiation.

17:30 TLR Agonist NKTR-262 Immunotherapy Combination with Bempegaldesleukin (NKTR-214) Harnessing Innate and Adaptive Immune System for the Treatment of Solid Tumors

Saul Kivimäe, PhD, Head, In Vivo Pharmacology Function, Research Biology, Nektar Therapeutics

NKTR-262 is a novel TLR agonist therapeutic designed to deliver intratumoral TLR7/8 engagement and is currently evaluated in Phase 1 dose escalation study with bempegaldesleukin, a CD122-preferential IL-2 pathway agonist. NKTR-262 combination treatment with bempegaldesleukin is designed to provide a synergistic effect of localized intratumoral innate immune stimulation with systemic, sustained T cell activation for comprehensive anti-tumor immune activation, mimicking a natural immune response.

18:00 Aberrant Glycosylation in Breast Cancer Results in Modulation of the Immune Microenvironment

Joy Burchell, PhD, Professor, Glyco-oncology, Head, Breast Cancer Biology Lab, Comprehensive Cancer Centre, School of Cancer and Pharmaceutical Sciences, King's College London

Cancers have developed a plethora of mechanisms to evade the immune response, including initiating a permissive local environment. For cancer cells to remodel their immune microenvironment, they need to acquire changes that include altering their glycosylation profile. We have shown that the interaction of a tumour-associated glycoform of MUC1, expressed by breast carcinomas with the lectin Siglec-9 found on monocytes and macrophages, can act as such an immune microenvironment remodeling trigger.

18:30 Targeting Immunosuppressive Sialoglycans in the Tumor Microenvironment Using a Novel Therapeutic Modality, EAGLE

Li Peng, PhD, Senior Vice President, Discovery and Early Product Development, Palleon Pharmaceuticals

The glyco-immune checkpoint axis (sialoglycan/Siglec pathway) has emerged as a novel mechanism of cancer immune escape. Here, we described a novel therapeutic modality, a bifunctional antibody-like molecule named EAGLE (Enzyme-Antibody Glyco-Ligand Editing), to target this axis by selectively removing immuno-suppressive terminal sialic acids on tumor cells. We demonstrated that EAGLE treatment led to robust anti-tumor activities and increased immune cell infiltration/activation in syngeneic mouse tumor models.

19:00 End of Modulating the Tumour Microenvironment





Winning Strategies for CAR T, TIL and TCR Therapy

Genome Editing to Improve Safety and Function

WEDNESDAY 20 NOVEMBER

07:45 Registration and Morning Coffee

QUEST FOR ALLOGENEIC CAR T CELLS

08:30 Chairperson's Opening Remarks

John Maher, FRCPATH, PhD, Consultant & Senior Lecturer, Immunology, Cancer Studies, King's College London

08:35 KEYNOTE PRESENTATION: Evolving Manufacturing Concepts and Approaches for Gene-Edited Off-the-Shelf Cell Therapy Product Candidates



Jean-Charles Epinat, PhD, CTO, Cellectis

This talk will discuss how gene editing is instrumental in moving cell therapies from grafts to off-the-shelf pharmaceuticals, evolving production and control concepts for gene-edited allogeneic cell product candidates, and how to approach manufacturing of genomically engineered designer cells.

09:05 Quest for Allogeneic CAR T Cells

Prasad S. Adusumilli, MD, FACS FCCP, Deputy Chief and Associate Attending, Thoracic Surgery; Director, Mesothelioma Program; Head, Solid Tumors Cell Therapy, Cellular Therapeutics Center (CTC), Memorial Sloan-Kettering Cancer Center; Associate Professor, Cardiothoracic Surgery, Weill Cornell Medical Center

The presentation will focus on advances in CAR T-cell therapy and the next steps in translation to clinic with specific focus on the quest for allogeneic CAR T cells. The methods will be discussed. The update on currently available modalities will be highlighted.

09:35 CRISPR-Edited Allogeneic T Cell Therapy

Waseem Qasim, PhD, NIHR Professor in Cell & Gene Therapy, Consultant in Paediatric Immunology/BMT, Institute of Child Health & Great Ormond Street Hospital

The wider application of engineered T cells may be advanced by incorporating genome editing steps to overcome HLA barriers to allow the generation of 'universal' CAR T cell banks. Transcription activator-like effector nucleases (TALEN) modified CAR19 T cells are already in clinical testing and further iterations using CRISPR/Cas9 editing are planned. Furthermore, precise chemical deamination effects can be delivered using RNA-guided deactivated Cas, offering the possibility of multiplexed editing with low risk of translocations.

10:05 Novel Mammalian Display Strategies for the Discovery of Antibody Therapeutics Targeting Integral Membrane Proteins

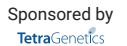
Nathan Robertson, PhD, Antibody Discovery, OXGENE

We present a novel method of mammalian display involving expression of an antibody library in a population of mammalian cells, wherein each cell displays the target polypeptide on the outer surface. This technology enables screening of large naive libraries against more intractable membrane proteins while displaying only physiologically relevant epitopes.



10:20 Discovery and Development of Therapeutic Antibodies Against Potassium Channels

Paul Colussi, Vice President, Research, TetraGenetics Inc.



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

TARGETING SOLID TUMOURS

11:15 Developing Next Generation Autologous and Allogeneic CAR T Cells without Gene Editing

Peggy Sotiropoulou, PhD, Director Research & Development, Celyad

Celyad uses an optimized shRNA technology to generate next-generation autologous and allogeneic CAR T cell therapies. The first autologous product developed is CYAD-02, our next-generation NKG2D-based CAR, showing increased *in vivo* persistence and anti-tumor activity in animal models. In the allogeneic CAR T cell field, Celyad leverages the shRNA platform to target CD3ζ and effectively knock down TCR expression. This protected animals against GvHD, while enhancing persistence of allogeneic CAR T cells compared to gene-editing approaches.

11:45 CARs, TRUCKs and Beyond: Novel Strategies to Target Solid Cancer

Univ.-Prof. Dr. Hinrich Abken, MD, PhD, RCI, Regensburger Centrum für Interventionelle Immunologie, Lehrstuhl für Gen-Immuntherapie, Universitätsklinikum Regensburg

Adoptive therapy with chimeric antigen receptor (CAR)-modified T cells achieved remissions of so far refractory leukemia/lymphoma, however treatment of solid cancer remains challenging. We engineered CAR T cells with an inducible expression cassette to release a heterologous protein upon CAR signaling. Such TRUCKs or "fourth generation" CAR T cells are going to change our concepts of treating solid tumors and delivering drugs to predefined lesions in the near future.

12:15 Clinical Strategies for Overcoming Challenges of Engineered T Cells in Solid Tumours

Fiona Thistlethwaite, MB, BChir, PhD, MRCP, Medical Oncology Consultant, Experimental Cancer Medicine Team (ECMT); Honorary Senior Lecturer, Division of Cancer Sciences, Faculty of Biology Medicine & Health, The University of Manchester; iMATCH Director, The Christie NHS Foundation Trust

The remarkable responses seen with CAR T therapy in haemato-oncology malignancies have yet to be replicated in the solid tumour setting. This talk will focus on approaches being taken to overcome the multiple challenges in solid tumours, including lack of truly tumour-specific surface antigens required for CAR T therapy. TCR T cell therapy is one approach where clinical responses have been demonstrated, indicating the potential for this approach in solid tumours.

12:45 Selected Poster Presentation: CARDIS: Next Generation CAR Discovery

Eleni Chantzoura, PhD, Senior Scientist, Immune Receptor Discovery, AgenTus Therapeutics, Inc.

13:00 Selected Poster Presentation: Half-Life Extended Soluble Adapters for Efficient Re-Targeting of Universal Switch On/Off CAR-T Cells (UniCAR) Against Leukemia and Solid Tumors

Jan Erik Meyer, PhD Student / Doktorand, GEMoAB Monoclonals GmbH



Winning Strategies for CAR T, TIL and TCR Therapy

13:15 Luncheon Presentation I: Specificity Screening of Cell Therapies Against Extensive Libraries of Plasma Membrane and Secreted Protein Targets

Diogo Rodrigues Ferreira, MSc, European Business Development Manager, Retrogenix Limited

Cell microarray screening of plasma membrane and tethered secreted proteins that are expressed in human cells enables rapid discovery of primary receptors, as well as potential off-targets for a variety of biologics, including: peptides, antibodies, proteins, CAR T, and other cell therapies. Case studies will demonstrate the utility of the technology in identifying novel, druggable targets, as well as in specificity screening to aid safety assessment and provide key data to support IND submissions.

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13:45 Talk Title to be Announced

James Keck, Senior Director, Innovation & Product Development, The Jackson Laboratory

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14:15 Session Break

14:35 TEGs: A New Avenue in Cellular Immunotherapy

Haakan Norell, PhD, Director, Discovery, Gadeta B.V.

Identification of generally applicable receptors that specifically target various malignancies remains challenging. Gadeta employs $\gamma\delta$ TCRs, which are not restricted to a single class of antigen-presenting proteins or dependent on mutation-induced neoantigens, to resolve this key bottleneck for broader application of engineered T cell therapies. Our product platform, TEG ($\alpha\beta$ T cells engineered to express a defined Gamma-delta receptor), achieves potent, yet highly specific reactivity across many different tumor types.

15:05 Non-Viral Genetic Engineering of Cytokine-Induced Killer (CIK) Cells with Chimeric Antigen Receptors (CARs) for the Targeting of Acute Myeloid Leukemia

Sarah Tettamanti, PhD, Centro Ricerca M. Tettamanti, Clinica Pediatrica Ospedale S. Gerardo, Università Milano-Bicocca

In AML, the CAR strategy is still in a challenging phase of clinical development. In this study, we aimed at arming, by the use of a cost-effective and safe non-viral approach, the effector population of Cytokine-Induced Killer (CIK) cells with CAR molecules targeting CD33 and CD123 AML overexpressed antigens. *In vitro* and *in vivo* characterizations have been performed to pre-clinically test this new platform on non-viral anti-AML CAR-CIK cells.

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

TCR THERAPIES AND THEIR DERIVATIVES

16:15 Using Insight into TCR Functioning for an Improvement of CARs

Prof. Dr. Wolfgang Schamel, Institute of Biology III (Molecular Immunology) and BIOS Centre for Biological Signaling Studies, University of Freiburg; Centre of Chronic Immunodeficiency, University Medical Centre Freiburg

We (Schamel group) study the mechanisms with which the TCR is activated by ligand binding for many years. Our main finding is that the TCR-CD3 complex exists in two different conformations: the resting inactive conformation and the active conformation. In fact, basal signaling by the TCR is suppressed by its quaternary structure. This is missing in chimeric antigen receptors (CARs). Furthermore, the different CD3 subunits contain different signaling domains. Again, in the CD3 ζ -based CARs, most of them are missing. Having this in mind, we (TCR2 Therapeutics and Schamel group) have engineered and studied a new format

of CARs called TCR fusion constructs (TRuCs). We show that an intact TCR complex can be effectively reprogrammed for cancer therapy by recombinantly fusing an anti-CD19 scFv to its TCR α , TCR β , CD3 ϵ , CD3 γ , or CD3 δ subunit. Respective scFv-TCR fusion constructs (termed TRuCs) were integrated into the TCR complex and expressed on the surface of T cells. In the presence of CD19-positive tumor cells, fusion constructs based on CD3 ϵ and CD3 γ could specifically and potently activate T cells. Despite the absence of extra signaling domains, TRuC-T cells showed similar *in vitro* cytotoxicity as CD28- and 4-1BB-based anti-CD19 CAR T cells. A single CD3 ϵ -TRuC-T cell dose greatly extended the survival of mice with Nalm-6 leukemia. In a subcutaneous Raji tumor model, CD3 ϵ -TRuC-T cells outperformed CAR T cells in terms of anti-tumor activity. Our novel technology for genetically engineering T cells provides an alternative to CARs that can engage the physiological and broad signaling capacity of the entire TCR complex.

16:45 Development of a Next Generation Immune Checkpoint Modulator towards the Clinic: A Humanized BTN3A Antibody (ICT01) Activating gamma9delta2 T Cells

Prof. Dr. René Hoet, PhD, CSO, ImCheck Therapeutics

ImCheck Therapeutics is advancing the first activating butyrophilin BTN3A (CD277) antibody towards the clinic. The humanized antibody to BTN3A, ICT01, specifically activates human gamma9delta2 T cells *in vitro* and *in vivo* and is planned to enter Phase I studies in early 2020. Additionally, therapeutic antibodies against 5 novel butyrophilins are currently validated. This opens a completely new space that is clearly different from the current B7/CD28 superfamily targets and has the potential to become the next generation immune checkpoint modulators.

17:15 TCR T Cell Therapies – What Have We Learned So Far and Where Next?

Helen Tayton-Martin, PhD, MBA, CBO, Adaptimmune

T cell therapy represents a new modality in the battle to treat cancer with immunotherapy as recent approvals have shown. However, the natural method by which T cells activate and kill infected or tumour cells involves engagement between the TCR and its cognate peptide-HLA complex on the surface of the cell. Starting from this fundamental principle, seeking to understand why it fails in cancer then moving to enhance the fundamental biology of the TCR to enable recognition and killing of cancer cells (and not normal cells) to produce a T cell product capable of benefiting patients in the real world, has been the focus of Adaptimmune for over 11 years. Today, the company has demonstrated the efficacy of this platform, termed SPEAR T cells (Specific Peptide Enhanced Affinity Receptor T cells) against solid tumours in synovial sarcoma with more than one product and has shown signs of activity with tumour shrinkage across multiple tumours with all of its three proprietary clinical programs. It has built a fully integrated capability to identify and validate TCR targets, produce and safely test engineer TCRs, optimise the viral vector to transfer them to patients' T cells, and the capability to manufacture and release those T cells products from its own facilities to patients across the US, Canada, the UK, and Europe. It has a Phase II (SPEARHEAD-1) study launching with its MAGE A4-targeted T cells (ADP-A2M4) in 2019 in synovial sarcoma and myxoid round cell liposarcoma (MRCLS) and has built a bank of translational and correlative immunology expertise informing optimisation of the T cell product for durable efficacy and efficient delivery across multiple tumours with its first second-generation SPEAR T cell product (ADP-A2M4CD8 – the SURPASS Trial) also launching this year. Every step is an evolution in understanding on the path to produce accessible and safe products capable of benefiting patients and this learning will be the focus of the presentation.

17:45 Networking Reception in the Exhibit Hall with Poster Viewing

18:45 Problem-Solving Breakout Discussions*

*See website for details.

19:45 End of Day





Winning Strategies for CAR T, TIL and TCR Therapy

THURSDAY 21 NOVEMBER

08:00 Registration and Morning Coffee

TILs AND GAMMA DELTA THERAPY

08:30 Chairperson's Remarks

John Maher, FRCPATH, PhD, Consultant & Senior Lecturer, Immunology, Cancer Studies, King's College London

08:35 Developing TIL-Based Treatment for Solid Tumours

Robert Hawkins, MB BS, MRCP, PhD, FRCP, Cancer Research UK Professor, Medical Oncology, University of Manchester; Honorary Consultant, Medical Oncology, Christie Hospital; Chief Executive Officer and Director, Immetacyte Ltd.

This talk will address the background to TIL therapy and potential benefits in solid tumours, clinical results in melanoma, pre-clinical data in other tumours, and engineering TIL to produce second-generation products.

09:05 Gamma Delta CAR T Cells Engineered for Avoidance of Toxicity and Dysfunction

John Anderson, PhD, GOSHCC Professor of Experimental Paediatric Oncology, Honorary Consultant Oncologist, UCL Great Ormond Street Institute of Child Health

Gamma delta T lymphocytes combine properties of innate and adaptive immunity. Through exploiting the natural ability of gamma delta T cell receptors to distinguish normal from diseased cells in a MHC unrestricted manner, engineering approaches can provide additional stimulatory signals in a tumour antigen-dependent manner that fine-tune tumour reactivity. Unlike conventional T cells, gamma delta T do not provoke graft versus host disease, so gamma delta CAR T are a promising approach for development of allogeneic universal cell products.

09:35 Innate T Cells for the Treatment of Disease

Derek G. Doherty, PhD, Associate Professor, Trinity College Dublin; Head, Discipline of Immunology, Trinity Translational Medicine Institute, St. James's Hospital

Innate T cells are unconventional T cells that recognise non-peptide antigens using semi-invariant T cell receptors. Some innate T cells have powerful antitumor activities and are being targeted in clinical trials in humans. They have advantages over conventional T cells in that they can be activated using conserved antigens; they rapidly, powerfully, and selectively activate adaptive immune responses; and they are unlikely to mediate allogeneic tissue rejection.

10:05 Sponsored Presentation (Opportunity Available)

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

11:15 NKTR-255: A Polymer-Conjugated IL-15 that Enhances CAR T Efficacy in Murine Models

Loui Madakamutil, PhD, Senior Vice President, Head of Biology and Preclinical Development, Nektar Therapeutics

CAR T cells have transformed the treatment paradigm in hematological malignancies, especially in the relapse refractory disease setting. Increasing evidence suggests that CD19 CAR T agents have issues with durability when infused in patients and better outcome is correlated with durable and enhanced uptake of CAR T cells after their infusion. Several studies indicate that T cell homeostatic cytokines, like IL-15 and IL-7, have correlation to CAR T cell survival and engraftment in patients by providing stemness and long-term survival for the CAR T cells. NKTR-255 is a polymer-conjugated IL-15 that retains binding affinity to IL15R α and exhibits reduced clearance to thereby provide a sustained pharmacodynamic response to CD8 memory T cells and NK cells. This presentation will cover our investigation of NKTR-255 to synergize and provide long term benefit for CAR T products in preclinical model systems.

11:45 CAR T-Cell Immunotherapy of Solid Tumours: Lessons from the Clinic and Lab in Parallel

John Maher, FRCPATH, PhD, Consultant & Senior Lecturer, Immunology, Cancer Studies, King's College London

12:15 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

13:15 Dessert Break in the Exhibit Hall with Poster Viewing

14:00 End of Winning Strategies for CAR T, TIL and TCR Therapy

17:00 Dinner Short Course Registration*

17:30 – 20:30 Dinner Short Courses

Recommended Short Course*

SC9: T Cell Therapies: Current Field, Challenges and Future Directions

**Separate registration required. See pages 6 & 7 for details.*





Agonist Immunotherapy Targets

Expanding Formats & Approaches for Better Targeting

THURSDAY 21 NOVEMBER

13:00 Registration

13:15 Dessert Break in the Exhibit Hall with Poster Viewing

ENHANCING TUMOR TARGETING AND AUTOIMMUNITY

14:00 Chairperson's Opening Remarks

Elizabeth Trehu, MD, FACP, CMO, Jounce Therapeutics

14:05 FEATURED PRESENTATION: Controlling STING, Infectious Disease, Inflammation and Cancer

Glen Barber, PhD, Professor, Cell Biology, University of Miami

Regulation of the immune system to facilitate anti-tumor cytotoxic T cell (CTC) responses is proving to be a powerful approach for the treatment of cancers. STING controls a key innate immune signaling pathway that influences cytokine production essential for robust CTC activity, although chronic signaling can invoke inflammation. Understanding these processes has shed significant insight into mechanisms of viral pathogenesis, inflammation as well as anti-tumor immunity and is leading to the generation of novel strategies to help treat such diseases.

14:35 Enhancing Antibody Tumor Targeting with Immunostimulation

Sean Hua Lim, PhD, CRUK Associate Professor, Honorary Consultant, Haematological Oncology, Antibody & Vaccine Group, CCI, University of Southampton

Tumour-targeting monoclonal antibodies have proven but limited anti-tumour efficacy. Here, we discuss how immunostimulatory antibodies can enhance the efficacy of tumour-targeting antibodies through bystander myeloid cell activation.

15:05 SELECTED POSTER PRESENTATION: Developing New Antibodies to Target Treg Cells Using the Patient Centric F.I.R.S.T.™ Platform

David Ermert, PhD, Senior Research Scientist, and Petra Holmkvist, PhD, Research Scientist, Antibody Discovery & Target ID, Bioinvent Intl AB

As many of the most well-established immune receptors such as CD40, OX40, CTLA4, and PD-1, have already been specifically targeted using conventional antibody generation approaches, alternative approaches are required to generate the next generation of novel immunomodulatory antibodies. We therefore applied an unbiased, phenotypic strategy to identify new first-in-class immunomodulatory antibodies. With our patient-centric F.I.R.S.T.™ platform we isolate tumor associated immune cells from primary tumour tissue, and use them to screen for novel antibodies from our fully human n-CoDeR® phage display library. This target-agnostic, holistic approach allows us to identify and develop first-(and best)-in-class antibodies directed to novel targets and antibodies, which by conventional target-focused approaches based on well-established known receptor functions would be neglected and disregarded.

15:35 Networking Refreshment Break

COMBINATION THERAPIES

16:00 Development of ONCR-177, a miR-Attenuated Oncolytic HSV-1 Designed to Potently Activate Systemic Anti-Tumor Immunity

Christophe Queva, PhD, CSO, Oncorus, Inc.

ONCR-177 is an oncolytic Herpes Simplex Virus engineered with complementary safety mechanisms, such as tissue-specific miR attenuation and UL37 mutation to reduce replication, neuropathic activity, and latency in normal cells, while preserving oncolytic ability in tumor cells. ONCR-177 is armed with five transgenes: IL-12, CCL4, FLT3LG, and antagonists to PD-1 and CTLA-4. Mouse ONCR-177 mediates potent anti-tumor efficacy in multiple syngeneic models, and elicit durable complete responses and protective immunity warranting its clinical investigation for the treatment of metastatic cancer.

16:30 Immunomodulatory Properties of the Glyco-Optimized Anti-EGFR Antibody Tomuzotuximab and Their Relevance for Combinatory Immunotherapy

Christoph Goletz, PhD, Associate Director, Preclinical Pharmacology & Cancer Immunology, GlycoTope GmbH

Tomuzotuximab (previously known as CetuGEX) is a defucosylated anti-EGFR antibody with enhanced capacity to mediate antibody-dependent cellular cytotoxicity (ADCC) compared to its fucosylated counterpart cetuximab. In this study, we evaluated the immune activation by tomuzotuximab beyond NK cell-mediated ADCC in comparison to cetuximab in order to build up rationales for combinatory therapies with agonistic and antagonistic antibodies targeting immune checkpoint molecules.

17:00 End of Day

17:00 Dinner Short Course Registration*

17:30 – 20:30 Dinner Short Courses

Recommended Short Course*

SC10: Engineering of Bispecific Antibodies and Multi-Specific Non-Antibody Scaffolds

*Separate registration required. See pages 6 & 7 for details.

FRIDAY 22 NOVEMBER

08:00 Registration and Morning Coffee

ICOS

08:30 Chairperson's Remarks

Peter Ellmark, PhD, Vice President Discovery, Alligator Bioscience AB



Agonist Immunotherapy Targets

08:35 KEYNOTE PRESENTATION: Agonists to the TNF Superfamily: Lessons Learned for TNFR2 for Autoimmunity



Denise L. Faustman, MD, PhD, Director, Immunology, Massachusetts General Hospital; Associate Professor, Medicine, Harvard Medical School

TNFR2 is a bi-directional switch for Treg expansion or contraction and therefore an attractive target for autoimmunity versus cancer therapies. Over the last 10 years we have worked on the perfection of agonistic antibodies to the TNF superfamily to identify candidates that do not require the natural ligand and do not require ADCC engagement, both traits that limit the clinical effectiveness due to ligand availability and could be associated with liver toxicity. New candidates with these traits have been identified to the human TNFR2 receptor and in autoimmune cells in culture restore the potent immunosuppression of Tregs that were weak prior to exposure to novel agonistic proteins.

09:05 Emergence of ICOS hi CD4 T Cells Correlates with Tumor Reduction, Progression-Free Survival, and Overall Survival in Advanced Cancer Patients Treated with Vopratelimab, an ICOS Agonist

Elizabeth Trehu, MD, FACP, CMO, Jounce Therapeutics

Vopratelimab is an ICOS agonist antibody intended to stimulate primed CD4 T effector cells. In the ICONIC trial, peripheral T cell phenotyping demonstrated emergence of an ICOS hi subset of activated CD4 T effector cells associated with tumor reductions and improved PFS and OS in mono and combo patients, with expansion of peripheral T cell receptor clones found in the original matched archival tumor. Future development focuses on settings in which CD4 T effector cells are primed to respond to vopratelimab.

09:35 GSK3359609- Anti-ICOS IgG4 Antibody Engineered for Optimized T Cell Agonist Effects Translating to Anti-Tumor Responses in the Clinic

Sapna Yadavilli, GSK Associate Fellow, Precision Medicine Lead, Clinical Biomarkers and Experimental Medicine, Oncology TA, GSK

ICOS is a T cell costimulatory receptor with unique function in T and B cell-mediated immune responses. GSK3359609 is a humanized IgG4PE with strong binding to ICOS without ADCC mediated T cell depletion which exhibits immune-stimulatory activity and efficacy in non-clinical tumor models. In the INDUCE-1 study, pharmacodynamic evaluation of GSK3359609 demonstrates dose-dependent changes in immune activation as well as promising clinical activity as monotherapy and in combination with PD1 blockade.

10:05 Networking Coffee Break

CD137/4-1BB

10:35 CTX-471, a CD137 Agonist Undergoing Clinical Development in Patients with Advanced Solid Tumors

Michael J. Schmidt, PhD, SVP & Head, Research, Compass Therapeutics

CTX-471 is a fully human monoclonal antibody that binds and activates a novel epitope of the co-stimulatory receptor CD137. Preclinical data suggest that CTX-471 has the potential to become a best-in-class CD137 agonist displaying curative monotherapy efficacy against multiple syngeneic tumor models and generation of long-term functional immunological memory. Most notably, CTX-471 is able to induce the complete eradication of large, established tumors where other preclinical CD137 antibodies and antibodies against PD-1, PDL-1, CTLA-4, and OX40 have minimal effect.

11:05 T Cell Enhancers for Focused CD137/4-1BB Co-Stimulation in the Tumor Microenvironment

James Legg, PhD, Senior Vice President, Research, Crescendo Biologics

Agonist antibodies binding to CD137 have shown great promise in preclinical models, but clinical development has been frustrated by severe toxicity and a narrow therapeutic index due to on-target, out-of-tumour activation leading to liver toxicity. Crescendo Biologics has initiated preclinical development of CB307, a novel tri-specific T cell enhancer targeting CD137, prostate specific membrane antigen (PSMA) and human serum albumin. This molecule has been designed to focus CD137 co-stimulation in the tumour and achieve an improved therapeutic index. The talk will describe the mechanism of action and preclinical characterisation of CB307 as well as an update on preclinical development.

11:35 Novel Strategies in Targeting CD137 in Solid Tumors

Erminia Massarelli, MD, PhD, Associate Clinical Professor, Medical Oncology and Therapeutics Research, City of Hope Comprehensive Cancer Center

CD137 is an attractive target in solid tumors to activate and enhance anti-cancer immune responses as well as suppress oncogenic cells. Anti-CD137 antibodies have shown safety and efficacy in selected solid tumors and trials are ongoing studying safety and efficacy of these antibodies in combination with other immunotherapy strategies. In this talk current knowledge of targeting CD137 strategies and future perspectives will be discussed.

12:05 Problem-Solving Breakout Discussions with a Light Snack*

*See website for more details.

CD40, GITR AND OX40

13:00 Chairperson's Remarks

Denise L. Faustman, MD, PhD, Director, Immunology, Massachusetts General Hospital; Associate Professor, Medicine, Harvard Medical School

13:05 Bispecific Agonistic Antibodies for Tumor Directed Immunotherapy

Peter Ellmark, PhD, Vice President, Discovery, Alligator Bioscience AB

Preclinical data on Alligator's bispecific programs will be presented, including a novel concept involving bispecific agonistic antibodies designed to increase the tumor-specific T cell repertoire. *In vitro* data and *in vivo* data using a transgenic mouse model will also be presented.

13:35 Development of a Novel Bi-Functional Fusion Protein: SIRPa-Fc-CD40L for Cancer Immunotherapy

George Fromm, PhD, Vice President, R&D, Shattuck Labs, Inc.

The SIRPa/CD47 axis has emerged as an exciting clinical target, whereby blockade could enhance antigen cross-presentation in immune-neglected (anti-PD1 refractory) tumors. The most potent antigen cross-presenters (DCs/Macs) express CD40, and stimulation of CD40 enhances CD8+ lymphocyte activation by these cells. Dual CD47-blockade and CD40-costimulation by SIRPa-Fc-CD40L performs both of these important functions, and has demonstrated superior activity compared to CD47/CD40 antibody combinations; which may position this compound to provide unique benefits to cancer patients.





14:05 Tumor Localized Agonistic Anti-CD40 Therapy and Beyond

Sara Mangsbo, PhD, Associate Senior Lecturer, Biologics, Uppsala University

Anti-CD40 agonistic therapy is a promising cornerstone in tumor immunotherapy. We have evaluated therapeutic effects of both agonistic CD40 antibodies along with CD40L expressing viruses in preclinical models, and some of our evaluated therapies have also reached clinical testing. Herein I will present the current work of our group with a focus on CD40 agonistic therapeutic strategies.

14:35 HERA-GITRL: A Unique Hexavalent GITR Agonist for Cancer Immunotherapy

Oliver Hill, PhD, Vice President, Drug Discovery/Lead Optimization, Apogenix AG

HERA-GITRL is a member of a novel class of hexavalent TNFR superfamily agonists that share the natural ligand conformation. The biological activities of HERA-GITRL, boosting antigen-specific T cell response and anti-tumor efficacy in mouse models, are crosslinking independent. As the Fc-mediated mixed mode of actions observed for antibodies are avoided, HERA-GITRL is an excellent candidate for further development into a next generation GITR agonistic immuno-oncology drug.

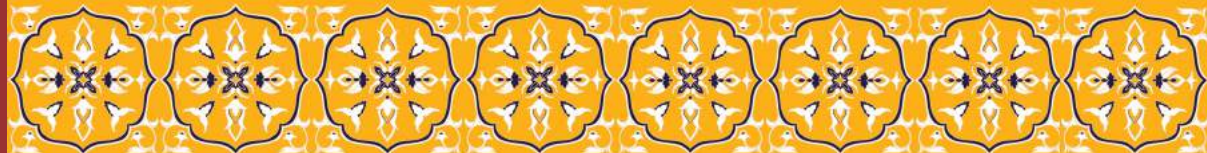
15:05 Multispecific and Multivalent Antibodies as OX40 Agonists

Mandar Bawadekar, PhD, Senior Scientist, Immunology, Invenra

OX40 and other TNFR-Super Family members are notorious for requiring secondary cross-linking strategies to achieve activity with monoclonal antibodies, and thus present significant clinical challenge. In this presentation, we will talk about the OX40 agonist antibodies developed using Invenra's B-Body™ platform, that exceed the potency of the OX40 ligand in NF-kB activation. Our lead agonist antibody has been optimized for activity and *in vivo* tumor efficacy and is currently under preclinical development.

15:35 End of Agonist Immunotherapy Targets





Cell Line and Systems Engineering

Expanding the Protein Engineering and Expression Toolbox

Recommended Short Course*

SC5: Use and Troubleshooting of Eukaryotic Expression Systems

*Separate registration required. See pages 6 & 7 for details.

MONDAY 18 NOVEMBER

12:00 Conference Registration

GENOME ENGINEERING

13:30 Organiser's Welcome

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

13:35 Chairperson's Opening Remarks

Cecília Maria Arraiano, PhD, Investigador Coordenador, ITQB-Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa

13:45 Engineering Vector Components and Host Cells for Next-Generation Bioproducts

David James, PhD, Professor, Bioprocess Engineering, Chemical and Biological Engineering, University of Sheffield

Engineering complex cellular performance characteristics is an unpredictable challenge made more difficult by the variability of CHO cell lines, protein products, and production processes. There is no one-size-fits-all solution. As a new paradigm for cell line development we are developing a hyper-variable design space for mammalian cell factory engineering that utilises directed and synthetic variation of chemical, genetic, and cellular input components as a core strategy to optimize cell functional performance beyond natural limits.

14:15 Synthetic Biology Applied to Modulate Heterologous Gene Expression Using Portable mRNA-Stabilizing 5'-UTR Sequences

Cecília Maria Arraiano, PhD, Investigador Coordenador, ITQB-Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa

Cell survival requires continuous degradation and synthesis of RNAs. Transcript stability is generally missed for manipulation in synthetic designs. By keeping transcription fixed and combining different 5' untranslated regions (5'UTRs) and constant RBS, mRNA decay was made the limiting factor of gene expression flow. This work resulted in a collection of well-characterized mRNA-stabilizing sequences that can be used as modules in any construct following the assembly rules of the Standard European Vector Architecture (SEVA) format.

14:45 Precise Genome Engineering of Hybridomas for Antibody Expression and Screening

Cristina Parola, PhD, Postdoctoral Research Scientist, Biologics Research, Sanofi

By taking advantage of precision genome editing with CRISPR-Cas9, we have developed a novel

mammalian cell platform for the expression of full-length antibodies in hybridoma cells. The Plug-and-(Dis)play (PnP) workflow included the initial generation of a reporter, antibody-negative cell line; in the subsequent reprogramming step, a novel specificity is introduced by means of a synthetic antibody. Finally, we optimized HDR efficiency to render the system amenable to the expression and screening of B cell repertoires: this feature allowed the *de novo* discovery of antibodies from immune libraries.

15:15 Challenges and Strategies in Expression of a Bi-Specific Antibody

Jay Sinha, PhD, Associate Director, Cell Culture Process Sciences, Global Biopharmaceutical Development, Incyte Corporation

A process has been developed for producing Phase I clinical study material. Several expression platforms were examined for expression of a model bispecific antibody. The product quality and titer were found to vary with changes to host-vector system. The challenges and strategies used for cell line and process development will be discussed.

15:45 Networking Refreshment Break

PLENARY KEYNOTE SESSION

16:15 Moderator's Opening Remarks



Kerry Chester, PhD, Professor, Molecular Medicine, University College London Cancer Institute

16:20 Bispecific, Soluble TCR as the Next Therapeutic Platform



Bahija Jallal, PhD, CEO and Director of the Board, Immunocore

Of the two adaptive immunity recognition motifs, only antibodies have been brought to patients. However, antibody therapeutics only recognize 10% of human proteome (surface-expressed). The other motif, T cell receptor (TCR), has potential to unlock 90% of the human proteome, but requires converting a low-affinity, specificity membrane receptor into a soluble therapeutic. IMCgp100, a soluble, TCR bispecific-targeting melanoma, is the most advanced soluble TCR therapeutic in development.

17:20 Attacking Cancer Cell Surfaceomes with Recombinant Antibodies



James A. Wells, PhD, Professor, Departments of Pharmaceutical Chemistry and Cellular & Molecular Pharmacology, University of California, San Francisco

The cell surface proteome (surfaceome) is the primary hub for cells to communicate with the outside world. Oncogenes are known to cause huge changes in cells and we find this translates to significant remodeling of the surfaceome. We generate recombinant antibodies to detect and then attack these cells by toxifying the antibodies or recruiting immune cells to kill. I'll discuss the technologies for surface protein analysis, an industrialized platform for rapid antibody generation using phage display, and using these tool reagents for target validation.





Cell Line and Systems Engineering

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

19:30 End of Day

Sponsored by
abcam

including monoclonal antibodies. The presented cell-free system is an integral part of a synthetic platform for *in vitro* glycoengineering of proteins by model-supported, cost-efficient and scalable biocatalytic processes being established by our group.

TUESDAY 19 NOVEMBER

07:45 Registration and Morning Coffee

CELL-FREE SYSTEMS

08:30 Chairperson's Remarks

Thomas Rexer, PhD, Team Lead, Dynamics of Complex Technical Systems, Bioprocess Engineering, Max Planck Institute

08:35 Integrating Cell-Free Expression, Purification, and Bioconjugation

Marco G. Casteleijn, PhD, Senior Researcher, Industrial Biotechnology, VTT Technical Research Institute of Finland

We aim to develop new tools for cell-free protein synthesis. For example, to integrate protein expression, purification, and bioconjugation in small volumes coupled with cell-free protein synthesis. We compared light triggered release with traditional affinity chromatography. Moreover, we explored transferring a moiety from a captured peptide to the target protein without further purification steps and used time gated Raman spectroscopy to evaluate protein quality.

09:05 Development of a High-Yield Cell-Free Synthesis Platform from *Pichia Pastoris*

Karen Polizzi, PhD, Reader in Biotechnology, Department of Chemical Engineering, Imperial College London

Pichia pastoris (syn Komagataella spp.) is a methylotrophic yeast used in recombinant protein manufacture because of its high volumetric productivity. We have developed a CFPS platform using *P. pastoris* via optimisation of reaction conditions and vector design and overexpression of global regulators of ribosome synthesis to increase overall yields. The result is a system that is suitable for prototyping vectors before strain development or manufacturing of proteins directly.

09:35 Problem-Solving Breakout Discussions*

*See website for details.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

CELL-FREE SYSTEMS (CONT.)

11:15 Synthetic Platform for *in vitro* Glycoengineering of Proteins by a Cell-Free, Compartmentalized Multi-Enzyme Cascade

Thomas Rexer, PhD, Team Lead, Synthetic Glycobiotechnology, Bioprocess Engineering, Max Planck Institute for Dynamics of Complex Technical Systems Magdeburg

N-linked glycans attached to proteins are involved in a wide range of processes such as biological recognition, protein stability, immunogenicity, and antigenicity. Therefore, the glycosylation of proteins is an important parameter to be considered in the optimization of animal cell culture-derived drugs

11:45 Cell-Free Based Approach for Rapid Screening of Antibody Fragment Libraries

Shayli Varasteh Moradi, PhD, Research Associate, Science and Engineering School, Queensland University of Technology

Cell-free protein expression system (CFPS) allows the robust production of recombinant proteins in a multiplexed format. We developed a rapid method for antibody fragment libraries screening based on eukaryotic *Leishmania tarentolae* (LTE) system in combination with AlphaLISA technology to study protein-protein interaction. The presented technique provides a powerful tool for rapid protein binders' selection with high sensitivity and throughput.

12:15 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

13:45 Dessert Break in the Exhibit Hall with Poster Viewing

CELL-LINE ENGINEERING

14:15 Chairperson's Remarks

Bjørn Voldborg, MSc, Director, CHO Cell Line Development, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark

14:20 KEYNOTE PRESENTATION: Unique Engineering Targets for Antibody Production Cell Lines: Selection, Cloning, Glycan Modifications, and Chromatin Readers



Volker Sandig, PhD, CSO, ProBioGen AG

Omics approaches are often applied to determine holistic strategies to improve key cell line attributes: yield, stability, robustness, and product quality. Instead, we have selected important junctions in known pathways to enhance cell line performance.

We will show how transgene cassettes embedded into transposons can be directed to most active genomic loci taking benefit of natural chromatin reader domains, discuss the impact for bispecific antibodies, and look into pathway deflection to set specific glycan features.

14:50 Development of a Pre-Glycoengineered CHO-K1 Host Cell Line for the Expression of Antibodies with Enhanced Fc Mediated Effector Function

Oliver Popp, Dr. rer. nat., Principle Scientist, pRED, Large Molecule Research, Roche Diagnostics GmbH, Roche Innovation Center Munich

Here, we present the development of a glycoengineered CHO-K1 host cell line, stably expressing β 1,4-N-Acetylglucosaminyltransferase III and α -mannosidase II, for the expression of a-fucosylated antibodies with enhanced Fc-mediated effector function.





Cell Line and Systems Engineering

15:20 Expanding the CHO Cell Line Development Toolbox to Enable Fast-Track Development of Innovative Biotherapeutics

Valerie Schmieder, PhD, Post-Doctoral Researcher, Cell Line Development, Bioprocess Development Biologicals, Boehringer Ingelheim Pharma GmbH & Co. KG

The increasing demand for novel biotherapeutics is driving the generation and implementation of innovative as well as disruptive tools for cell line development (CLD) in CHO. Additionally, more and more complex molecules, such as multi-specific antibodies, are further challenging the production of therapeutic proteins from CHO. Here, we present our recent achievements in the use of state-of-the-art technologies to overcome current and future challenges in CLD.

15:50 GPEX Boost: A Novel Approach for High-Expressing CHO Cell Line Engineering

Gregory T. Bleck, PhD, Global Head, Research & Development, Biologics, Catalent Pharma Solutions

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BIOLOGICS

16:20 Refreshment Break in the Exhibit Hall with Poster Viewing

CELL-LINE ENGINEERING (CONT.)

17:00 Combining a CRISPR Library with Phenotypic Enrichment to Identify Gene Engineering Targets in CHO Cells

Niamh Keogh, Research Scientist, Niall Barron Laboratory, Chemical and Bioprocess Engineering Department, National Institute for Bioprocessing Research & Training

CRISPR Technology has the ability to fundamentally change the capabilities of genetic engineering. My work focuses on using CRISPR/CAS 9 to generate individual knock outs of genes as well as using a CRISPR Library approach to create genome-wide loss of gene function studies with the overall aim of discovering potentially beneficial gene targets for CHO cell line engineering.

17:30 Studying the Impact of Genetic Alterations Using a Targeted Integration CHO Host Cell Line

Mark Trautwein, Dr. rer. nat., Senior Scientist, Biologics Research, Bayer AG

Both the chromosomal environment of the integration site as well as the genetic elements of a transgene expression cassette contribute to the degree of high and stable transgene expression. We have used targeted integration host cell lines for evaluation of different genetic elements of the transgene construct as well as for Crispr/Cas9-based implementation of targeted (epi)genetic modifications. This approach facilitates optimization of product-specific expression configurations.

18:00 Rethinking Gene Expression Using the Synthetic C3P3 Transcription System

Philippe H. Jais, MD, PhD, President and CSO, Eukarÿs SAS

Eukarÿs has developed the first ever artificial expression system by synthetic biology that is named C3P3 (cytoplasmic chimeric capping prone-phage polymerase). This enzymatic system, currently in its 3rd generation, synthesizes *in vivo* high amounts of mature messenger RNA and, consequently, protein of interest in mammalian cells. Besides its uses for therapeutics, the C3P3 system is used as a potent tool for the bioproduction of viruses and proteins.

18:30 Cell- and Vector-Engineering for Manufacturing Gene Therapy Lentiviral Vectors from Constitutive Producer Cell Lines

Ana Filipa Rodrigues, PhD, Research Scientist, Animal Cell Technology Unit, Cell Line Development and Molecular Biotechnology Laboratory, iBET - Instituto de Biologia Experimental e Tecnológica

Lentiviral vectors (LV) are currently the first choice for cell and gene therapy applications when long-term expression is required. To support robust LV manufacture, we present three novel approaches: i) LentiPro26, stable and constitutive packaging cells, based on a mutated lentiviral gag-pro-pol and a stringent selection method; ii) high-titer chimeric envelopes for three different pseudotypes, based on protein engineering; and iii) producer cell genome editing and engineering for increased robustness to vector component's cytotoxicity.

19:00 End of Cell Lines and Systems Engineering





Optimising Expression Platforms

Employing Cell Factories for the Production of Biotherapeutics

WEDNESDAY 20 NOVEMBER

07:45 Registration and Morning Coffee

DIFFICULT-TO-EXPRESS PROTEINS

08:30 Chairperson's Opening Remarks

Peter Schmidt, PhD, Director, Recombinant Technologies, CSL Behring

08:35 KEYNOTE PRESENTATION: Tag-on-Demand: Exploiting Amber Codon Suppression Technology for the Enrichment of High-Expressing Membrane Protein Cell Lines



Trevor Wilkinson, PhD, Associate Director, Antibody Discovery & Protein Engineering, AstraZeneca Biopharmaceuticals Unit

Multi-spanning membrane proteins such as G-protein-coupled receptors and Ion Channels are of significant therapeutic interest. Targeting these proteins with Monoclonal Antibodies has proven particularly challenging, in part due to the difficulties in obtaining high-level expression of these membrane protein antigens. In this presentation we will explore case studies illustrating how these challenges may be overcome, including how a Tag-on-Demand strategy can facilitate enrichment of high-expressing membrane protein cell lines.

09:05 Technologies for High-Level (Membrane) Protein Production in Mammalian Cells

Jonathan Elegheert, PhD, Team Leader, Interdisciplinary Institute for Neuroscience (IINS), CNRS, University of Bordeaux

Structural, biochemical, and biophysical studies of soluble and membrane proteins typically require their production in milligram quantities. Difficult-to-produce eukaryotic proteins are generally best expressed from close-to-native mammalian cell types. I will compare different approaches for the production of soluble and membrane proteins from mammalian cells and discuss their strengths and weaknesses in function of the protein target and application, as well as their practical implementation.

09:35 High-Yield Production of "Difficult-to-Express" Proteins in an Improved Cell-Free System

Takanori Kigawa, DSci, Team Leader, Center for Biosystems Dynamics Research, RIKEN

We have developed a new method of *E. coli* cell extract-based cell-free protein synthesis optimal at lower temperatures (20-25 °C) achieving high-yield production comparable to the conventional method (30-37 °C). This method is suitable for expressing proteins that tend to aggregate and/or be insoluble at optimal temperatures for the conventional method (30-37 °C). Therefore, our new method is particularly useful for expressing "difficult-to-express" proteins.

10:05 Accelerating Discovery and Development of Next-Generation Therapeutic Antibodies using the Beacon Platform

John Proctor, PhD, Senior Vice President, Berkeley Lights, Inc.

The Beacon platform dramatically accelerates the discovery and development of next-generation antibody therapeutics. The presentation will demonstrate how Berkeley Lights' customers are using



Plasma B Cell Antibody Discovery to perform target-to-lead candidate selection in just 1 day. Once lead candidates have been selected, Beacon Cell-Line Development enables the selection of production cell lines with >99% monoclonality assurance in less than 1 week.

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

11:15 Production of Hard-to-Produce Proteins Using Genome Engineered CHO Cells

Bjørn Voldborg, MSc, Director, CHO Cell Line Development, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark

Using our in-house developed high throughput CHO cell line engineering platform, we have engineered the glycosylation machinery to make a panel of CHO cell lines for the expression of recombinant proteins with tailored N-glycans. Using these cells, we have produced a therapeutic protein that until now has only been available from natural human sources. The produced protein resembles the human derived proteins with respect to N-glycan profile and activity.

11:45 The IC-Tagging Platform and Its Use for the Expression of Difficult Proteins

Jose M. Martinez-Costas, PhD, Profesor Titular, Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS); Departamento de Bioquímica e Bioloxía Molecular, Universidade de Santiago de Compostela

We have developed a platform that programs cells to construct nano/microspheres that integrate any protein of interest and that are easily purified. Between the multiple applications of this technology, we have recently shown its potential in the expression of difficult/toxic proteins by expressing, between others, the highly demanded diabetogenic auto-antigen protein IGRP opening the possibility of further studies on type 1 diabetes.

12:15 HEK293 Cell Lines Allow Rescue of Proteins that are Difficult to Produce in CHO – Learning Lessons from Endogenous Secretory Pathway Expression

Magdalena Malm, PhD, MSc, Researcher & Lab Manager, Wallenberg Center for Protein Research, KTH Royal Institute of Technology

Evaluation of the recombinant expression of 24 secreted human difficult-to-express proteins showed generally improved expression in HEK293 compared to CHO cells. Transcriptomic analysis was used to identify key differences between the secretory pathways of the two cell lines and to study genes differentially activated upon transgene expression. The findings suggest lessons to be learnt from each cell line based on endogenous secretory pathway gene expression.

12:45 Optimization of *E. Coli* Solupro® Using Synthetic Biology to Generate a Scalable, High-Yield Chassis Microbe

Melissa Patterson, Purification Group Leader, Downstream Process Development, AbSci



13:00 ALiCE - Makes Production of Difficult-To-Express Proteins Easy

Ricarda Finnern, PhD, Research & Development, LenioBio GmbH

ALiCE is the first eukaryotic cell-free platform, scalable according to customer's needs. Combining the best properties of cell-based, cell-free, eukaryotic and prokaryotic systems, ALiCE is the most versatile protein production system. It allows single step production of proteins that have been difficult to make using other technologies in unrepresented quantities.





Optimising Expression Platforms

13:15 Luncheon Presentation I: Utilising Directed Evolution and Droplet Microfluidics to Increase Titres and Accelerate Cell Line Development Timelines
Devika Kalsi, Principal Scientist, MCC Upstream Process Development, FUJIFILM Diosynth Biotechnologies

Sponsored by

13:45 Luncheon Presentation II: ExpiSf™ Expression system: A Chemically Defined Baculovirus-Based Expression System for Enhanced Protein and Virus Production in Sf9 Cells

Sponsored by

Kenneth Thompson, Manager, Research & Development, Cell Biology, Thermo Fisher Scientific
 The Baculovirus Expression Vector System is a versatile platform for expression of individual recombinant proteins, membrane proteins, virus-like particles and Adeno-associated virus (AAV). Here, we describe the ExpiSf™ Expression System, the first chemically defined insect system that enables high-yield production of proteins and viral particles at small and large scales. The system includes an improved transfection reagent and updated protocol for faster baculovirus generation and a chemically defined enhancer to boost protein and virus production.

14:15 Session Break

RECOMBINANT PROTEINS

14:30 Chairperson's Remarks

Richard Altman, MS, Staff Scientist, Life Science Solutions, Thermo Fisher Scientific

14:35 The Use of Design of Experiments in Recombinant Protein Production: Concepts and Case Studies

Barry Ryan, BSc (Hons), PGDip, MSc, MA, PhD, Lecturer, Food Science and Environmental Health, College of Health and Science, Technological University Dublin

Many factors, both intrinsic and extrinsic, can influence recombinant protein yield; however, identifying the most important factors, individually or synergistically, for optimum yield can be time consuming and expensive. Statistical models, such as Design of Experiments (DoE), can be used as efficient approaches to recombinant protein production optimisation. Fundamental concepts of DoE, with supporting case studies, will underpin an overview of the potential of this method for enhanced recombinant protein production.

15:05 Playing a Round with Recombinant Protein Production: What is PAR for the Course

Douglas Browning, PhD, Senior Research Fellow, Institute of Microbiology and Infection, School of Biosciences, University of Birmingham

Many promoters used for recombinant protein production (RPP) in *Escherichia coli* are capable of high-level protein expression but are often too strong for expressing proteins that are difficult to fold or targeted to the membrane or periplasm. To circumvent this, we have engineered a suite of bacterial promoters (the PAR promoters) and strains that can be used to tailor the expression of target proteins to maximize RPP and product yield.

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

16:15 Overview of a High-Throughput Pipeline for Streamlining the Production of Recombinant Proteins for Structural Biology

Raymond J. Owens, PhD, Professor, Research Complex at Hartwell & Rosalind Franklin Institute, University of Oxford

There has been a transformation in the power and throughput of structural methods delivered by large-scale facilities, such as synchrotrons. This has placed an increasing demand on the supply of high-quality samples (purified proteins and protein crystals) for structural studies. To meet this requirement, protein production has been streamlined to improve efficiency and throughput. Our experience will be reviewed and new trends discussed.

16:45 Improved Production of Recombinant Proteins from Insect Cells through Promoter, Virus, and Strain Enhancements

Dominic Esposito, PhD, Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research
 Baculovirus-based insect cell expression platforms are often successfully used for production of pharmaceutically relevant proteins. However, the insect cell system remains suboptimal in terms of technology development related to controlling the level of protein production, stability of baculoviruses for large-scale production, and modification of host insect cell lines for improved performance. We have begun to address some of these deficiencies and demonstrate the use of these improved systems for production of clinically relevant drug targets.

17:15 Choosing Right between Transient and Stable Protein Expression Systems While Supporting Fast-Paced Biologics Discovery

Kinjal Mehta, PhD, Principal Scientist, Protein Sciences, Jounce Therapeutics

Within the fast-paced realm of biotechnology, research groups are often tasked with generating large amounts of proteins with the highest quality possible while continuously shortening turnaround times. This becomes a challenge with therapeutic candidates because factors like glycosylation patterns and consistency with biophysical/chemical properties become critical. Choosing between transient and stable protein production becomes an important step at each stage. We have developed a platform where we use a CHO-GS KO cell line, typically used under stable conditions, and have adapted it to a transient system with a robust protocol that is consistently results in high titers.

17:45 Networking Reception in the Exhibit Hall with Poster Viewing

18:45 Problem-Solving Breakout Discussions*

*See website for details.

19:45 End of Day

THURSDAY 21 NOVEMBER

08:00 Registration and Morning Coffee

ANTIBODIES

08:30 Chairperson's Remarks

Renate Kunert, PhD, Professor, Department of Biotechnology, University of Natural Resources and Life Sciences (BOKU)





Optimising Expression Platforms

08:35 Producing High-Quality Bispecific Material from Transients for Developability Assessment

Claire Pearce, PhD, Senior Research Scientist, CHO Expression Team Leader, Biopharmaceutical Development, Kymab Ltd.

Antibody developability continues to be a hot topic, with the ability to develop and manufacture a molecule having equal importance to its research properties. This presentation will detail the supply and developability assessment of a panel of bispecific molecules expressed from a rapid transient platform, and the comparability of this material to that expressed from a stable process.

09:05 Novel Highly Productive Production System for Biotherapeutics: Filamentous Fungus *Myceliophthora thermophila* C1

Markku Saloheimo, PhD, Senior Principal Scientist, Industrial Biotechnology and Food Research, VTT Technical Research Centre of Finland

We are developing the industrial enzyme production host C1 into an efficient and versatile therapeutic protein production platform. A major topic in our research has been reduction of the host protease level. This has enabled superb production levels of Mabs, Fc-fusion proteins, bispecifics and vaccine proteins in a 6- to 7-day process in C1. Glycoengineering is also under way to humanize the glycosylation pathway of this production host.

09:35 Rapid Selection of CHO Clones Secreting Chimeric Antibody-Antigen Fusion Constructs Based on 2A-Peptide Cleavage and GFP

Bert Devriendt, PhD, Postdoctoral Scientist, Department of Virology, Parasitology, Immunology, Physiology, Ghent University

To enable large-scale recombinant antibody production, a high producer cell line is essential. Selecting such a cell line is however time consuming and labor intensive. By combining the design of a tri-cistronic vector expressing GFP and both antibody chains, separated by a GT2A sequence, with single cell sorting and automated image analysis, a CHO cell line was rapidly selected producing high amounts of recombinant antibodies, which showed minimal degradation.

10:05 Scaling Up and Scaling Out: Pushing the Boundaries of Transient Protein Production

Ian Wilkinson, CSO, Absolute Antibody Ltd.

Whilst transient yields have improved drastically in the last decade, scalable systems are time-consuming and costly to implement. Absolute Antibody has developed systems which scale up and scale out protein expression and purification, enabling the rapid and cost-effective production of milligram-to-gram quantities of large panels of proteins.

Sponsored by

10:20 High Density (HD) Expression Platform: The One-Stop-Solution for Recombinant Antibody Production

Bowu Luan, PhD, Product Manager, GenScript USA, Inc.

GenScript has developed a novel reagent "Cocktail" compatible with HD expression system, which improves antibody yield by increasing cell viability and facilitating protein folding. This HD system works well with all species and low expressers, readily to scale down and up. Automatic workflow from transfection to purification ensures the quality.

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

ANTIBODIES (CONT.)

11:15 Influence of Somatic Mutations on mAb Expression and Thermal Stability Properties

Renate Kunert, PhD, Professor, Department of Biotechnology, University of Natural Resources and Life Sciences (BOKU)

The production potential of monoclonal antibody (mAb) expressing cell lines depends on the intrinsic antibody structure and its interaction with cellular compartments especially the folding and secretion machinery. To get a better understanding of such relations we expressed different mAbs under isogenic conditions in recombinant CHO cells and studied cellular biology and physicochemical properties of mAbs.

11:45 High Throughput Antibody Production and Purification: Day to Day Challenges and How to Overcome Them

Peter Schmidt, PhD, Director, Recombinant Technologies, CSL Behring

Monoclonal antibodies are the fastest growing segment in the drug market. The development of mAbs requires purification of large numbers of variants with sufficient yield. However, established high-throughput purification strategies have been limited by the binding capacity of established affinity matrices. The presentation will address some of the known and less known issues and suggest ways to overcome them.

12:15 Luncheon Presentation I: Establishment of a CHO Transient Expression Platform for Bispecific Fusion Protein Developability Assessment

Thibaut Angevin, PhD, Pieris Pharmaceuticals GmbH

Pieris Pharmaceuticals' proprietary molecules, the Anticalin® proteins, are small therapeutics derived from human lipocalins. They can be genetically linked to antibodies to generate different bispecific fusion proteins. Those proteins display different developability profiles. Pieris' developability assessment platform has been established in order to screen bispecific constructs at an early stage, with an aim of identifying candidates that are best suited for advancement to stable cell line development or further optimization of such constructs.

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12:45 Luncheon Presentation II: GlycoExpress® - An Alternative Host for Difficult to Express Proteins

Lars Stöckl, PhD, Senior Director BD and Technology, Glycotope GmbH

The era of classical IgG molecules in bio-pharma development is shifting rapidly to more challenging complex biopharmaceuticals. With CHO being a good production cell line for IgG molecules, they might fail to produce more challenging candidates. The GlycoExpress® (GEX®) system represents an ideal alternative for the production these difficult to express protein molecules and will provide case studies which demonstrate the superiority in productivity and product quality vs CHO cell expression.

Sponsored by

13:15 Dessert Break in the Exhibit Hall with Poster Viewing

14:00 End of Optimising Expression Platforms

17:00 Dinner Short Course Registration*

17:30 – 20:30 Dinner Short Courses





Protein Purification Technologies

Streamlining Processes

THURSDAY 21 NOVEMBER

13:00 Registration

13:15 Dessert Break in the Exhibit Hall with Poster Viewing

CONTINUOUS PROCESSES

14:00 Chairperson's Opening Remarks

Ana Correia, PhD, Scientist, Biologics Optimization, Amgen, Inc.

14:05 KEYNOTE PRESENTATION: Hot Topics in Continuous Chromatography for Protein Purification



Massimo Morbidelli, Professor, Chimica, Materiali e Ingegneria Chimica, Giulio Natta, Politecnico di Milano

Continuous countercurrent chromatography is recognized as the technology of choice for a number of instances in the area of protein purification. Approaching its maturity stage, this technology has to be reconsidered with respect to crucial aspects for its future development. In particular, we discuss issues related to scalability in the GMP environment, model-based process characterization and validation, as well as process automation, control and digitalization particularly in the context of continuous integrated manufacturing.

14:35 Continuous Chromatography Purification Process: From Small Peptides to Virus-Based Biologics

Ricardo Silva, PhD, Scientist, Animal Cell Technology, Instituto de Biologia Experimental Tecnológica (iBET)

Alternative purification strategies that can improve the purification yield, such as continuous chromatography, are regarded nowadays as potential tools to overcome the capacity bottleneck in biomanufacturing. The current talk will focus on the development of continuous purification processes targeted at small peptides and novel biologics such as virus for vaccines and gene therapy applications.

15:05 Overcoming Limitations of Conventional Tag Systems – Strep-Tactin®XT Applications

Mike Rothe, PhD, CEO, IBA Lifesciences

The Strep-Tactin®XT: Twin-Strep-tag®-purification system enables protein purification at high yields and purity under physiological conditions. Providing the highest binding affinity among all affinity tag systems, the technology fulfills the demands of detections and monitoring of biomolecular interactions in real time and is available for applications like SPR and Octet®/BLITZ®.

Sponsored by



15:20 Novel Solutions for HTP Antibody and Protein Purification Using Magnetic Beads

Roumen Bogoev, Marketing Director, Catalog Products, GenScript

GenScript has partnered with Amgen to design the AmMag SA, an automatic platform using magnetic beads for purifying antibodies and proteins. The system facilitates increased throughput for drug screening. It also eliminates the need for centrifugation and filtration of samples prior to processing, saving significant amount of time and labor.

Sponsored by
GenScript

15:35 Networking Refreshment Break

BREAKTHROUGH TECHNOLOGIES

16:00 A Microfluidic Platform for Antibody Manufacturing Optimization

Raquel Aires Barros, PhD, Full Professor, Bioengineering, IBB – Institute for Bioengineering and Biosciences, Instituto Superior, Universidade de Lisboa

The number of biotechnology-based pharmaceuticals in the late-stage pipeline has been increasing more than ever in particular monoclonal antibodies (mAbs) representing a quarter of all biopharmaceuticals in clinical trials. As a result, there is an enhanced demand for more efficient and cost-effective processes for antibody manufacturing. Here, the potential of miniaturization as a high-throughput screening tool to speed up process development of antibodies is explored.

16:30 Taking Chromatography to the Next Level - A Novel Fiber Based Protein A Chromatography Platform

Linnea Troeng, Product Manager, Protein Preparation and Purification, GE Healthcare Bio-Sciences AB

Sponsored by
GE

In this presentation we show the development of a novel cellulose fiber-based chromatography solution "Fibro", that combines high binding capacity with high flowrates to enable increased productivity from industrial research, process development, to clinical & commercial mAb purification. The technology is scalable and enables true single-use chromatography solutions. Here we will present data on binding capacity, purification performance and scalable performance

17:00 Protein Separation by Magnetic Particles at the Technical Scale

Paula Fraga Garcia, PhD, Scientist, Mechanical Engineering, Bioseparation Engineering, Technical University of Munich

Biocompatible magnetic nanoparticles are a promising material that has shown applicability in a wide range of areas. This work paves the way for an innovative, economical purification process for biotechnologically produced proteins and contributes to a deeper understanding of bio-nano interactions.

17:30 End of Day

17:00 Dinner Short Course Registration*





Protein Purification Technologies

17:30 – 20:30 Dinner Short Courses

Recommended Short Course*

SC7: Protein Aggregation: Mechanism, Characterization and Consequences

**Separate registration required. See pages 6 & 7 for details.*

FRIDAY 22 NOVEMBER

08:00 Registration and Morning Coffee

MEMBRANE PROTEIN PURIFICATION

08:30 Chairperson's Remarks

Dirk Linke, PhD, Professor, Molecular Microbiology, Biosciences, University of Oslo

08:35 The Gram-Negative Bacterial Cell Surface: How to Study Its Protein Components and How to Remove Endotoxin

Dirk Linke, PhD, Professor, Molecular Microbiology, Biosciences, University of Oslo

In our recent work, we have developed methods to express bacterial outer membrane proteins in ways that allow direct NMR studies in the native environment. As experts in membrane protein purification, we constantly develop expression strains and methods for quality control. In that regard, we recently found a small protein with high affinity for bacterial endotoxin, that we hope can be used for endotoxin detection and removal.

09:05 Sane in the Membrane – Salipro One-Step Reconstitution of Membrane Proteins

Jens Frauenfeld, PhD, CEO, Salipro Biotech AB

Membrane proteins are important drug targets (GPCRs, ion channels), yet are notoriously difficult to work with. We have developed a novel one-step approach for the incorporation of membrane proteins directly from crude cell membranes into lipid Salipro particles. This direct approach presents new opportunities for the analysis of novel drug targets. Furthermore, we present how the Salipro system can be used to generate antibodies against important membrane proteins.

09:35 A Tricky Endeavour: Production of Membrane-Bound P450s

Oliver Spadiut, PhD, Associate Professor, Chemical, Environmental and Bioscience Engineering, Integrated Bioprocess Development, Vienna University of Technology (TU Wien)

Cytochrome P450s (P450s) comprise one of the largest known protein families. They occur in every kingdom of life and catalyze essential reactions, such as carbon source assimilation, synthesis of hormones and secondary metabolites, or degradation of xenobiotics. Due to their outstanding ability of specifically hydroxylating complex hydrocarbons, there is a great demand to use these enzymes for biocatalysis. However, this requires a great understanding of these enzymes – thus we need to know their protein crystal structure. In this talk I will present how we recombinantly produced and purified a plant cytochrome P450.

10:05 Networking Coffee Break

PURIFYING BISPECIFIC ANTIBODIES

10:35 Overcoming Some Challenges in the Purification of Bispecific Antibodies

Ana Correia, PhD, Scientist, Biologics Optimization, Amgen, Inc.





Protein Purification Technologies

Bispecific antibodies are an emerging class of therapeutics which are engineered to simultaneously bind two distinct targets. Production and purification of these molecules is challenging due to the presence of byproducts such as aggregates and half-antibodies, which are difficult to eliminate by conventional chromatographic techniques. Here I show results from a novel Protein A chromatography strategy that removes these impurities, thereby reducing processing cycle-time and improving product quality.

11:05 Novel Protein A Small and Large-Scale Purification Platforms for Bispecific Antibodies

Afshin Mahmoudi, MS, Biotherapeutics, Signal Pharmaceuticals, LLC (a wholly owned subsidiary of Celgene Corp.)

Our goal was to develop a robust 1-2 step process that can be applied for the purification of most bispecific antibodies (BsAbs). In this study, we present a BsAb purification process consisting of affinity capture using a novel Protein A chromatography resin, and subsequent screening of chromatography resins (ion exchangers, HIC or multimodal resins) for additional polishing. Recovery and purity indicate a robust purification platform for BsAb programs. This novel platform simplifies process development, reduces time and expense, and ultimately time to market.

11:35 POSTER SPOTLIGHT:

Isolation and Characterization of Light Chain Misassembled Bispecific Antibody Variants by Hydrophobic Interaction Chromatography and Knowledge Use for Production Cell Line Optimization

Thomas von Hirschheydt, Dr. rer. nat., Principal Scientist and Technical Development Leader, Roche Diagnostics GmbH

12:05 Problem-Solving Breakout Discussions with a Light Snack*

*See website for more details.

INNOVATING PURIFICATION STRATEGIES

13:00 Chairperson's Remarks

Oliver Spadiut, PhD, Associate Professor, Chemical, Environmental and Bioscience Engineering, Integrated Bioprocess Development, Vienna University of Technology (TU Wien)

13:05 A Development and Manufacturing Platform for Non-Platform Proteins

Matthias Berkemeyer, PhD, Associate Director, Downstream Development, NBE and Biosimilars, Biopharma Process Science Austria, Boehringer Ingelheim RCV GmbH & Co KG

13:35 Advanced Chromatography-Free Protein Purification Strategies Enabling High-Resolution Structure Determination of Large, Labile Multi-Subunit Biological Assemblies and Drug Discovery

Ashwin Chari, PhD, Project Group Leader, Structural Dynamics, Max Planck Institute for Biophysical Chemistry

Biochemical purification of large, labile assemblies remains a formidable challenge and often fails when strategies suitable for single biomolecules are adapted to larger complexes. Here, I will present the development of chromatography-free purification strategies, which enable the purification of large biological assemblies in high-yield and high-quality. The strategies reported here have enabled the structure determination of proteasomes and fatty acid synthases at unprecedented resolution and opened up new venues for drug discovery.

14:05 Improved Downstream Processing of Recombinant Proteins Using Aqueous Two-Phase Systems Composed of Ionic Liquids

Augusto Pedro, PhD, Postdoctoral Fellow, Chemistry, CICECO – Aveiro Institute of Materials, University of Aveiro

Previous studies have shown that ionic liquids display highly interesting features concerning protein stabilization, and by properly tailoring their anion/cation pairs, increased selectivity towards the target protein can be achieved in IL-ATPS. Process intensification and scale-up of IL-ATPS for the purification of recombinant proteins can be achieved by centrifugal partition chromatography (CPC), in which the stationary phase is also liquid and kept by centrifugal force.

14:35 Purification of Viruses and Virus-Like Particles for Structural Studies

Thilo Stehle, PhD, Professor, Interfaculty Institute of Biochemistry, University of Tübingen

Structure-function studies of viruses require large amounts of intact particles of either complete, infectious virus or infection-deficient virus-like particles. I will report on strategies that we use in my group to express and purify such particles, and I will present data on the structural analysis of these particles.

15:05 End of Protein Purification Technologies





Advancing Bispecifics and Combination Therapy to the Clinic

Refinements for Improved Safety and Efficacy

WEDNESDAY 20 NOVEMBER

07:45 Registration and Morning Coffee

BISPECIFICS FOR T CELL ENGAGEMENT DEMONSTRATING SUPERIOR PROPERTIES

08:30 Chairperson's Opening Remarks

Paul W.H.I. Parren, PhD, Executive Vice President, Head, R&D, Lava Therapeutics B.V.

08:35 Progress with Bispecific V γ 9V δ 2-T Cell Engagers

Paul W.H.I. Parren, PhD, Executive Vice President, Head, R&D, Lava Therapeutics B.V.

V γ 9V δ 2-T cells constitute the largest $\gamma\delta$ -T cell subset in human peripheral blood and are powerful anti-tumor immune effector cells that can be identified in many different tumor types. Our V γ 9V δ 2-T cell engager platform brings important advantages over existing (CD3-based) T cell engagers. Recent preclinical development data including potency, mechanism of action, activity with patient-derived tumor cells, and safety will be discussed.

09:05 Preclinical Combinations of T Cell Bispecifics Targeting Solid Tumors and Hematological Malignancies

Marina Bacac, PhD, Head, Cancer Immunotherapy Department 2 (CIT-2), Roche Innovation Center Zurich

We give an overview of preclinical activity of CEA-TCB and CD20-TCB, two clinical stage T cell bispecific antibodies based on the "2:1" IgG format. In addition, we present combination strategies of these two TCBs with checkpoint inhibitors and novel targeted costimulatory molecules.

09:35 A Novel Mucin 16 Bispecific T Cell Engaging Antibody for the Treatment of Ovarian Cancer

Alison Crawford, PhD, Senior Staff Scientist, Oncology and Angiogenesis, Regeneron Pharmaceuticals, Inc.

REGN4018 binds both Mucin 16 (MUC16) and CD3. REGN4018 induced T cell killing of MUC16-expressing tumor cells *in vitro* in the presence of CA-125. REGN4018 potently inhibited tumor growth in a xenogeneic mouse model, as well as in immuno-competent mice genetically engineered to express human CD3 and human MUC16. Toxicology studies in cynomolgus monkeys revealed no overt toxicity, supporting clinical evaluation of REGN4018 in patients with advanced ovarian cancer.

10:05 Renmab™ Mouse: A Leading Platform for Fully Human Antibody Generation

Chaoshe Guo, Vice President, PhD, Global Head, Business Development, Biocytogen



Biocytogen has recently developed RenMab Mouse, a fully human antibody mouse with its entire variable regions replaced by human Ig heavy chain and light chain. The RenMab™ model has also demonstrated a similar immune response to the wildtype strain as it carries the full human antibody repertoire. Combined with existing inventory of single, double or triple target humanized mouse models, Biocytogen is poised to provide an one-stop solution from target validation to IND application.

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

11:15 KEYNOTE PRESENTATION: Bispecific Antibodies: Discovery, Development, and Next Generation



Tomoyuki Igawa, PhD, CEO, Head, Research, Global Biologics Leader, Chugai Pharmabody Research Pte. Ltd.

Emicizumab, a humanized anti-FIXa/FX bispecific antibody for hemophilia A, is the first bispecific IgG antibody which was approved by the FDA. Now, many T cell-redirecting bispecific IgG antibodies are being developed. In my presentation, I will talk about the discovery and development of these bispecific IgG antibodies, and how novel antibody engineering can further improve the properties of these molecules.

11:45 Discovery and Optimization of a Novel T Cell Bispecific for the Treatment of Solid Tumors

Adam Root, MSc, Senior Principal Scientist, BioMedicine Design, Pfizer, Inc.

12:15 Targeting Cancer with BiTE® Antibody Constructs

Roman Kischel, MD, Director, Research, Amgen Research (Munich) GmbH

The presentation will discuss the structure and mode of action of BiTE antibody constructs, provide an update on the development of the BiTE antibody platform, and showcase early clinical data for a novel BiTE antibody construct targeting myeloma.

12:45 The Journey to "the" Antibody: Tailoring for Success

María González Pajuelo, CSO, FairJourney Biologics

To maximize the possibility to select "the" antibody, at FJB we have taken antibody discovery to an unprecedented level by creating a versatile toolbox that allows the selection by phage display of antibody fragments of different species from large naïve and immune repertoires. Ultimately, these fragments can be engineered and converted to mono- and bi-specific formats that are produced in CHO cells.



13:15 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

14:15 Session Break

INNOVATIVE APPROACHES YIELDING PRODUCTS HEADING FOR THE CLINIC

14:30 Chairperson's Remarks

Adam Root, MSc, Senior Principal Scientist, BioMedicine Design, Pfizer, Inc.

14:35 Developing Bi- & Multi-Specific Immune-Modulatory Biologics to Address Unmet Needs

Tariq Ghayur, PhD, Distinguished Research Fellow, AbbVie Bioresearch Center

This will examine the technical challenges of making bi-/multi-specific biologics that have been (or can be) solved, and address the key challenges, namely to design molecules that match the disease biology and meet clinical needs. We are developing methods and tool molecules to understand the biology of the various aspects of cancer, ranging from the immunity cycle to the design of therapeutic molecules. Examples of these efforts will be discussed.





Advancing Bispecifics and Combination Therapy to the Clinic

15:05 Benefits of Chicken-Derived Antibodies for Combination Immunotherapy

Klaus Koefoed, PhD, MSc, Director, Antibody Technology, Symphogen A/S

Development of novel antibodies and more powerful therapeutic combinations for immunotherapy is an intense area of focus. However, difficult and/or conserved targets, finding antibodies with unique functionality, and generating early PoC pose challenges to the development of novel antibody therapeutics. Symphogen's approach to discovery and development of potent antibody combinations for cancer immunotherapy using different species, including chicken, will be presented. Examples from our clinical pipeline will be shown.

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

16:15 DuoHexaBody-CD37, a Novel CD37-Targeting Bispecific Antibody with a Hexamerization-Enhancing Mutation, Demonstrating Superior Preclinical Activity Against Malignant B Cells *in vitro*, *ex vivo*, and *in vivo*

Laurens Kil, PhD, Senior Scientist, Translational Research, Genmab B.V.

DuoHexaBody™-CD37 is a bispecific antibody with a hexamerization-enhancing mutation that targets two different epitopes on CD37. DuoHexaBody-CD37 was designed to induce highly potent cytotoxicity of B cells in a variety of B cell malignancies through enhanced complement-dependent cytotoxicity (CDC) and other Fc-mediated effector functions. Here we will present studies on the rational design, mechanism of action, and pre-clinical efficacy of DuoHexaBody-CD37.

16:45 Towards RNA-Based Cancer Immunotherapy: Advances in the Development of mRNA Encoded Therapeutic Antibodies

Ursula Ellinghaus, PhD, Scientist, Bispecific Antibodies, BioNTech RNA Pharmaceuticals GmbH

BioNTech's RiboMAB® platform, based on *in vitro*-transcribed non-immunogenic mRNA encoding for a variety of antibodies, is circumventing the production challenges and manufacturing cost of protein-based monoclonal antibodies. Systemic administration of RiboMABs formulated in LNPs results in sustained antibody levels and elimination of advanced tumors in mice as efficient as the corresponding purified antibody. Given the feasibility and safety of RiboMABs, we created an exciting platform technology for cancer immunotherapy.

17:15 Anticalin Proteins and Their Application in Respiratory Disease

Christine Rothe, PhD, Vice President, Discovery & Alliance Management, Pieris Pharmaceuticals GmbH

Anticalin® proteins are based on human lipocalins and can be formulated as inhalable biologics, allowing local delivery to the lung. This was demonstrated with AZD1402/PRS-060, an IL-4Ra antagonist that Pieris is developing in collaboration with AstraZeneca for the treatment of moderate-to-severe asthma. A first-in-human study has revealed a promising clinical profile. The ability to generate bi- and multi-specific Anticalin proteins offers the potential to address more than one target in a disease pathway and thus improve efficacy and/or broaden the patient population for a range of respiratory diseases.

17:45 Networking Reception in the Exhibit Hall with Poster Viewing

18:45 Problem-Solving Breakout Discussions*

*See website for details.

19:45 End of Day

THURSDAY 21 NOVEMBER

08:00 Registration and Morning Coffee

CHECKPOINT BLOCKADE IN COMBINATION WITH ANTAGONISTS/AGONISTS

08:30 Chairperson's Remarks

Tariq Ghayur, PhD, Distinguished Research Fellow, AbbVie Bioresearch Center

08:35 PD-1 x LAG-3 (MGD013) and PD-1 x CTLA-4 (MGD019): Two Clinical-Stage DART® Molecules Designed to Simultaneously Block Two Checkpoint Pathways

Alexey Berezhnoy, PhD, Scientist, Cell Biology & Immunology, MacroGenics, Inc.

Tumor-infiltrating lymphocytes frequently co-express multiple immune checkpoint receptors, whose co-blockade provides additional benefits in immunotherapy. Here we applied a bispecific platform to increase stringency and specificity of immune checkpoint co-blockade. Two clinical-stage bispecific DART molecules, PD-1 x CTLA-4 (MGD019) and PD-1 x LAG-3 (MGD013), will be discussed in this presentation, including format selection, preclinical pharmacology, IND-enabling studies, and clinical trial design.

09:05 A Novel, Monovalent Tri-Specific Antibody-Based Molecule that Simultaneously Modulates PD-L1 and 4-1BB Exhibits Potent Anti-Tumoral Activity *in vivo*

Stefan Warmuth, PhD, Head, CMC, Therapeutic Program Lead, Numab Therapeutics AG

Targeting PD-L1 and 4-1BB with multi-specific antibodies holds the promise of increased potency, while improving the safety profile compared to combination therapy. Numab develops a molecule that potently blocks PD-L1/PD-1 signaling and elicits further T cell activation through its costimulatory domain solely in the proximity of cells that overexpress PD-L1. Preclinical data show efficacy on tumor growth in combination with an enhanced intratumoral CD8+ T cell activation when compared to the combination of the PD-L1 and 4-1BB modalities.

09:35 Development of a Novel Bi-Functional Fusion Protein Platform (Agonist Redirected Checkpoint or ARC) for Cancer Immunotherapy

George Fromm, PhD, Vice President, Research & Development, Shattuck Labs, Inc.

The ARC platform was developed to solve the challenge of incorporating immune-checkpoint blocking functional domains and tumor necrosis factor (TNF) superfamily agonists (OX40, CD40, 4-1BB, etc.) into single therapeutics. This was achieved by engineering hexameric TNF ligands, which uniquely activate TNF receptors compared to mono- or di-valent antibody-based approaches. The ARC platform has provided a means to unlock this family of costimulatory molecules, which is currently being evaluated in a clinical study.





Advancing Bispecifics and Combination Therapy to the Clinic

10:05 Next-Generation Reporter Technologies for Immunotherapy Discovery and Potency Testing

Jamison Grailer, Senior Research Scientist, Research & Development, Promega Corporation

Immunotherapy strategies, including immune checkpoint monoclonal antibodies (mAbs), bispecific molecules, and chimeric antigen receptor T (CAR T) cells, are promising new approaches for treating cancer, autoimmunity, and other diseases. A major challenge in immunotherapy drug development is access to quantitative and reproducible functional assays for screening (e.g. TCR screening), measurement of target cell-specific killing, and potency testing. Here we will present a variety of next-generation reporter technologies to address these needs in the context of mAb-mediated ADCC, bispecific molecules, and TCR-mediated cell therapies.

Sponsored by



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

SCREENING AND IDENTIFICATION OF BISPECIFIC COMBINATIONS / FOCUS ON CYTOKINE RELEASE

11:15 Unbiased Functional Screening of Large Bispecific Antibody Panels to Unlock Novel Biology

Pieter Fokko van Loo, PhD, Director, Oncology-Immunology, Merus N.V.

Our technology platform leverages the natural human IgG1 format; enabling high throughput functional screening to discover drug candidates with excellent anti-tumour properties. The discovery of two clinical stage pipeline candidates will be discussed that highlight the power of this functional screening approach: MCLA-117, a CLEC12AxCD3 T cell engaging antibody for acute myeloid leukemia and MCLA-145, CD137xPD-L1 bispecific antibody that recruits and supercharges tumor infiltrating lymphocytes.

11:45 An International Collaborative Study to Establish a 1st Reference Panel for Cytokine Release Assays

Sandrine Vessillier, PhD, Principal Scientist, Head, Immunotoxicology Cellular Immunology, Biotherapeutics, National Institute for Biological Standards and Control, UK

Cytokine release assays (CRAs) are key for hazard ID of immunotherapeutics, such as cytokine release syndrome (CRS). To gain a better understanding of the comparability between different CRA formats, NIBSC recently produced a panel of lyophilised recombinant antibodies known to induce CRS of different intensities and three isotype-matched negative controls. The relative potency of these antibodies to stimulate cytokine release was evaluated in an international collaborative study.

12:15 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

13:15 Dessert Break in the Exhibit Hall with Poster Viewing

14:00 End of Advancing Bispecifics and Combination Therapy to the Clinic

17:00 Dinner Short Course Registration*

17:30 – 20:30 Dinner Short Courses

Recommended Short Course*

SC10: Engineering of Bispecific Antibodies and Multi-Specific Non-Antibody Scaffolds

**Separate registration required. See pages 6 & 7 for details.*





Engineering Bispecifics

Next-Generation Approaches for Discovery, Screening and Optimizing Bispecifics

THURSDAY 21 NOVEMBER

13:00 Registration

13:15 Dessert Break in the Exhibit Hall with Poster Viewing

INSIGHTS INTO EFFECTIVE BISPECIFIC MECHANISMS

14:00 Chairperson's Opening Remarks

Mark Chiu, PhD, Associate Director, BioTherapeutics Analytical Development, Janssen Research & Development LLC

14:05 KEYNOTE PRESENTATION: Turning Receptors Off and On with Bispecific Agents: Mechanistic Insights from Biophysics and Biochemistry



Andreas Plückthun, PhD, Professor & Director, Biochemistry, University of Zurich

Seemingly similar bispecific molecules, binding to the same receptors, can show very different biological behavior with dramatic consequences for their therapeutic suitability. Thus, bispecific agents may affect in opposite ways interaction with neighboring receptors, downstream signaling, internalization and subsequent degradation. A series of advanced biophysical methods have been developed to shed light on these phenomena, laying out blueprints for designing effective therapeutics.

14:35 Lisbon Wasn't Built in a Day – Alternative Scaffolds Gain Momentum

H. Kaspar Binz, PhD, Binz Biotech Consulting

The advent of alternatives to antibodies has been observed with large skepticism by the mAb community. It was while turning the academic ideas into businesses that the differentiating strengths of novel scaffolds crystallized. With safety doubts dispelled with clinical data, we now start to see alternatives to antibodies deliver differentiated drugs addressing unmet medical need in novel ways.

15:05 TCER® Platform: Targeting of Tumor-Specific HLA Ligands Using T Cell Receptor Bispecifics

Sebastian Bunk, PhD, Immunology, Immatics Biotechnologies GmbH

Bispecific T cell-engaging receptors (TCER) are soluble fusion proteins consisting of an affinity-matured T cell receptor targeting human leucocyte antigen-bound peptides and an antibody for recruitment of T cells and half-life prolongation. The design of the potent TCER molecules allows redirection of human T cells towards peptide-HLA targets showing highly selective expression in tumor tissue as validated by our target discovery engine, XPRESIDENT®. We present data supporting proof-of-concept of this novel class of T cell engagers.

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15:35 Networking Refreshment Break

NEW PLATFORMS FOR DISCOVERY, PRODUCTION, AND IDENTIFICATION OF SYNERGISTIC TARGET PAIRS

16:00 A Simple IgG-like Discovery Platform for a Complex IgG-like (1+1) Format

Régis Cebe, MSc, Scientific Technical Leader, Novartis Biologic Centre, Novartis Institute of Biomedical Research

A variety of bispecific antibody formats are being developed at Novartis. The IgG-like (1+1) format is often preferred when maximal tolerability is in focus. Over the past years, we have been developing a technology platform that enables efficient discovery, engineering, and production of such bispecific format. Based on illustrative case studies, the power of this platform in advancing therapeutic bispecific projects will be highlighted.

16:30 A New Platform for the Identification of Synergistic Bispecific Combinations

Elke Glasmacher, PhD, Head, Immunobiology, Large Molecule Research, pRED, Roche Innovation Center

Bi- and multi-specific antibodies enable the exploration of new biological concepts and treatment strategies. Within Roche, such next generation biologics have found broad application prospects in various disease areas. The presentation will focus on how format matters when designing multi-specific onco-immunological antibodies and how this affects its biological activity, and FORCE - a novel large-scale combinatorial platform to rapidly generate bispecific antibodies of different format and with different binders.

17:00 End of Day

17:00 Dinner Short Course Registration*

17:30 – 20:30 Dinner Short Courses

Recommended Short Course*

SC10: Engineering of Bispecific Antibodies and Multi-Specific Non-Antibody Scaffolds

*Separate registration required. See pages 6 & 7 for details.





Engineering Bispecifics

FRIDAY 22 NOVEMBER

08:00 Registration and Morning Coffee

ENGINEERING TO OVERCOME VIRAL RESISTANCE, TO CROSS THE BLOOD BRAIN BARRIER, AND FOR AUTOIMMUNE DISEASE

08:30 Chairperson's Remarks

H. Kaspar Binz, PhD, Binz Biotech Consulting

08:35 Multi-Specific Agent to Overcome Potential Resistance to Influenza

Mark Chiu, PhD, Associate Director, BioTherapeutics Analytical Development, Janssen Research & Development LLC

A multi-specific agent was designed to target multiple epitopes on pan influenza strains. The engineering to prepare the relevant therapeutic product profile involving viral neutralization, immune effector function, and optimal pharmacokinetic profile will be presented.

09:05 Brain Penetrant Bispecific Agonist Antibodies to Neurotrophin Receptors TrkB and TrkC

Frank S. Walsh, PhD, CEO, Ossianix, Inc.

Neurotrophins are attractive therapeutic targets for neurodegenerative disease, but their utility has been restricted by an inability to deliver therapeutic levels of the natural ligands, such as BDNF and NT3, to the CNS. We have used agonist antibodies to the receptors TrkB and TrkC and made them brain penetrant using VNARs to the transferrin receptor. The bispecific antibodies retain agonist activity *in vitro* and *in vivo*.

09:35 Preclinical Development of XmAb27564, a Long-Acting IL2-Fc Fusion Protein, as a Novel Treg-Selective Therapy for Autoimmune Diseases

Suzanne Schubert, PhD, Lead Scientist, Cell Biology, Xencor, Inc.

Regulatory T cells are critical for maintaining immune homeostasis, and their deregulation is associated with autoimmunity. Low-dose IL-2 is used therapeutically to expand Tregs, but suffers from rapid clearance and a narrow therapeutic index. To solve these problems, we developed XmAb27564, an IL2-Fc fusion protein with reduced potency and longer persistence. XmAb27564 selectively expands Tregs in human PBMCs in mice and monkeys, supporting its clinical development in autoimmune diseases.

10:05 Networking Coffee Break

HIGH THROUGHPUT SCREENING APPROACHES FOR BISPECIFICS

10:35 Bispecific Target Discovery by High-Throughput Functional Screening

Pallavi Bhatta, PhD, Principal Scientist, Bispecific Target Discovery, UCB

To exploit the potential of bispecific antibodies to discover new target pairs and invoke novel biology, we have developed technology that enables unbiased functional screening with large, combinatorial panels of bispecific antibodies. Our novel mix-and-match bispecific format allows grid-screening of thousands of bispecifics to hundreds of antigen combinations in high-throughput, disease-relevant assays. We will describe the discovery of several 'obligate' bispecifics across multiple disease areas, including autoimmunity, fibrosis, and oncology.

11:05 NestLink Technology to Determine Key Pharmacokinetic Parameters of Hundreds of Bispecifics Simultaneously

Pascal Egloff, PhD, Platform Leader, Medical Microbiology, University of Zurich

NestLink enables the simultaneous characterization of thousands of different binding proteins without the need to handle individual clones at any stage of the process. The technology was previously applied *in vitro* for the efficient identification of high-affinity binders against integral membrane proteins in the cellular context. In this talk, I will show that NestLink can be applied *in vivo* as well, such as to simultaneously determine pharmacokinetic parameters of more than one hundred individual bispecific binding proteins in a single model organism.

11:35 Next-Generation CLD Platform for Advanced Bispecific Antibodies Expression

Severine Fagete, Director, Cell Line Services, Selexis SA

Despite technologies that have advanced the forced heterodimerization of bi-specific antibodies (bsAb) and innovative purification procedures that remove homodimer by-products, new solutions that improve the bsAb production during the cell line development step are still needed. Here, we present a breakthrough cell line development platform using a single-cell system to express any bsAb format. Scalability and stability issue will be discussed and a case study of rescued bsAb program originally poorly expressing will be presented.

12:05 Problem-Solving Breakout Discussions with a Light Snack*

*See website for more details.

FOCUS ON T CELL ACTIVATION, SPECIFICITY, PK, AFFINITY, AND MAXIMIZING THE THERAPEUTIC INDEX

13:00 Chairperson's Remarks

Annelise Vuidepot, PhD, Vice President, Pipeline Research, Immunocore

13:05 Specificity of Bispecific T Cell Receptors (TCR) and Antibodies Targeting Peptide-HLA

Annelise Vuidepot, PhD, Vice President, Pipeline Research, Immunocore

Maintaining peptide selectivity is essential for the development of therapeutic agents targeting peptide-HLA complexes on cancer cells. Using multiple approaches, we assessed the selectivity of two novel classes of T cell redirecting pHLA-targeting bispecifics based on TCR-mimic antibodies or high-affinity TCRs. We show that peptide selectivity is associated with a broad and balanced energetic binding observed predominantly in TCR-pHLA interactions, whereas higher levels of cross-reactivity are associated with more focused 'hotspot' binding.

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Engineering Bispecifics

13:35 Dual Agonist Bispecific Antibody Targeting OX40 and CD137 Mediates Anti-Tumour Immunity and Synergises with PD-1/PD-L1 Blockade to Improve Survival in a Syngeneic Mouse Model

Omer Stern, PhD, Discovery, F-star

CD137 (4-1BB) and OX40 are key mediators of costimulatory signals and they play important roles in driving anti-tumour immunity, but combination of CPI with costimulatory agonists has not delivered significant clinical benefit. The activity of Fcγ receptor-dependent agonists may be limited by suboptimal costimulation of T cells and inadequate clustering via Fcγ receptors. We have developed FS120, a dual agonist bispecific antibody that drives potent activation of T cells via co-engagement of CD137 and OX40 and independent of Fcγ receptor binding.

14:05 Optimization of Preclinical Safety and Efficacy of Anti-HER2/CD3

Teemu Junttila, PhD, Senior Scientist, Translational Oncology, Genentech, Inc.

Systemic cytokine release and on-target/off-tumor toxicity on normal tissues are the main adverse effects limiting the applicability of T cell-redirecting bispecific antibodies. We have investigated how affinity to HER2 and CD3 impacts anti-tumor efficacy, distribution, and preclinical safety of anti-HER2/CD3 TDB and describe that affinity has a major impact on tolerability. Our studies suggest that fine-tuning the affinities to both the antigen and CD3 is likely critical to maximize therapeutic index in clinical use.

14:35 Concept to Clinic: Development of Fc-Containing XmAb Bispecific Antibodies for Immunotherapy

Umesh Muchtal, PhD, Director, Molecular Biology & Protein Sciences, Xencor, Inc.

We present a robust and modular heterodimeric Fc platform, engineered for efficient development of bispecific antibodies and Fc fusion therapeutics. These XmAb bispecific molecules are effective, stable, and easy to manufacture, and allow for the design of potent and/or tunable molecules with enhanced therapeutic index and safety profile. Several tumor-targeting CD3 bi-specifics and dual checkpoint-blocking molecules developed using this platform are in early clinical testing.

15:05 Targeted Antibody-Prodrugs

Ulrich Brinkmann, PhD, Expert Scientist, Large Molecule Research, Roche Pharma Research & Early Development, Roche

Antibody-prodrugs will be presented, which become selectively activated on target cells by novel mechanisms. Various examples and different formats for this principle will be presented, including targeted activation of mechanisms that trigger cytotoxicity on tumor cells, as well as options to improve PK properties and/or the therapeutic window.

15:35 End of Engineering Bispecifics



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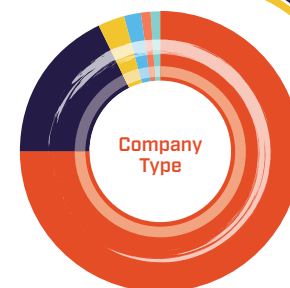
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CONFERENCE VENUE:

Lisbon Congress Center
(Centro de Congressos de Lisboa)
Praca Das Industrias
Lisbon, 1300-307, Portugal
Tel: +351 218-921-400



For Additional Information go to the Travel Page of PEGSummitEurope.com

HOST HOTEL:

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One short course	€625	€375	€125
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Monday, 18 November Morning, 9:00 – 12:00	Thursday, 21 November Dinner, 17:30 – 20:30
SC1: Advanced Introductory Course on Making Antibody Libraries in Phage and Yeast	SC6: Selection, Screening and Engineering for Affinity Reagents
SC2: The Tumour Microenvironment and Response to Cancer Immunotherapy	SC7: Protein Aggregation: Mechanism, Characterisation and Consequences
SC3: Mutation and Selection Strategies Beyond Affinity Optimisation	SC8: Advanced Analytical Technologies for Developability and Early Formulation Assessments
SC4: Surfactants in Biotherapeutics: Can't Live with Them, Can't Live without Them	SC9: T Cell Therapies: Current Field, Challenges and Future Directions
SC5: Use and Troubleshooting of Eukaryotic Expression Systems	SC10: Engineering of Bispecific Antibodies and Multi-Specific Non-Antibody Scaffolds

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ENGINEERING	C1A: Display of Biologics	C1B: Engineering Antibodies	C1C: Engineering Bispecifics
ONCOLOGY	C2A: Next-Generation Antibody-Drug Conjugates	C2B: Advancing Bispecifics and Combination Therapy to the Clinic	C2C: Novel Targets for Cancer and Emerging Targets
ANALYTICAL	C3A: Optimisation & Developability	C3B: Analytical Characterisation of Biotherapeutics	C3C: Protein Aggregation & Stability
IMMUNOTHERAPY	C4A: Modulating the Tumour Microenvironment	C4B: Winning Strategies for CAR T, TIL and TCR Therapy	C4C: Agonist Immunotherapy Targets
EXPRESSION	C5A: Cell Line and Systems Engineering	C5B: Optimising Expression Platforms	C5C: Protein Purification Technologies
BISPECIFICS		C2B: Advancing Bispecifics and Combination Therapy to the Clinic	C1C: Engineering Bispecifics
Training SEMINARS	TS6A: Antibody Deep Sequencing and Single Cell Analysis	TS6B: Genome Editing with CRISPR: Toward Novel Research, Translational and Clinical Applications	
	TS7A: Intro to Bispecifics: History, Engineering, and Applications	TS7B: Rational Approaches to Biologics Formulation and Delivery	

*Pre-doctoral, full-time student

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