11th Annual

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

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- Genome Editing with CRISPR  
- Biologics Formulation and Delivery |
The best biologics technology meeting in Europe: 
A must-attend conference for novel biologics.

Rakesh D., PhD, VP, AstraZeneca
PLENARY KEYNOTE SESSION

Monday 18 November | 16:15 - 18:20

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.

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.
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 Frendéus, 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, MB BS, PhD, CSO, 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 Koulou, 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. Chieu, PhD, Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific

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

**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:_

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, Affilogic
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.
TS6A: Antibody Deep Sequencing and Single Cell Analysis

Instructors: Brandon DeKosky, PhD, Assistant Professor, Department of Pharmaceutical Chemistry, Department of Chemistry and Life Sciences, Kansas University

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

In this training seminar, participants will learn about recent developments in the field of 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 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.

WEDNESDAY, 20 NOVEMBER AND THURSDAY, 21 NOVEMBER

DAY 1

8:30 – 12:45, Training Seminars in Session
12:45 – 13:30, Lunch Provided
13:30 – 18:20, Training Seminars in Session
18:20 – 19:30, Networking Reception

DAY 2

8:30 – 12:45, Training Seminars in Session
12:45 – 13:30, Lunch Provided
13:30 – 18:20, Training Seminars in Session
18:20 – 19:30, Networking Reception

Refreshment breaks and exhibit hall viewing hours also provided.
A Novel scFv Antibody Fragment to Misfolded Alpha Synuclein as a Potent Modulator of Neuroinflammation by in vivo Intras nal 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 medicated neuroinflammation.

15:15 Streamlined Discovery and Production of Therapeutic Antibodies

Lauri Pell, 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.
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 Alexandria, Isogenica’s Fully Synthetic Human Fab Library

Alexandria is Isogenica's fully synthetic human Fab library, containing a high diversity of heavy and kappa chain germlines and optimized for superior developability. Here, we will showcase a variety of antibody discovery campaigns to demonstrate its utility in generating viable lead panels to therapeutically relevant targets.

13:15 Alexandria, Isogenica’s Synthetic Antibody Discovery against Native Antigens by CRISPR/Cas9-Induced Mutagenesis

Guy Hermans, PhD, CSO, Isogenica Ltd.

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.

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Display of Biologics

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
We demonstrated that our RNAntibody technology is able to generate therapeutically effective amounts sufficient to provide fast protection against lethal rabies infection or botulinum intoxication. Additionally, single injection of antibody-encoding mRNA rapidly leads to high neutralizing antibody titers in animals, associated with the use of recombinant proteins in protein therapies. Recently, we demonstrated that a structural-guided approach we have designed, generated and demonstrated that these novel bispecific multi-specific antibodies, Ab-cytokine fusion proteins, non-Ig scaffolds, chimeric antigen receptors (CARs) and 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.

**NEW MODALITIES AND PLATFORMS**

**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.

**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 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*

TNFα is implicated in a host of chronic autoimmune inflammatory diseases. Therapeutic targeting and subsequent neutralisation of TNFα 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 TNFα 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.

**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.
Engineering Antibodies

13:15 Luncheon Presentation I to be Announced

13:45 Luncheon Presentation II to be Announced

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

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.
Commonality Despite Exceptional Diversity in the Baseline Human Antibody Repertoire
Bryan Briney, PhD, Assistant Professor, Immunology & Microbiology, Scripps Research Institute

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.

Talk Title to be Announced
Sherie Duncan, PhD, Manager Partners & Programs, AbCellera

Coffee Break in the Exhibit Hall with Poster Viewing

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.

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’.

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.

Luncheon Presentation II: Synthetic Biology Capabilities of the BioXp™ 3200 System
John Gill, Senior Director of Research & Development, Research & Development, 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.

Dessert Break in the Exhibit Hall with Poster Viewing

End of Engineering Antibodies

Dinner Short Course Registration*

Recommended Short Course*
SC6: Selection, Screening and Engineering for Affinity Reagents
*Separate registration required. See pages 6 & 7 for details.
11th Annual

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
Sebastian Bunk, PhD, Immunology, Immatics Biotechnologies GmbH
Bispecific T cell-engaging receptors (TCER) are soluble fusion proteins consisting of an affinity-maturated 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
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 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 Schubbert, PhD, Lead Scientist, Cell Biology, Xencor, Inc.

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 Presentation to be Announced

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

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.

*See website for more details.
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.

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.

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.

End of Engineering Bispecifics
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

13:00 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 by the end of 2019.

15:15 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 the 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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18 - 19 NOVEMBER 2019

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 Sponsored Presentation (Opportunity Available)

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

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/Garterra), 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 (Sponsorship Opportunity Available)

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 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.
Next-Generation Antibody-Drug 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 Sponsored Presentation (Opportunity Available)

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

NOVEL TECHNOLOGIES

17:00 Overcoming Limitations of Current Antibody-Drug Conjugates (ADCs) by a Novel Linker Technology
Philipp Spycher, PhD, 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

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 Vγ9Vδ2-T Cell Engagers
Paul W.H.I. Parren, PhD, Executive Vice President, Head, R&D, Lava Therapeutics B.V.
Vγ9Vδ2-T cells constitute the largest γδ-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 Vγ9Vδ2-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 Presentation to be Announced

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.

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 tools 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 Koevoed, 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
Laurens Kij, 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
BioNTechs 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. Systematic 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
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.

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

The Biclonics® 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 biomolecules 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
Janet Sim, PhD, Vice President, Protein Science, ALX Oncology
OmniChicken facilitated discovery of high affinity antibodies against the myeloid checkpoint receptor SIRPa
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
Christian Klein, PhD, Head of Oncology Programs & Department Head of Cancer Immunotherapy Discovery, Roche Innovation Center Zurich, Roche Pharmaceutical Research and Early Development (pRED)
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 FcgR-binding.

17:00 End of Day

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.
Novel Targets for Cancer and Emerging Therapeutic Areas

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

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 Schlößer, 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.

13:35 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

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 post-translational 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.

Fredtøf 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, missetargeted inflammation directed against healthy tissue underpins autoimmune disease pathogenesis. Investigating how regulatory
Novel Targets for Cancer and Emerging Therapeutic Areas

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 Presentation to be Announced

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
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

11:10 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 Presentation to be Announced

12:45 Luncheon Presentation I to be Announced

13:15 Luncheon Presentation II (Sponsorship Opportunity Available)

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 Combining Deep Sequencing and High Throughput B Cell Technologies to Maximize Functional Activity Guided Antibodies Discovery and Optimization
Gabriel WC Cheung, PhD, Senior Director, BioMedicine Design, Pfizer, Inc.

Successful biotherapeutic discovery follows some basic principles. At Pfizer, we strategically integrate technologies to enable fast and focused interrogation of B cell repertoire with functionally relevance.
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 Talk Title to be Announced
Anthony Stajduhar, Business Development Manager, Rapid Novor, Inc.

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.

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

17:00 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.

ASSESSING CQAs AND OPTIMISING BIOPHYSICAL CHARACTERISTICS

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
Fouda 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 swichSENSE® Biosensor
Ulrich Rant, PhD, CEO, Dynamic Biosensors GmbH

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 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.
Analytical Characterisation of Biotherapeutics

12:45 Presentation to be Announced

13:15 Luncheon Presentation I to be Announced

13:45 Automated Multi Attribute Method Analyses for Process Development and Characterization of mAbs
Martin Hoffmann, Senior Scientist, Research & Development – 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) - 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. Focus of the presentation will be the automated data analysis with the Genedata Expressionist software.

14:15 Session Break

HCP QUANTITATION

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

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
John Stults, PhD, Director, Protein Analytical Chemistry, Genentech, Inc.

Specification acceptance criteria are typically based on the understanding of critical quality attributes, clinical experience, and manufacturing capability. With shortened development timelines and few clinical lots, justifications of acceptance criteria are focused on science- and risk-based assessments of patient impact, providing a balance between appropriate control over high-risk attributes to ensure product quality for the patient, and flexibility for low-risk attributes, as appropriate, for a robust supply chain.

09:35 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.

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 to be Announced

12:45 Luncheon Presentation II (Sponsorship Opportunity Available)

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.
**PEGSummitEurope.com**

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**6th Annual**

**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 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?**

*John Proctor, PhD, Vice President, Marketing, Halo Labs*

Come 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.

15:20 **Modeling Protein Properties Using pH-Dependent Conformational Sampling**

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

mAb candidates present liabilities for developability; aggregation-prone regions or poor solution behavior. We optimized an integrin a11 binding mAb using rational design where reducing hydrophobic patches improved HIC behavior. Retrospective analysis shows conformational sampling and multi-parameter models can screen candidates and enrich libraries with favorable properties for biotherapeutics.

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.

17:00 End of Day
Protein Aggregation & Stability

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, Novo Nordisk 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 Biopharmaceuticals, 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 pharmacopoeias (EP, USP, JP) are the most widely used surfactants in biopharmaceutical products. Chinese pharmacopoeia (ChP) requires an oleic acid content of ≥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

11:35 Talk Title to be Announced
Dhananjay Jere, PhD, Senior Principal Scientist, Principal Group Leader, Drug Product Services, Lonza Pharma & Biotech

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

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.
Protein Aggregation & Stability

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 though 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
Dieter Willbold, PhD, Director, Structural Biochemistry, Forschungszentrum Jülich
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 subvisible 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 mAbs 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
Jeremy Wright, PhD, Principal Scientist, Immunomodulatory Drug Discovery, Agenus
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 Presentation to be Announced

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 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 tools reagents for target validation.

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

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 FcyRII
Björn Frendéus, PhD, CSO, BioInvent 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 Sponsored Presentation (Opportunity Available)

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 Frendéus, PhD, CSO, BioInvent International AB

14:20 Modifying the TME to Overcome Resistance to Immunotherapy
RJ Tesi MD, CEO/CMO Inimmune Bio, La Jolla
Resistance to immunotherapy is common and frustrating for patients and their clinical teams. Immunotherapy resistance mechanisms have a different etiology from resistance to chemotherapy. Targeting the cause of the immunologic resistance allows the re-use of the first-line immunotherapy. Two case studies will be presented: i) reversing resistance to immune checkpoint inhibitors caused by elevated MDSC and ii) reversing resistance to trastuzumab in women with HER2+ breast cancer.
14:50 Selectively Inhibiting CD47 in the Tumor Microenvironment
Nicholas 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
Amrak 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.

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

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

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
Riccardo Baptista, PhD, Director, Process and Analytical Development, 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 Cas9 offering the possibility of multiplexed editing with low risk of translocations.

10:05 Presentation to be Announced

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

11:00 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 NGK2D-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 CD3ε 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-Immunkonfektion, Universitätsherrnlinik Regensburg
Adaptive 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 Centre, Institute of Cancer Research London; The University of Manchester; iMATCH Director, The Christie NHS Foundation Trust
The remarkable responses seen with CAR T therapy in haematological 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 Polyfunctional Single Cell Analysis as a Key to Discovery and Predicting Patient Outcome
Peter Djali, European Director, Sales, IsoPlexis
Single-cell polyfunctionality has been shown as a potential predictor of patient response to CAR T cell therapy (Blood 2018). Here we present this and additional data from discovery to the clinic, showing how multiplexed cytokine secretion measurements can be used to characterise treatments and predict responses.

13:00 Sponsored Presentation (Opportunity Available)
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 Ferreirinha, 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.

13:45 Luncheon Presentation II (Sponsorship Opportunity Available)

14:15 Session Break

14:30 TEGs: A New Avenue in Cellular Immunotherapy Haakan Norell, PhD, Director, Discovery, Gadaeta B.V.
Identification of generally applicable receptors that specifically target various malignancies remains challenging. Gadeta employs y6TCRs, 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 (qβT 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 characterization assays 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 BIOSS 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 CD3ζ-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 TCRα, TCRβ, CD3ε, CD3γ, or CD3δ subunit. Respectively, 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 CD3e and CD3γ 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 CD3ε-TRuC-T cell dose greatly extended the survival of mice with Nalm-6 leukemia. In a subcutaneous Raji tumor model, CD3ε-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 HumanizedBTN3A 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
TCR 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 correlational 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.
Winning Strategies for CAR T, TIL and TCR Therapy

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

TILs AND GAMMA DELTA THERAPY

08:30 Chairperson's Remarks
John Maher, FRCP, 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, FRCPath, 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 IL15Rα 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 PANEL DISCUSSION: CARs vs. TCRs for Solid Tumours
Moderator: John Maher, FRCP, 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

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 Sponsored Presentation (Opportunity Available)

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 Goeltz, 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

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
**Agonist Immunotherapy Targets**

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, PhD, 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 immuno-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, PD-L1, 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, off-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.

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 *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/CD40 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.

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**CD40, GITR AND OX40**

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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

**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

**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.

**15:45** Networking Refreshment Break

**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
Cell Line and Systems Engineering

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-LINE ENGINEERING

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

Thomas Rexer, PhD, Team Lead, Synthetic Glycobiology, 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 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.

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

Shayli Varasteh Moradi, PhD, Research Associate, School of Earth, Environmental and Biological Sciences, 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 Presentation to be Announced

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 production platform. It combines the best properties of cell-based, cell-free, eukaryotic and prokaryotic systems, making it the most versatile protein production system. It allows production of proteins that have been difficult to make using other technologies in unprecedented quantities, in a single step.

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

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

Oomics 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 β1,4-N-Acetylglucosaminyltransferase III and α-mannosidase II, for the expression of a-fucosylated antibodies with enhanced Fc-mediated effector function.
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.

Sponsored Presentation (Opportunity Available)

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

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.

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.

Rethinking Gene Expression Using the Synthetic C3P3 Transcription System
Philippe H. Jais, MD, PhD, President and CSO, Eukary’s SAS
Eukary’s 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.
### 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*

**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, DSc, 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 Presentation to be Announced**

**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, Professor 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 Sponsored Presentation (Opportunity Available)**

**13:15 Luncheon Presentation I to be Announced**

**13:45 Luncheon Presentation II to be Announced**

**14:15 Session Break**
Optimising Expression Platforms

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 Tuning Recombinant Protein Expression to Match Secretion Capacity
Neil Dixon, PhD, Research Group Leader, Manchester Institute of Biotechnology, University of Manchester
Translocation of recombinant protein across cellular membranes can greatly facilitate the isolation of high quality and highly pure product. However, translocation processes are a major cellular bottleneck that are prone to capacity overload. Here we will report upon recent advances to avoid this capacity overload. Specifically, how we can employ fine-tuning of gene expression to match the secYEG-dependent secretion capacity in E. coli for the production of antibody fragments.

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

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)

08:35 Developing a Fit-For-Multi-Purpose Rapid Material Supply Process
Claire Pearce, PhD, Senior Research Scientist, CHO Expression Team Leader, Biopharmaceutical Development, Kymab Ltd.
Pre-clinical material supply demands microgram amounts of several hundred potential lead molecules through to gram amounts of the top 2-5 lead candidates. This presentation will detail progress on the development of an in-house rapid material supply platform to meet these needs.

09:05 Humanization and Simultaneous Optimization of Monoclonal and Bispecific Antibody
Christine X. Koo, PhD, Senior Scientist 1, Lead Optimization, Chugai Pharmabody Research
Antibody humanization is an essential technology for reducing the potential risk of immunogenicity. For developing an antibody molecule as a pharmaceutical, simultaneous optimization of critical antibody properties with humanization help to shorten the period necessary to identify a qualified clinical candidate. In addition, a system for purification of non-standard format antibodies such as bispecifics by using protein L chromatography is used to avoid over-engineering of antibody amino acid sequences.

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.
Optimising Expression Platforms

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.

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.

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

10:45 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.

11:05 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.

11:25 Luncheon Presentation I to be Announced

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.

12:45 Luncheon Presentation II: GlycoExpress® - An Alternative Host for Difficult to Express Proteins
Lars Stöckl, PhD, Senior Director BD and Technology, Glycotope GmbH

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

14:00 End of Optimising Expression Platforms

14:30 Dinner Short Course Registration*

17:00 Dinner Short Courses
Expression Stream

4th Annual

Protein Purification Technologies

Streamlining Processes

THURSDAY 21 NOVEMBER

13:00 Registration

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

CONTINUOUS PROCESSING

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 Tailor-Made Solvent Systems for Continuous Aqueous Two-Phase Extraction of Biomolecules
Christoph Brandenbusch, PhD, Group Leader, Biochemical and Chemical Engineering, Technische Universität Dortmund (TU Dortmund)
Extractions based on aqueous two-phase system (ATPS) were shown to have an enormous potential for the extraction of biomolecules. It is essential to identify a suitable tailor-made ATPS using profound knowledge on the molecular interactions in solution to influence the partitioning of the biomolecule and allow for the highest possible yield. We will present a novel method for this purpose as well as a new technology for a continuous ATPE.

15:05 Overcoming Limitations of Conventional Tag Systems – Strep-Tactin®XT Applications
Sarah Ludwig, PhD, Application Specialist, 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®.

15:20 Presentation to be Announced

15:35 Networking Refreshment Break

BREAKTHROUGH TECHNOLOGIES

16:00 A Microfluidic Platform for Antibody Manufacturing Optimization
Raquel Aires Barros, PhD, Full Professor, Bioengineering, IBB – Instituto de Bioengenharia 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 Protein Separation by Magnetic Particles in the Technical Scale
Sonja Berensmeier, PhD, Professor, 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 a new, economical purification process of biotechnologically produced proteins and contributes to a deeper understanding of bio-nano interactions.

17:00 End of Day
Protein Purification Technologies

FRIDAY 22 NOVEMBER

08:00 Registration and Morning Coffee

MEMBRANE PROTEIN PURIFICATION

08:30 Chairperson’s Remarks
Christoph Brandenburg, PhD, Group Leader, Biochemical and Chemical Engineering, Technische Universität Dortmund (TU Dortmund)

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 recombiantly 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.
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 Taking Chromatography to the Next Level - A Novel Fiber Based Protein A Chromatography Platform
Linnea Troeng, Product Manager, Protein Preparation and Purification, GE Healthcare Biosciences AB

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

INNOVATING PURIFICATION STRATEGIES

13:00 Chairperson’s Remarks
Sonja Berensmeier, PhD, Professor, Mechanical Engineering, Bioseparation Engineering, Technical University of Munich

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 Bioconjugates: Development of an Efficient and Scalable Maleimide Linker Stabilization Method
Pegah Saremirad, PhD, Scientist, Process Development, AstraZeneca
Conjugation of Active Pharmaceutical Ingredients (APIs) to macromolecules via Maleimide (Mal) conjugation to a sulfhydryl is used for generating medicines with selective delivery and prolonged half-life. However, deconjugation often occurs for Mal linkers, resulting in product heterogeneity and decreased shelf-life. De-conjugation can be mitigated via the hydrolysis of the Mal-linker. Here we report development of a controlled and scalable process for Mal linker hydrolysis. Process efficiency, scale up suitability and impact on the molecule was investigated, followed by demonstration of linker stabilization under different storage conditions.

15:35 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 Vγ9Vδ2-T Cell Engagers
Paul W.H.I. Parren, PhD, Executive Vice President, Head, R&D, Lava Therapeutics B.V.
Vγ9Vδ2-T cells constitute the largest γδ-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 Vγ9Vδ2-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 Presentation to be Announced

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.

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 Koe foed, 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 Kii, 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*  
BioNTechs RiboMAB® platform, based on in vitro-transcribed non-immunogenic mRNA encoding for a variety of antibodies, is antibiotics that provide a production challenge 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
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.

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.*

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***

*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

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.

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-maturated 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
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 Bintz, 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 Schubbert, 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 individual bispecific binding proteins in a single model organism.

11:35 Presentation to be Announced

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
Mihriban Tuna, PhD, Senior Vice President, Drug 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 Fcy receptor binding.
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 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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