Plenary Keynotes

Bicycles and Bicycle Drug Conjugates
Sir Gregory Winter, PhD, FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics

Paracrine Delivery: Therapeutic Biomolecules Produced in Situ
Andreas G. Plückthun, PhD, Professor and Director, Department of Biochemistry, University of Zürich

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- Rakesh D., PhD, VP, R&D, MedImmune
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- Engineering Bispecifics

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PEGSummitEurope.com
16:15 Moderator’s Opening Remarks
Janine Schuurman, PhD, Corporate Vice President, Research & Innovation, Genmab BV

16:20 Bicycles and Bicycle Drug Conjugates
Sir Gregory Winter, PhD, FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics
Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles’ unique properties have been used to develop Bicycle Drug Conjugates™ (BDCs), a novel toxin delivery platform which greatly improves toxin loading into tumour tissues. A BDC is expected to enter clinical trial in Q1 2018.

17:20 Paracrine Delivery: Therapeutic Biomolecules Produced in Situ
Andreas G. Plückthun, PhD, Professor and Director, Department of Biochemistry, University of Zürich
Cancer will have to be fought with cocktails of therapeutics acting locally, which may have to include therapeutic antibodies against receptors, checkpoint inhibitors, as well as cytokines to modify the tumor microenvironment. We have recently developed a technology of using non-replicative adenovirus carrying no viral genes, engineered to target desired cells and also to be shielded from the immune response, as a vehicle for simultaneous delivery of multiple genes of therapeutic proteins, produced and secreted by the infected cells.
SC1: Transient Protein Expression: A Key Tool to Enable Rapid Protein Engineering
Richard Altman, MS, Scientist, Protein Technologies, Amgen
Henry C. Chiou, PhD, Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific
Dominic Esposito, PhD, Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research

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

SC2: Making Antibody Libraries in Phage and Yeast
Andrew R.M. Bradbury, MB BS, PhD, CSO, Specifica, Inc.

In this short course, students will learn about antibody basics, including structure, genetics and the generation of diversity, as well as the creation of naïve antibody libraries in the phage and yeast display formats. This will include a description of phage and yeast display technologies, the creation of naïve libraries from natural and synthetic sources. The seminar will be fully interactive with students provided ample opportunities to discuss technology with instructors.

SC3: Introduction to the Tumour Microenvironment and Response to Cancer Immunotherapy
Mark Cragg, PhD, Professor, Experimental Cancer Biology, Antibody & Vaccine Group, Cancer Sciences Unit, University of Southampton
Frederick Arce Vargas, MD, PhD, MRCS, Group Leader, Translational Research, Autolus

The tumour microenvironment (TME) is a complex, dynamic environment in which extracellular matrix (ECM), soluble factors, immune cells, stromal cells and tumour cells interact. Each of these components is key to the establishment and growth of the tumour, as well as impacting tumour cell behaviour and response to treatment. For example, stromal cells such as fibroblasts and macrophages display tumour promoting properties, driving proliferation and survival whilst propagating an immunosuppressive environment. In this short course, we will discuss the nature of the TME, how the tumour promotes an immunosuppressive environment and what opportunities this presents for reversing immune suppression to deliver effective immunotherapy.

SC4: Mutation and Selection Strategies beyond Affinity Optimisation
Brian Fennell, PhD, Senior Principal Scientist, BioMedicine Design (BMD), Pfizer Dublin
Fred Darmanin Sheehan, PhD, Senior Principal Scientist, Biomedicine Design, Pfizer Dublin

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, genetic 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.

SC5: Surfactants in Biotherapeutics: Can’t Live with Them, Can’t Live without Them
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
Satish Singh, PhD, Head, Drug Product Process Development, Drug Product Services, Lonza Pharma and Biotech

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 pseudolamellar assembly. 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 biopharmaceutical products.

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

MONDAY 12 NOVEMBER AND TUESDAY 13 NOVEMBER

DAY 1
13:30 - 18:20
18:20 - 19:30
Training Seminars in Session
Welcome Reception

DAY 2
08:30 - 18:30
12:45
Training Seminars in Session
Lunch Provided

TS6A: Basic Technologies in a Protein Production Lab
This seminar is designed to introduce basic technologies, strategies and considerations in recombinant protein production in E. coli, insect and mammalian cells for multiple research and development applications. The seminar supplies a basic toolbox for management of multiple and diverse projects.

Instructors:
Tsak Danieli, PhD, Director, BioGV Excubator & Head, Protein Expression Facility, The Hebrew University of Jerusalem; Mario Lebendiker, PhD, Head, Protein Purification Facility, The Hebrew University of Jerusalem

Panelists:
Richard Allman, MS, Scientist, Protein Technologies, Amgen; Nicola Burgess-Brown, PhD, Principal Investigator, Structural Genomics Consortium (SGC), University of Oxford; Henry C. Chou, PhD, Director, Cell Biology, Thermo Fisher Scientific; Dominic Esposito, PhD, Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research; Bjorn Voldborg, MSc, Director, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark

TS7A: Introduction to Bispecifics: History, Engineering, and Application
Intro to Bispecifics will be organized as an informative and practical guide to get up to speed on critical aspects of bspecific 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 bspecifics as targeted and immunomodulatory approaches will be discussed.

Instructor:
G. Jonah Rainey, PhD, CEO, Oriole Biotech

TS8A: Introduction to Protein Engineering
CHI’s Introduction to Protein Engineering training seminar offers a comprehensive tutorial in the concepts, strategies and tools of protein engineering – and explains the role of this discipline in the progression of biotechnological research and development. The class is directed at scientists new to the industry or working in support roles, academic scientists and career protein scientists wanting a detailed update on the current state of the field.

Instructor:
David Bramhill, PhD, Founder, Bramhill Biological Consulting, LLC and Research Corporation Technologies

TS6B: Rational Approaches to Biologics Formulation & Delivery
This course will give participants an understanding of the basic principles of biologics formulation development and achieving long term product stability. Participants will gain an understanding of biochemical and biophysical properties of proteins and peptides, and how excipients and other strategies can be used to mitigate degradation. Focus will be on maximizing efficiency while maintaining regulatory compliance. Following which, we will discuss more complex formulation development topics and strategies for compatibility studies.

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

TS7B: Next-Generation Sequencing for Antibody Discovery and Engineering
Part 1 of the training introduces antibody repertoire exploration, genetic background, generation of diversity, sequencing technologies and the computational tools available for analysis of antibody repertoire NGS data. Part 2 will focus on preprocessing and analysis of data, elucidating each step using the programming language R using examples from existing bioinformatics pipelines. Repertoire analysis content will provide statistical quantification and visualization of high-dimensional data. The course will be fully interactive with case studies.

Instructors:
Sai Reddy, PhD, Assistant Professor, Biosystems Science and Engineering, ETH Zurich, Switzerland; Simon Friedensohn, MSc, Research Assistant, Biosystems Science and Engineering, ETH Zurich, Switzerland

THURSDAY 15 NOVEMBER AND FRIDAY 16 NOVEMBER

DAY 1
14:00 - 17:00
Training Seminars in Session

DAY 2
08:30 - 15:35
Training Seminars in Session
Lunch Provided

TS6C: Potency and Comparability for Cell and Gene Products
Extending potency assay concepts to cell, gene and tissue products is more challenging and often the most difficult aspect of characterising these products. Whenever changes are made, it is necessary to confirm they do not adversely impact the quality and therefore safety and efficacy of the product; this requires data beyond meeting current specifications. This training seminar will discuss the implementation and use of tools to enable characterisation, comparability and process development.

Instructor:
Christopher A. Bravery, PhD, Consulting Regulatory Scientist & Director, Advbios

TS7C: Introduction to CAR-T Engineering for Protein Scientists
This course is intended for academic and industry scientists new to the field of CAR-T immunotherapy, and it offers an overview of basic concepts, strategies and tools in CAR-T development. Topics will include the history of the CAR-T field, CAR structure and function, approaches to CAR gene delivery, target selection, the impact of CAR linkers and structural domains on function, multi-targeting CAR constructs, and the emerging technologies for temporal and spatial control of CAR-T function.

Instructor:
Dina Schneider, PhD, Manager, Cell Biology Lentigen Technology, Inc.
Bispecific antibodies have become an important class of antibody drugs with application in a variety of therapeutic areas. Here, we will discuss identification of agonist targets and combinations. CAR T, TIL & TCR Therapy will be discussed as well.

The tumour microenvironment is a critical factor in the development of cancer therapies. We will explore how to modify the microenvironment to make it more receptive to treatment.

Phage display is a powerful tool for drug discovery, vaccine development, antibody engineering, epitope mapping, gene/drug delivery or enzyme technology. Thanks to phage display, bacteriophages can be used as promising tools in engineering genetics, mainly thanks to its human antibody discovery and optimization platform.

Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles® molecule-like tissue penetration, tunable exposure and chemical synthesis are important.

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TUESDAY 13 NOVEMBER

07:45 Registration and Morning Coffee

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

08:35 Virus-Like Particle Display of HER2 Induces Potent Anti-Cancer Responses
Arianna Palladini, PhD, Department of Experimental Diagnostic and Speciality Medicine (DIMES), University of Bologna

09:05 Anticalin Drug Candidates Selected against Therapeutic Targets with Innovative Formats and Modes of Action
Arne Skerra, PhD, Professor & Chair, Technical University of Munich

09:35 Direct Functional Screening for Antibody-Drug Conjugates Using Transpo-mAb Mammalian Cell Display
Roger R. Beerli, PhD, CSO, NBE-Therapeutics AG

11:15 Discovery of a Cryptic Peptide Binding Site on PCSK9 and Design of Antagonists
Yingnan Zhang, PhD, Senior Scientific Manager, Early Discovery Biochemistry, Genentech

11:45 Microfluidics and Genomics for Polyclonal and Monoclonal Antibody Drugs for Infectious Disease
David S. Johnson, PhD, Founder and CEO, GigaGen, Inc.

12:15 The Journey to “the” Antibody: Accessing a Versatile Toolbox
Maria González-Pajuelo, PhD, CSO, FairJourney Biologics, S.A.

12:45 The Screening Smarter to Derive Data Driven Decisions Faster
Sarah Payne, PhD, Product Manager, Marketing, TTP Labtech

13:15 Luncheon Presentation: Accelerate your Antibody Discovery and Cell Line Development Workflows with Cyto-Mine®
Xin Liu, PhD, Principal Scientist, Biology, Sphere Fluidics

NOVEL USES OF DISPLAY TECHNOLOGIES

Chairperson
David Lowe, PhD, Senior Director, R&D, Antibody Discovery and Protein Engineering, MedImmune Ltd.
14:15 Chairperson's Remarks
Gregory A. Weiss, PhD, Professor, Chemistry, Molecular Biology & Biochemistry, University of California, Irvine

14:20 KEYNOTE PRESENTATION: Single Cell Selections of Recombinant Antibodies Binding to Circulating Tumor Cells
Peter Kristensen, PhD, Associate Professor, Department of Chemistry and Bioscience, Aalborg University

Metastatic cancer is closely linked to circulating tumor cells. The mechanisms behind the dissemination of cancer through these metastatic seeds however remain incompletely understood. To reveal novel biomarkers, and gain a better understanding of the underlying mechanisms of cancer metastasis, we have used an advanced single cell selection on circulating tumor cells from patients diagnosed with metastatic colorectal cancer. In the presentation, the potential of single cell selection of recombinant antibodies will be discussed.

14:50 Dual Display: Phage Selection Driven by Co-Engagement of Two Targets
Oliver Hartley, PhD, Associate Professor, Department of Pathology and Immunology, Faculty of Medicine, University of Geneva

This presentation will describe the design and preliminary evaluation of a new phage display approach enabling compatible pairs of antibody fragments to be co-selected based on co-engagement of their respective targets. Phagemids encoding a first scFv fused to phage g3p protein via a first leucine zipper are rescued in bacteria expressing a second scFv fused to a complementary leucine zipper, which is incorporated into phage during assembly.

15:20 Phage Display Selection of Chemically Cyclized Peptides for the Development of Therapeutics
Christian Heinis, PhD, Professor, Laboratory of Therapeutic Peptides and Proteins, Ecole Polytechnique Federal de Lausanne (EPFL)

My laboratory is engaged in the discovery and development of cyclic peptides for therapeutic application. A major focus is the generation of ligands based on bicyclic peptides by phage display. In my talk, I will present new chemical reactions that we have applied to generate structurally highly diverse cyclic peptide libraries, and I will show recent data on the therapeutic activity of bicyclic peptides in vivo.

15:50 Validation of Llamma, Isogenica's Humanized Single Domain Antibody Library
Guy Hermans, PhD, CSO, Isogenica Ltd.

We have previously discussed the design and validation of Ilamda, Isogenica’s fully synthetic camelid single domain antibody library. Here, we will disclose novel data on the design and validation of a humanized variant of the library. Examples will be provided on how this library, combined with our CIS Display enabled high throughput screening method, can generate high affinity lead panels in weeks rather than months.

16:20 Refreshment Break in the Exhibit Hall with Poster Viewing
3rd Annual
Engineering Antibodies
Designing Next-Gen Molecules

WEDNESDAY 14 NOVEMBER

07:45 Registration and Morning Coffee

ANTIBODIES AGAINST INTRACELLULAR AND CHALLENGING TARGETS

08:30 Chairperson's Remarks
Ulrich Brinkmann, PhD, Expert Scientist, Molecular Engineering, Roche

08:35 KEYNOTE PRESENTATION: Grp 94, an Intracellular Target of Antibody-Based Immunotherapy of Malignant Diseases – Opportunities and Challenges
Soldano Ferrone, MD, PhD, Professor, Surgery, Massachusetts General Hospital, Harvard Medical School
The scFv W9 has been isolated from a phage display human antibody library. This antibody has the unique specificity to recognize an extracellular epitope of the heat shock protein Grp94. The characteristics and functional properties of this antibody will be described. In addition, the obstacles to the clinical applications of this and the strategies to overcome them will be discussed.

09:05 Engineering Alphabodies to Target Intractable Intracellular Cancer Targets
Yvonne McGrath, PhD, CSO, Complix
Alphabodies comprise a triple helical protein scaffold that can be engineered to bind target proteins with high specificity and affinity. Further modifications allow these biologics to traverse the cell membrane and inhibit disease-associated intracellular targets. A panel of these Alphabodies has been engineered to bind and inhibit important oncology intracellular targets hitherto considered intractable with conventional small molecules. Functional assessment of a selection of these Alphabodies will be presented.

09:35 Generating Potent and Selective Inhibitors of Kv1.3 Ion Channel by Fusing Venom Derived Mini Proteins into Peripheral CDR Loops of Antibodies
Aneesh Karatt-Vellatt, PhD, Group Leader, Antibody and Protein Engineering, IONTAS Ltd.
Pathogenic TEM cells drive many autoimmune disorders and are uniquely dependent on the Kv1.3 channel. A number of venom derived cysteine-rich mini-protein inhibitors of Kv1.3 are being developed as potential drug candidates, but can suffer from manufacturing difficulties, short half-lives and a lack of specificity. Using proprietary KnotBody technology, IONTAS has developed a panel of potent and selective Kv1.3 inhibitors that can be further developed as long acting immunomodulators for the treatment of autoimmune disorders.

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

STRATEGIES TO IMPROVE TARGETING, BINDING AND BIOACTIVITY OF MOLECULES

11:15 Targeting the Matrix Metalloproteinase (MMP)-14/MMP-2/Integrin αvβ3 Axis with Multispecific N-TIMP2-Based Antagonists for Cancer Therapy
Niv Papo, PhD, Group Leader, Assistant Professor, Biotechnology Engineering, Ben-Gurion University
The MMP-14/MMP-2/integrin αvβ3 axis thus constitutes a putative target for therapeutic interventions, but inhibitors that target this axis remain to be developed. Based on screening of a N-TIMP2 mutant library, we generated efficient protein monomers and heterodimer antagonists that contain monovalent and bivalent binding epitopes to MMP-14 and integrin αvβ3. These results enabled us to investigate the individual roles of the three signaling molecules in various malignant processes.

11:45 Multiple Mechanism of Ligand Blocking by Antibodies
Fernando Garces, PhD, Senior Scientist, Therapeutic Discovery, Amgen
Antibodies can be generated and selected to block the binding of a protein receptor to its protein ligand. In such cases, the set of molecules generated usually show low sequence diversity and a common inhibition mechanism. Here we present a case study, where we have structurally characterized multiple antibodies, with high sequence diversity that recognize a protein receptor and block protein/ligand binding via several inhibition mechanisms.

12:15 The Molecular Landscape of the Immune Response following Treatment with Biologics
Yariv Wine, PhD, Assistant Professor, School of Molecular Cell Biology and Biotechnology, Tel Aviv University
The mechanisms that lead to the generation of ADAs and their molecular composition are unknown. We developed a new immunoassay to determine ADA level and their neutralizing capacity. We found that therapeutic mAb infusion mounts a vaccine boost like response reflected in a rapid rise of lymphocytes post-infusion. B Cells were isolated and their repertoire features were determined by NGS. Collectively we found: i) an increase in lambda/kappa antibody light chain ratio in the neutralizing ADA compartment; ii) an increase in ADA clonal polarization post-infection.

12:45 An Integrated Approach to Managing Immunogenicity Risk and Optimum Protein Design
Jeremy Fry, DPhil, Director, Sales, Proimmune
Integrated platforms can be used to mitigate immunogenicity risk and characterize immune responses during the drug design and development stages. Proimmune offers mutational activity mapping for optimal protein design, DC-T/T cell proliferation assays for biologic lead selection/optimization, a Mass Spectrometry
assay for characterization of antigen presentation; HLA-peptide binding assays to characterize individual epitopes & undiluted whole blood cytokine storm assays.

13:15 Luncheon Presentation I: Build Better Biologics with Machine Learning and Synbio
Claes Gustafsson, Co-Founder and CCO, ATUM (formerly DNA2.0)
This presentation will showcase how ATUM combines recent developments in genome engineering, automation, big data and product analytics to increase efficiency of engineering and developability of biologics and cell lines. Cell lines generated using the LeapIn® transposase combined with optimized vector constructs, proprietary codon optimization and QSAR-based protein engineering allow for an information rich and efficient optimization of mAbs, bispecifics, CAR-T molecules, and the increasingly complex biologics approaching the market place.

13:45 Luncheon Presentation II: Overcoming Tolerance by Deep Mining of Natural Immune Repertoires
Veronique Lecault, PhD, Co-Founder, AbCellera
Antibodies from natural immune responses are widely regarded as superior to those generated by display technologies; however, immune tolerance poses a serious challenge for targets with high inter-species homology. Insoluble and poorly immunogenic targets such as membrane proteins exacerbate this challenge. We show how AbCellera’s ultra-deep screening technology overcomes these challenges, producing hundreds of diverse rodent antibodies against targets with 100% rodent-human homology, including G protein-coupled receptors.

14:15 Session Break

NOVEL FORMATS AND ALTERNATIVE PLATFORMS

14:30 Chairperson’s Remarks
Philip M. Kim, PhD, Associate Professor, Donnelly Centre, University of Toronto

14:35 Use of Small and Stable Antibody Scaffold Fv-clasp to Facilitate Structural Studies of Drug-Target Molecules
Junichi Takagi, PhD, Professor, Laboratory, Protein Synthesis and Expression, Institute for Protein Research, Osaka University
“Fv-clasp” is an artificially designed, small (~37 kDa) two-chain antibody fragment format compatible with bacterial expression and is applicable to any IgG antibodies. The conformational rigidity and high heat stability of Fv-clasp contributed to its superior “chaperoning” activity over conventional Fab fragment, and facilitated the structure determination of many drug target proteins with high conformational flexibility.

15:05 Multi-Specific, Multi-Valent and Bi-Paratopic Nanobodies: Progress toward the Clinic
Carlo Boulton, PhD, Director, Technology & Information Management, Ablynx NV
Small Nanobodies with their modular design are a perfect starting point for generating multivalent and multispecific therapeutics in a wide range of human diseases. The formatting flexibility of the platform allows the development of the most optimal drug formats. The development of Nanobodies® and their progress towards the clinic will be shown by a number of examples.

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

16:15 V565 Is an Orally-Administered, Protease-Resistant, Anti-TNF Domain Antibody for the Treatment of Inflammatory Bowel Disease
Kevin Roberts, PhD, Senior Scientist, VHSquared Ltd.
V565 is an anti-TNF domain antibody for oral administration in IBD patients, engineered to resist intestinal proteases. Oral dosing of V565, formulated in enteric-coated minitablets, resulted in micromolar levels of active V565 in the ileal fluid of volunteers fitted with ileostomy bags and in the faeces of Crohn’s disease patients. Oral administration to five ulcerative colitis patients for 6 to 7 days resulted in V565 localisation to the lamina propria and inhibition of mucosal inflammatory processes.

16:45 Development of mRNA-Encoded Bispecific Antibodies Targeting Solid Tumors
Hayat Bahr-Mahmud, PhD, Deputy Head, Bispecific Antibodies, BioNTech
Successful application of many T cell-engaging bispecific antibodies is hindered by manufacturing challenges and short serum half-life. We circumvented these limitations by treating mice with in vitro-transcribed (IVT) pharmacologically optimized and nucleoside-modified mRNA encoding the antibody. We achieved sustained endogenous synthesis of the antibody, which eliminated advanced tumors as effectively as the corresponding purified bispecific antibody. Due to the fast manufacturing process of pharmaceutical mRNA, the RiboMAB approach could accelerate the clinical development of novel bispecific antibodies.

17:15 Development of Highly Potent T Cell Receptor Bispecifics Targeting Tumor-Specific HLA Ligands
Sebastian Bunk, PhD, Director, Immunology, Immatics Biotechnologies GmbH
T cell receptor (TCR)-based immunotherapy has emerged as a promising treatment modality for malignant diseases. Immatic’s bispecific TCR molecules utilize affinity matured and selective TCRRs for targeting of tumor-specific, human leukocyte antigen (HLA)-bound peptides as identified by the target discovery engine XPRESIDENT®. The TCRs are engineered into our highly active bispecific TCR scaffold comprising a T cell-engaging antibody for potent redirection and activation of T cells and resulting in stable molecules with extended serum half-life.

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
08:35 From Antibody-Targeted Toxins to Gene Editing: Disruption of Diphthamide Synthesis Genes and Resulting Toxin Resistance as a Robust Technology for Quantifying and Optimizing CRISPR/Cas9 Approaches
Ulrich Brinkmann, PhD, Expert Scientist, Molecular Engineering, Roche
Activity of antibody fusions harboring Pseudomonas Exotoxin derivatives requires diphthamide on eEF2. Diphthamide therefore serves as biomarker for immunotoxin efficacy; cells without diphthamide are toxin resistant. This phenotype can also be applied to identify and quantify events that result from CRISPR/Cas9 editing. DPH gene editing followed by toxin selection provides a simple robust method to differentiate and quantify homologous/ heterologous inactivation and integration events, and to optimize specificity and efficacy of editing procedures.

09:05 High-Throughput Antibody Engineering in Mammalian Cells by CRISPR/Cas9-Mediated Homology-Directed Mutagenesis
Sai Reddy, PhD, Assistant Professor, Biosystems Science and Engineering, ETH Zurich
Homology-directed mutagenesis (HDM) extends the concept of CRISPR/Cas9-mediated homology-directed repair to generate site-directed mutagenesis libraries in mammalian cells. Following cleavage by the Cas9 protein, single-stranded oligonucleotides containing degenerate codons serve as the repair template, providing integration of sequence diversity into the genome. We used HDM to generate libraries in the antibody CDRH3, and combined this with a mammalian surface display platform for high-throughput screening.

09:35 A Case Study in Adaptability: Exemplification of the Power of UCB’s Core Discovery Platform through the Discovery of a Potent Anti-Tau Antibody
Dale Starkie, MSc, Senior Scientist, UCB Celltech
Here we describe the use of a number of cutting-edge antibody discovery technologies to efficiently interrogate the B cell repertoire of immunised animals and humans to identify rare antibodies with desirable characteristics. We employ a high-throughput automated B cell culture screening platform to mine out the memory B cell repertoire and a novel fluorescence-based proximity secretion assay to sample the plasma cell repertoire. We will discuss the use of multiple immunisation strategies utilising several forms of antigen and the discovery of an anti-tau lead antibody candidate capable of blocking uptake and aggregation of tau from three distinct human tauopathies in a novel robust and quantitative Tau seed uptake cellular assay.

10:05 Antibody Protein Sequencing with Mass Spectrometry
Mingjie Xie, CEO, Rapid Novor, Inc.
Many applications in antibody engineering require the direct sequencing of antibody proteins. At Rapid Novor (rapidnovor.com), we have developed a robust workflow and routinely sequenced antibody proteins. Here we share the success experiences, examine common mistakes novices make, and present our practices to ensure the correctness of every amino acid.

10:20 The SCORE Technology, a Novel Label-Free HTS Tool for Drug discovery
Florian Proell, PhD, CEO, Biametrics GmbH
In high-throughput screening, the more you can screen, with the most sensitive technology, the higher likelihood of finding the best candidates. SCORE technology combines a microarray approach with kinetics to offer richer data sets that improve target identification. This results in better lead candidates, accelerating your drug discovery pipeline.
10th Annual

**Engineering Bispecifics**
Enhanced Targeting and Functionality

**THURSDAY 15 NOVEMBER**

13:00 Registration

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

**FOCUS ON T-CELL ENGAGERS**

14:00 Chairperson's Opening Remarks
Thomas Van Blarcom, PhD, Associate Research Fellow, Protein Engineering, Pfizer, Inc.

**14:05 KEYNOTE PRESENTATION:** Novel T Cell Engagers for Targeted Recruitment of Effector Cells to Tumors
Yoram Reiter, PhD, Head, Molecular Immunology, Technion-Israel Institute of Technology

We have developed a new class of recombinant chimerical molecule that serve as T cell engagers to re-direct potent immune effector functions to specifically kill tumor cells. These T cell engagers are based on the genetic fusion of antibody fragments, specific for tumor cell surface antigens to monomeric HLA molecules that carry immunodominant peptides that can recall potent effector T cells. The molecular feature of these molecules/approaches and their in vitro and in vivo activities will be described.

14:35 Engineering of a T-Cell Dependent Bispecific to Broaden the Therapeutic Index for Solid Tumors
Christoph Spiess, PhD, Senior Scientist, Antibody Engineering, Genentech, Inc.

I will present the engineering of the bispecific to achieve selective binding to tumor cells and provide data demonstrating improved tumor infiltration in vitro and in vivo and preclinical safety.

15:05 Presentation to be Announced

15:35 Networking Refreshment Break

**16:00 Creating a Novel T-Cell Engaging Bispecific Antibody Platform: Fine Tuning Anti-Tumor Activity with Sequence-Based Discovery and Machine Learning**
Nathan Trinklein, PhD, VP, Discovery, Teneobio

Using a multiple myeloma tumor cell line along with primary human PBMCs, we demonstrate a spectrum of in vitro tumor cell killing activity with varied levels of cytokine release using our bispecific molecules with diverse CD3 binding activities. In summary, we have created a T-cell engaging bispecific antibody platform with tuned T-cell agonism that can be used to optimize the therapeutic index for a variety of tumor antigens.

16:30 Developing Humabody VH Therapeutics for Immuno-Oncology
James Legg, PhD, Vice President, R&D, Crescendo Biologics

This presentation describes our approach to developing immune-oncology therapeutics, in particular Humabody VH products, small highly adaptable multifunctional proteins which can be developed into differentiated therapeutics with excellent characteristics for tumour targeting. It includes the development of a Biparatopic PD-1 inhibitor showing efficacy in a Pembrolobuzumab insensitive in vivo model, a Bispecific PD-1, LAG3 inhibitor and a targeted IO approach in which T-cell co-stimulation is focused away from the periphery and into the tumour microenvironment.

17:00 End of Day

17:00 Dinner Short Course Registration*

17:30 – 20:30 Dinner Short Courses

**Recommended Short Courses**

SC8: Selection, Screening and Engineering for Affinity Reagents
SC10: Engineering of Bispecific Antibodies

*Separate registration required. **Click here** for details.

**FRIDAY 16 NOVEMBER**

08:00 Registration and Morning Coffee

**FC ENGINEERING FOR ENHANCED PRODUCT PROPERTIES AND FOR BRAIN DELIVERY**

08:30 Chairperson’s Remarks
Martin Bader, PhD, Head, Biochemical and Analytical Research, Pharma Research and Early Development, Roche

08:35 Glyco-Optimization of Antibodies Targeting Immune Checkpoint Molecules: Case Studies of an Agonist and an Antagonist
Christoph Goletz, PhD, Associate Director, Preclinical Pharmacology & Cancer Immunology, Glycopte GmbH

Glyco-engineering is an established strategy to improve tumor antigen-targeting antibodies, e.g. anti-CD20, anti-EGFR, regarding their ADCC activity. In two case studies of an agonistic anti-CD40 and an antagonistic anti-PD-L1 antibody, we show that glyco-optimization can also be applied to enhance activity of antibodies targeting immune checkpoint molecules.

09:05 Development of a Novel Fc Heterodimerization Technology
Fabian Richter, PhD, Post-Doc, Biomedical Engineering, Cell Biology and Immunology, University of Stuttgart

The innovative heterodimerization technology “Fc1k” (Fc-one-kappa) was created and used for the generation of monovalent as well as polyvalent and multi-specific...
antibody-like molecules. We demonstrated the applicability in a monovalent Fv-Fc1k format, used for cytokine receptor blockade and in a bispecific scFv2-Fc1k molecule, simultaneously targeting two antigens. This novel platform technique provides for covalent heterodimerization of immunoglobulin domains, based on fully human and naturally occurring sequences.

09:35 Identification of a PD-L1 Binding Fcab: A Potent Inhibitor of Immunosuppressive Signals
Jose Munoz Olaya, PhD, Principal Scientist, Drug Discovery, F-star

Checkpoint inhibitors have been very popular and successful targets in the field of immuno-oncology. Here we describe the isolation of an Fcab, an antibody Fc domain modified to bind to a target, specific to PD-L1. The Fcab exhibits high affinity to human PD-L1 that translates into strong potency in cell-based functional assays. An anti-murine surrogate molecule, with similar potency, also exhibits activity in an MC38 syngeneic tumour model. This activity is improved when the Fcab is paired with Fabs targeting other immune checkpoint regulators.

10:05 Networking Coffee Break

10:35 Antibody Transport Vehicle (ATV): A Novel Brain Delivery Platform
Mark S. Dennis, PhD, Fellow, Denali Therapeutics

The Antibody Transport Vehicle (ATV) enables the delivery of large molecule therapeutics to the brain for the treatment of neurological diseases. The ATV platform contains an engineered Fc domain that binds the transferrin receptor and utilizes receptor-mediated transcytosis to cross the BBB. Transport in nonhuman primates was assessed by the inhibition of β-secretase 1 (BACE1) in brain which was robustly inhibited by ATV:BACE1 leading to a sustained reduction in amyloid beta levels.

11:05 Turning Affibody Molecules into Efficient Peptide Binders by Dimerization
John Lofblom, PhD, Associate Professor, Engineering Sciences in Chemistry, Biotechnology and Health, KTH Royal Institute of Technology

Affibody molecules are small three-helical affinity proteins. Generating binders for the amyloid beta peptide yielded a variant with 20-pM affinity, and with a unique 2:1 stoichiometry mode of binding as well as structural rearrangements in both the affibody domains and the amyloid beta peptide that is sequestered in a tunnel-like cavity. Engineered binders for other peptides show similar structural rearrangements and mode of binding, indicating that the new dimeric scaffold is well suited for such molecular recognitions.

11:35 Industrializing IO Therapeutic Discovery Platforms: Multispecifics, Engineered TCRs and CARs
Maria Wendt, PhD, Head, Science 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.

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

TECHNOLOGIES FOR DISCOVERY AND SCREENING, CMC, TARGETING, POTENCY AND LOW RISK OF TOX

13:00 Chairperson's Remarks
Mark S. Dennis, PhD, Fellow, Denali Therapeutics

13:05 Case Studies on How Digital and Automated Solutions Transform the Discovery and Development of Next-Generation Antibodies
Martin Bader, PhD, Head, Biochemical and Analytical Research, Pharma Research and Early Development, Roche

We systematically introduced automated and digital solutions along our antibody discovery and development chain. A number of examples will be highlighted that demonstrate how automation and data science speed up 1) developability predictions to enable fast selection of clinical leads, 2) automation during functional characterization, and 3) machine learning during cell line selection and bioprocess modeling. As a consequence, output during the antibody discovery and development phase increases substantially.

13:35 Simultaneously Multiple Interaction T Cell Engagers (SMITEs): Improving Bispecific Therapies through T Cell Costimulation
Colin Correnti, PhD, Senior Research Scientist, Clinical Research, Fred Hutchinson Cancer Research Center

14:05 Redefinition of ErbB2/3 Tumor Targeting: How to Design Truly Potent Bispecific and Biparatopic Agents
Rastislav Tamaskovic, PhD, Head, TC Facility, Senior Scientist, Biochemistry, University of Zurich

Due to adaptiveness of oncogenic networks, tumors readily develop resistance against targeted therapies. Recently, we have described major compensatory routes, which become activated in therapy of ErbB2-positive cancer - and developed a new class of bispecific and biparatopic anti-ErbB2/3 targeting agents endowed with capabilities to overcome the adaptive resistance. Analogously, we build a new platform for tumor RTK fingerprinting aimed at identification of prospective therapeutic leads and truly synergistic combination therapies.

14:35 Productive Common Light Chain Libraries Yield Diverse Panels of High Affinity Bispecific Antibodies
Thomas Van Blaricom, PhD, Associate Research Fellow, Protein Engineering, Pfizer, Inc.

Here we describe the design of a synthetic human antibody library based on common light chains to generate antibodies with biochemical and biophysical properties that are indistinguishable to traditional therapeutic monoclonal antibodies. We used this library to generate diverse panels of well-behaved, high affinity antibodies toward a variety of epitopes across multiple antigens including mouse 4-1BB in order to investigate the therapeutic potential of biparatopic bispecific antibodies.
15:05 **DuoBody Technology: A Versatile Platform for Bispecific Antibody Discovery and Development**

*Rick Hibbert, MBA, PhD, Assistant Director, Protein Production and Chemistry, Genmab B.V.*

The DuoBody® platform represents a versatile, elegant and robust technology for generating bispecific antibodies. The post-production process is based on controlled Fab-arm exchange and yields bispecific antibodies that retain the molecular structure and quality attributes of therapeutic IgGs. The process is robust, high-throughput compatible and shows linear scalability from bench to manufacturing scale. This presentation will highlight recent insights in the preclinical and CMC development of DuoBody products.

15:35 **End of Summit**
3rd Annual
Next-Generation Antibody-Drug Conjugates

Engineering Strategies

**Recommended Short Course***

**SC2: Making Antibody Libraries in Phage and Yeast**

*Separate registration required. Click here for details.

**MONDAY 12 NOVEMBER**

**12:00 Conference Registration**

**FIGHTING CANCER WITH ADCs**

**13:30 Organizer’s Welcome**

Mary Rubbery, Senior Conference Director, Cambridge Healthtech Institute

**13:35 Chairperson’s Opening Remarks**

Christian P. R. Hackenberger, PhD, Professor and Department Head, Chemical Biology II, Leibniz-Research Institute for Molecular Pharmacology (FMP) and Humboldt University Berlin

**13:45 FEATURED PRESENTATION: Delineating the Role of Normal Tissue Target Expression on PK and Anti-Tumor Activity with a Mouse Cross-Reactive ADC**

Jan Pinkas, PhD, Vice President, Translational Research & Development, ImmunoGen, Inc.

We have developed a mouse cross-reactive ADC that we have employed to understand the role of normal tissue target expression on PK and anti-tumor activity. Our findings are broadly applicable to the development of ADCs for solid tumor targets. In this talk, I will share the data that has been generated.

**14:15 Clinical and Preclinical Evaluation of Anti-Tumor Antibody-Toxin Fusion Proteins**

Gregory P. Adams, PhD, CSO, Eleven Biotherapeutics, Inc.

Anti-tumor antibody fragments genetically fused to protein toxins that block translation can overcome many of the limitations of current generation ADCs. Their ability to drive immunogenic cell death and potentially stimulate host anti-tumor immune responses also makes them attractive candidates for combination with immuno-oncology agents. Preliminary results from an ongoing mono therapy Phase III clinical trial in patients with high-grade non-muscle invasive bladder cancer will be presented along with preclinical results of earlier-stage agents.

**14:45 Radionuclide Therapy Using Peptide Nucleic Acid (PNA)-Mediated Pretargeting of HER2-Expressing Tumors**

Amelie Eriksson Karlström, PhD, Professor, Protein Science, Engineering Sciences in Chemistry, Biotechnology and Health, KTH Royal Institute of Technology

In vivo pretargeting is a promising approach to reduce unfavorable biodistribution leading to side effects during treatment with radiolabeled tumor-targeting antibodies or alternative scaffold proteins. We have developed a concept where the primary, tumor-targeting agent is conjugated to a peptide nucleic acid (PNA) strand, which binds with high affinity to a secondary, radiolabeled, complementary PNA strand. We also applied the same pretargeting system to tumor targeting with the monoclonal antibody trastuzumab and demonstrated a high contrast between tumor and non-tumor tissue.

**15:15 Sponsored Presentation (Opportunity Available)**

**15:45 Networking Refreshment Break**

**PLENARY KEYNOTE SESSION**

**16:15 Moderator’s Opening Remarks**

Janine Schuurman, PhD, Corporate Vice President, Research & Innovation, Genmab BV

**16:20 Bicycles and Bicycle Drug Conjugates**

Sir Gregory Winter, PhD, FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics

Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles’ unique properties have been used to develop Bicycle Drug Conjugates™ (BDCs), a novel toxin delivery platform which greatly improves toxin loading into tumour tissues. A BDC is expected to enter clinical trial in Q1 2018.

**17:20 Paracrine Delivery: Therapeutic Biomolecules Produced in Situ**

Andreas G. Plückthun, PhD, Professor and Director, Department of Biochemistry, University of Zürich

Cancer will have to be fought with cocktails of therapeutics acting locally, which may have to include therapeutic antibodies against receptors, checkpoint inhibitors, as well as cytokines to modify the tumor microenvironment. We have recently developed a technology of using non-replicative adenovirus carrying no viral genes, engineered to target desired cells and also to be shielded from the immune response, as a vehicle for simultaneous delivery of multiple genes of therapeutic proteins, produced and secreted by the infected cells.

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

**19:30 End of Day**
THE NEXT GENERATION OF ADCs

**08:35 KEYNOTE PRESENTATION: Strategies & Challenges for the Next Generation of ADCs**

Alain Beck, PhD, Senior Director, Analytical Chemistry, NBEs, Centre d’Immunologie Pierre Fabre; Associate Editor, mAbs

The development of ADCs has benefited from general improvements in the design of therapeutic mAbs and from specific improvements in methods for conjugate synthesis. Diversification of linking strategies and warheads has provided new opportunities to improve drug delivery to tumors while reducing drug exposure to normal tissues. Protein structural characterization tools such as mass spectrometry are allowing better understanding of ADC structures, stability and biotransformations. This knowledge contributes to the identification of early-developability criteria for all of the ADC components.

**09:05 The Power of Chemoselectivity: Powerful Conjugation Technologies for Next-Generation ADCs**

Christian P. R. Hackenberger, PhD, Professor and Department Head, Chemical Biology II, Leibniz-Research Institute for Molecular Pharmacology (FMP) and Humboldt University Berlin

We develop novel protein functionalization technologies for the generation of site-specific conjugates with high stability and defined activities. With Tub-tag labeling, we recently introduced a novel and versatile chemoenzymatic method for the C-terminal functionalization of biomolecules. It is based on the microtubule modifying enzyme tubulin tyrosine ligase (TTL) and facilitates one- or two-step functionalization procedures. Moreover, we have developed a new thiol-selective protein conjugation chemistry, that is characterized by strongly increased conjugate stability compared to previous approaches. Both methods are applied for the generation of defined ADCs with improved stability and potent cytotoxicity.

**09:35 Problem-Solving Breakout Discussions* **

*See website for details.

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

**11:15 New Payloads for Antibody-Drug Conjugates**

Thomas Pillow, PhD, Senior Scientist, Discovery Chemistry, Genentech, Inc.

This presentation will highlight the most recent work on ADCs at Genentech. It will cover our newest effort to deliver targeted protein degraders as a new modality for ADCs as well as new linkers developed to enable this platform.

**11:45 Preclinical Validation of Site-Specifically Conjugated ADCs with Potent Anthracycline Payloads in Solid and Hematologic Tumor Models**

Rémy Gébéieux, PhD, Scientist II, NBE-Therapeutics Ltd.

I will address next-generation ADC technology with an update on preclinical development of our program NBE002, targeting ROR1 in TNBC and lung adenocarcinoma. My talk will cover the validation of a novel ultra-potent anthracycline-toxin in ADCs, including validation of NBE’s lead ADCs in preclinical tumor models, and the characterization of the immuno-oncology function of NBE’s ADCs. The audience will gain insights into both a novel site-specific conjugation platform as well as a highly potent payload technology.

**12:15 Lead-Finding and Optimization of CLIPS Constrained Peptides using High- and Medium-throughput Peptide Libraries**

Michael Goldflam, PhD, Head, Peptide Discovery, Pepscan

CLIPS constrained peptides are a compound class that combines the specificity and high-affinity properties of antibodies with the advantageous features of small molecules, such as deep tissue penetration and low manufacturing costs. Pepscan developed a platform for the discovery and optimization of CLIPS peptides suitable as therapeutics, drug conjugates, diagnostics or affinity reagents.

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

**09:35 Problem-Solving Breakout Discussions* **

*See website for details.
15:20 Utility of PK-PD Modeling and Simulation (M&S) in the Discovery and Development of Next-Generation Immunoconjugates (ICs) for Cancer Therapy
Aman P. Singh, PhD, PK-PD Scientist/Biologics Development Leader, Janssen Biotech
We have experienced an expeditious emergence in the development of novel immunoconjugates (ICs) in cancer therapy, including the success of Antibody-Drug Conjugates (ADCs), with more than 60 molecules currently in clinical development, where the payload is designed to either inhibit the growth of replicating tumor cells (e.g., microtubule inhibitors) or intercalate with the DNA (e.g., DNA damaging agents). A more emerging subcategory of ICs includes radio-immunoconjugates (RICs), where DNA damaging alpha or beta ray emitting radionuclides are conjugated to antibodies.

15:50 Sponsored Presentation (Opportunity Available)

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

17:00 Functional Disulfide Re-Bridging Enables Native Full Antibody DAR 2, 4 & 8 Formation, Site-Selective Orthogonal Dual Modification and Homogeneous Fragment Drug Conjugates, as well as Bi- and Tri-Specific Scaffolds
Vijay Chudasama, PhD, Lecturer, Chemistry, University College London
Our latest data on next-generation maleimide (NGM) and pyridazinedione (PD) reagents for the site-selective modification of antibodies will be detailed (including robust serum stability, in vitro selectivity, in vivo efficacy with options for DAR 2, 4 & 8, dual drug conjugates and fragment drug conjugates). Also presented will be our latest work on using chemical linkers to form bi- and tri-specific scaffolds, as well as applications to nanoparticle modification.

17:30 Site-Specific Antibody Functionalization at the Antibody NBS
Nathan J. Alves, PhD, Assistant Professor, Emergency Medicine and Biomedical Engineering, Indiana University School of Medicine
Antibody modification is often necessary to endow antibodies with non-native capabilities from antibody-drug conjugates (ADCs) for targeted therapeutics to fluorescent reporter molecules for use as diagnostic or tracking tools. This session will explore site-specific antibody modification through conjugation to the conserved antibody nucleotide binding site (NBS) and will demonstrate how various linkers and conjugation strategies can be utilized to leverage the UV-NBS technology for use in next-gen antibody pharmaceuticals.

18:00 Generation of Potent Anti-HER1/2 Immunotoxins by Protein Ligation Using Split Inteins
Harald Kolmar, PhD, Professor and Head, Applied Biochemistry, Technical University of Darmstadt
We developed a route for the generation of immunotoxins based on full length antibodies using self-splicing split inteins and were able to generate a set of specific and highly potent conjugates. Our robust and generic method for generation of immunotoxins relies on protein conjugation via split intein ligation. This strategy overcomes notorious problems with immunotoxin production and the resulting conjugates with intrinsic bivalency and longer in vivo half-life display promising properties for further clinical development.

18:30 End of Next-Generation Antibody-Drug Conjugates
10th Annual
Advancing Bispecifics and Combination Therapy to the Clinic
New Approaches with Exciting Results

WEDNESDAY 14 NOVEMBER

07:45 Registration and Morning Coffee

ENGAGEMENT OF NK CELLS / CHECKPOINT INHIBITORS IN COMBINATION

08:30 Chairperson's Remarks
Marina Bacac, PhD, Head, Cancer Immunotherapy, Roche Innovation Center Zurich

08:35 Multi-Specific Antibody Technology Engaging NK Cells in Oncology
Laurent Gauthier, PhD, Senior Director, Research and Development, Innate Pharma

We report the design and generation of new multi-specific antibodies which selectively recruit NK cells against tumour targets (NKCE). NKCEs bind to NKp46 on NK cells and can potentially co-engage other activating receptors like CD16 to induce tumor target killing. NKCEs show good developability profile, anti-tumour activity in vitro and in vivo preclinical models and provide new therapeutic options for cancer treatment.

09:05 ATOR-1015, a Next-Generation, Bispecific CTLA-4 x OX40 Targeting Antibody for Tumor Directed Immunomunotherapy of Cancer
Christina Furebring, PhD, Senior Vice President, Research, Alligator Bioscience AB

ATOR-1015 is a next-generation CTLA-4 x OX40 bispecific immune activating antibody developed for tumor-directed immunotherapy. ATOR-1015 binds both targets simultaneously, promoting cell-cell interactions expected to enhance the immuno-stimulating effect of the compound. The mode of action of ATOR-1015 is a combination of regulatory T-cell (Treg) depletion and effector T-cell activation. ATOR-1015 is currently in preclinical development and clinical trials will start in the second half of 2018.

09:35 Development of an Agonist Redirected Checkpoint, SIRPa-FcCD40L, for Cancer Immunotherapy
George Fromm, PhD, VP, R&D, Shattuck Labs

We will present the generation of a novel, two-sided human fusion protein incorporating the extra cellular domains of SIRPs and CD40L. SL-172154 binds both CD47 and CD40 with high affinity, activates CD40 signaling in the absence of Fc receptor cross-linking, outperforms CD47 and CD40 antibodies in multiple tumor models and was safe in non-human primates. SL-172154 will enter the clinic in 2019 in multiple indications.

10:05 Development and Application of MOA-Based Reporter Bioassays for Immunotherapy Drug Development
Mei Cong, Director, Custom Assay Services, Promega Corporation

Having a functional bioassay that is MOA-based, accurate, precise, robust and reproducible is critical for the development of antibody-based biologics. We have developed reporter bioassays that meet these criteria for a broad range of antibody modalities including Fc effector function, immune checkpoint modulation, bispecific antibody engagement, cytokine modulation, and others. Here we will present the latest technology advancements and demonstrate how these bioassays can be used for a broad range of applications.

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

COMBINATION THERAPIES / T-CELL ENGAGEMENT

11:15 KEYNOTE PRESENTATION: Development of Effective Combination Therapies for Immuno-Oncology
Rakesh Dixit, PhD, Vice President, Safety Assessment, Medimmune, Inc.

This presentation will cover: the rationale for combination therapies in immunotherapy; the challenges of selecting the combination drugs that would give synergism; translational and precision medicine approaches in combination immune-oncology, and safety considerations in development of the combination drugs.

11:45 Development of Novel Fully Human Bispecific Antibodies for Oncology
Eric Smith, PhD, Director, Bispecific Antibodies, Regeneron, Inc.

This presentation will describe Regeneron's bispecific platform and present preclinical data on T-cell redirecting bispecifics being developed for solid and liquid tumor indications. In addition, a brief update on the status of REGN1979, Regeneron's CD20xCD3 bispecific in Phase I clinical trials, will be presented.

12:15 CD20 TCB (RG6026), a Novel “2:1” T-Cell Bispecific Antibody for the Treatment of B-Cell Malignancies
Marina Bacac, PhD, Head, Cancer Immunotherapy, Roche Innovation Center Zurich

We give an overview of preclinical data of CD20-TCB, a novel CD20-targeting T-cell bispecific antibody on the “2:1” IgG format that consistently demonstrated superior potency compared to other CD20-TCBs with conventional “1:1” IgG format. In addition, we present a novel approach enabling safer administration of such potent drug consisting of a single administration of obinutuzumab (Gazyva pre-treatment, Gpt) prior to the first infusion of CD20-TCB.

12:45 Affimer Therapeutics: A Novel Human Scaffold for the Generation of Bi-Specific Molecules
Amrik Basran, PhD, CSO, Avacta

Affimer therapeutics are based on the human protein Stefin A, a small (12kDa) intracellular protease inhibitor. We have built large (1x10^10) phage display libraries and generated highly selective Affimer binders to range of targets including those that are difficult to bind with antibodies or small molecules.
therapeutically relevant targets such as PD-L1 and LAG-3. We have shown that the Affimer scaffold can be formatted as in-line fusions, to the Fc domain or a full antibody to create bispecific molecules are able to engage both target antigens.  

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

14:15 **Session Break**

**COMBINATION THERAPIES / T-CELL ENGAGEMENT**

14:30 Chairperson's Remarks  
*Eric Smith, PhD, Director, Bispecific Antibodies, Regeneron*

14:35 **Targeting B-Cell Malignancies with a CD3 Bispecific Antibody - Preclinical Evaluation of DuoBody-CD3xCD20**  
*Ida Hiemstra, PhD, Lead Scientist, Translational Research, Genmab B.V.*

An overview will be presented of preclinical data identifying DuoBody-CD3xCD20 as the most potent B-cell-targeting CD3 bispecific antibody in an in vitro functional screen covering a comprehensive panel of B cell targets. DuoBody-CD3xCD20 induced potent T cell activation and cytotoxic activity in the presence of malignant B-cells in vitro and in vivo. The capacity of DuoBody-CD3xCD20 to deplete B cells from blood and lymphoid organs, after intravenous or subcutaneous administration, was assessed in cynomolgus monkeys as part of the non-clinical safety studies. A clinical study evaluating the DuoBody-CD3xCD20 is currently enrolling.

15:05 **APVO436: A CD3 Engager with Low Cytokine Release Profile Targeting CD123 for AML**  
*Catherine J. McMahan, PhD, Senior Director, Pharmacology and Cell Sciences Research and Non-Clinical Development, Aptevo Therapeutics*

APVO436 is a CD123 x CD3 bispecific ADAPTIR antibody designed to treat AML. It contains an Fc region for extended half-life and has bivalent binding to both the tumor target and CD3. APVO436 was optimized for manufacturability, specificity and low levels of cytokine release compared to other bispecific formats. APVO436 induces robust proliferation of T-cells and target tumor lysis in vitro and in vivo xenograft models.

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

**IMMUNOSTIMULATORY CYTOKINES FOR TUMOUR TARGETING AND CONTROL OF TOXICITY**

16:15 **Engineering Bispecific Cytokine-Fc Fusions to Create Safer and More Effective Immuno-Oncology Therapies**  
*David Szymkowski, PhD, Vice President, Cell Biology, Xencor*

Immunostimulatory cytokines such as IL-2 and IL-15, while extremely potent, suffer from poor tolerability and rapid clearance, limiting their potential as cancer treatments. Using our clinically-validated bispecific Fc domain, we generated a heterodimeric IL15/IL15Ra-Fc with reduced potency and longer half-life. IL15/IL15Ra-Fc demonstrates improved exposure and stimulates multiple effector-cell responses in mice and monkeys. Such cytokine-Fc biologics may possess better tolerability and improved efficacy with less-frequent dosing than recombinant cytokines.

16:45 Immunostimulatory Properties of a Novel IL-15-Based Tumor-Targeted Immunocytokine  
*Anika Jäkel, PhD, Director, Preclinical Pharmacology & Cancer Immunology, Glycotope GmbH*

Interleukin-15 (IL-15), a potent stimulator of NK and CD8 T-cells, is considered to be one of the most encouraging immunotherapeutics for cancer treatment. We created novel IL-15-based immunocytokines with different potencies and Fc effector functions binding to a tumor-specific carbohydrate antigen to potentiate tumor targeting. By applying a comprehensive screening approach considering PK, PD and cytokine profile, we seek to identify a promising lead candidate suitable for mono or combinatorial therapy of solid tumors.

17:15 Development of Novel Interleukin-2 Variants for Immunotherapy of Cancer and Autoimmune Diseases  
*Ekkehard Moessner, PhD, Head, Protein Engineering, Large Molecules Research, Roche Innovation Center Zurich*

The development of interleukin-2 muteins throughout the preclinical development will be described, for two different approaches. In one approach the IL-2 will be used for cancer immunotherapy, and in the other, the IL-2 is engineered for applications in autoimmune diseases.

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

18:45 Problem-Solving Breakout Discussions*  
*See website for details.

19:45 End of Day

**THURSDAY 15 NOVEMBER**

**BISPECIFICS IN THE CLINIC**

08:30 Chairperson's Remarks  
*David Szymkowski, PhD, Vice President, Cell Biology, Xencor*

08:35 Update on BiTE® Antibody Constructs Currently in Clinical Development  
*Virginie Nägele, PhD, Senior Scientist, BiTE Technology, Amgen Research (Munich) GmbH*

The BiTE® technology is a clinically explored approach targeting malignant cells by T-cells with blinatumomab being the first bispecific T-cell engager (BiTE) approved for the treatment of patients with relapsed or refractory B-precursor acute lymphoblastic leukemia (B-ALL) in the US. More recently, blinatumomab has also received accelerated approval for the treatment of B-ALL minimal residual disease. This presentation will give an update on the current clinical development of BiTE antibody constructs at Amgen focusing on hematologic malignancies like acute myeloid leukemia and multiple myeloma, and on solid tumor indications.

09:05 DVD-Ig Platform: Clinical Lessons and Future Directions  
*Tariq Ghayur, PhD, Distinguished Research Fellow, Foundational Immunology, AbbVie Bioresearch Center*

Several DVD-Ig molecules have been tested in preclinical models and in clinic for mono or combinatorial therapy of solid tumors.
autoimmune and oncology indications. Emerging data suggests that the DVD-Ig format per se is not immunogenic. However, target biology may play an important role in anti-drug antibody response (ADA, immunogenicity). Lessons learned from these studies may be broadly applicable and will be discussed.

09:35 Development of a Potent Anti-Cancer Bispecific Antibody Targeting VEGF and DLL4
Weon-Kyoo You, PhD, Head, R&D, Vice President, ABL Bio, Inc.
Simultaneous blockade of VEGF/VEGFR and DLL4/Notch signaling pathways is known to lead potent inhibition of tumor progression. In this presentation, we will talk about ABL Bio’s bispecific antibody platforms and development processes of the most advanced asset, a bispecific antibody targeting VEGF and DLL4 (ABL001) which is currently ongoing a Phase I clinical study. We will cover an overview of preclinical data as well as interim clinical data of ABL001.

10:05 SMAB: a Novel Bispecific Antibody Platform for Therapeutic Development
Janice Jin, Head, Project Management Center, Project Management Department, GenScript
Urgent demands for new therapeutic strategies, such as novel modalities are raised during explosive growth of therapeutic antibody drugs. In this presentation, we will introduce GenScript proprietary SMAB bispecific antibody platform which minimizes the immunogenicity and manufacture concerns of current bispecific antibody platforms while enabling bi-valent and multi-valent therapeutics.

10:20 Sponsored Presentation (Opportunity Available)
10:35 Coffee Break in the Exhibit Hall with Poster Viewing

DESIGN TO PROOF-OF-CONCEPT
11:15 Case Study on New Product: Biology and Proof-of-Concept
Mihriban Tuna, PhD, Vice President, Drug Discovery, F-star

11:45 Tumor-Localized T-Cell Co-Stimulation Using Antibody-Anticalin Fusion Proteins: From Flexible Design to Proof-of-Concept and Beyond
Marina Pavlidou, PhD, Project Leader, Discovery, Pieris Pharmaceuticals GmbH
We describe the generation of bispecific molecules by fusing T-cell targeting Anticalin proteins to tumor targeting antibodies. We show superior potency of the bispecific over the combination of building blocks and the combination of benchmark molecules. The activity of the bispecific is dependent on the expression of the tumor target showing the potential of providing a tumor localized activation of the immune system with high efficacy and reduced peripheral toxicity.

12:15 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own
NEW APPROACHES TO SOLID TUMORS

14:05 TGFβ Drives Immune Evasion in Genetically Reconstituted Colon Cancer Metastasis

Daniele Tauriello, PhD, Institute for Research in Biomedicine (IRB Barcelona), The Barcelona Institute of Science and Technology

We crossed mice bearing conditional alleles of four main colorectal cancer mutations in intestinal stem cells. From the resulting tumours, we derived organoids to transplant in syngeneic, immunocompetent mice. Cancers display key hallmarks of human microsatellite-stable colorectal cancers. Inhibition of TGFβ unleashed a potent cytotoxic T-cell response against tumour cells, preventing metastatic initiation in mice with progressive liver metastatic disease, blockade of TGFβ signalling rendered tumours susceptible to anti-PD-1/PD-L1 therapy.

14:35 Developing an ROR1 Bispecific T-Cell Engager for Treatment of Solid Tumors

Amit C. Nathwani, PhD, Professor, Haematology, University College London Cancer Institute

We have developed a humanized Bi-Specific T-Cell Engager (BITE) targeting Receptor Tyrosine Kinase Like Orphan Receptor 1 (ROR1), a cell surface antigen present on a broad range of malignancies, many with significant unmet therapeutic needs. In preclinical studies, the ROR1 BITE-mediated T cell and tumour antigen-specific cytotoxicity of a range of histologically distinct, ROR1 expressing solid tumour cell lines at exceedingly low concentrations (0.1ng/mL) and low effector to target ratios. In vivo studies showed that the ROR1-BITE prevented engraftment of tumour in xenograft murine models and significantly reduced the size of established subcutaneous tumours. To validate its wider therapeutic potential, we next demonstrated significant cytotoxicity against ovarian cancer in an in vitro and in vivo setting and T cell mediated killing. Final preclinical data to support a clinical trial will be presented together the obstacles encountered in the generation of clinical grade ROR1-BITE, a promising immunotherapy approach.

15:05 Developing an Integrated Summary of Immunogenicity (ISI) to Effectively Manage Regulatory Risks in Product Development

Josefin Beate Holz, PhD, NDA Associate Clinical Consultant, NDA Group AB

Therapeutic proteins have the potential to induce immunogenicity in humans. Such findings in clinical development would be regarded as an unfavourable effect if they are associated with a negative impact on the benefit-risk conclusion. The determination of the immunogenicity potential and its impact is an essential element of the development of a protein therapeutic. The Integrated Summary of Immunogenicity is a highly effective approach that provides regulatory reviewers with all data on immunogenicity for assessment.

15:35 Networking Refreshment Break

NEW APPROACHES TO COMBINATION THERAPY

16:00 Empirical Determination of Optimal Combination Therapies Targeting Immunological Pathways

Michael Schmidt, PhD, Vice President of Antibody Discovery & Engineering, Compass Therapeutics

At Compass, we combine high-throughput antibody discovery with proprietary platforms for multi-specific generation and screening to empirically determine optimal combinations for drugging immunological pathways. Here, we apply this approach to generate novel combination therapies targeting members of the TNFR superfamily, Nectin/Nectin-1 checkpoint pathways, and NK cell activation.

16:30 Novel mAb-Fc Receptor Mechanism of Action

Jeremy Waight, PhD, Principal Scientist, Immunomodulatory Drug Discovery, Agensia Inc.

17:00 End of Day

17:00 Dinner Short Course Registration*

17:30 – 20:30 Dinner Short Courses

Recommended Short Course*

SC8: Selection, Screening and Engineering for Affinity Reagents

*Separate registration required. Click here for details.
FRIDAY 16 NOVEMBER

08:00  Registration and Morning Coffee

IMMUNOCYTOKINES: CLINICAL APPLICATIONS, SUCCESSES TO DATE AND HURDLES TO BE OVERCOME

08:30  Chairperson's Remarks
Soldano Ferrone, MD, PhD, Division of Surgical Oncology, Surgery, Massachusetts General Hospital, Harvard Medical School

08:35  Clinical Approaches for Immunocytokine Therapy Based on Antibody and Cytokine Modifications
Stephen D. Gillies, PhD, Founder & President & CEO, Provenance Biopharmaceuticals Corp.

Immunocytokines target cytokines with anti-tumor activity to the tumor microenvironment. The earliest immunocytokines to be studied in the clinic were based on human IgG1 with full effector functions that, in some cases, led to dose-dependent toxicities. Later generation immunocytokines had various modifications in structure that eliminated effector functions, modified the bioactivity of the cytokine, or were dosed subcutaneously or intra-tumorally. The pros and cons of these approaches will be discussed.

09:05  Cancer-Targeted IL-12 Controls Human Rhabdomyosarcoma by Senescence Induction and Myogenic Differentiation
Karin Schilbach, PhD, Hematology/Oncology, University Children’s Hospital, Tübingen

Interleukin 12 is the major Th1-polarizing cytokine for innate and adaptive immunity. The antibody-IL-12 fusion protein NHS-IL12 binds histones of necrotic cells. NHS-IL12 therapy of human sarcoma in humanized mice combined with either IL-7 (FcIL-7) or IL-2 (IL-2MAB602) induced massive tumor infiltration and innate and adaptive antitumor immunity, permanently arrested cancer cell proliferation and initiated myogenic differentiation in rhabdomyosarcoma cells. NHS-IL12 significantly improved survival and induced long-term remissions when combined with IL-2.

09:35  Unexpected Effects of Directed Therapy on Immune Recognition of Cancer Cells
Mar Valés-Gómez, PhD, Spanish National Research Council, CSIC; Spanish National Center for Biotechnology

Directed therapies can affect the recognition of tumour cells by Natural Killer cells due to the modulation of NKG2D ligands. These proteins are present in cancer patient sera both as soluble molecules and recruited to extracellular vesicles. NKG2D ligands can be used as markers of tumour progression and we propose that it is important to consider them as a factor contributing to tumour immune response and evasion.

10:35  Affinity Modulation of Various Antibodies Using Universal Allosteric Switch Modules
Stefan Diedel, PhD, Professor & Head, iTUBS Innovationsgesellschaft Technical University Braunschweig

Insertion of mutated variants of calmodulin to substitute the linker of scFv fragments allowed to modulate antigen binding affinity of five different antibodies. Regulation was achieved without the need of ion concentration or pH changes, and worked both for VH-VL and VL-VH architecture. We expect that this switch linker design provides a universal allosteric regulation principle which can easily be applied to many different scFv antibodies.

11:05  Recombinant Human B Cell Repertoires Enable Screening for Rare, Specific, and Natively Paired Antibodies
Saravanan Rajan, PhD, Scientist II, Antibody Discovery & Protein Engineering, MedImmune

The human antibody repertoire is increasingly being recognized as a valuable source of therapeutic grade antibodies. However, methods for mining primary antibody-expressing B cells are limited in their ability to rapidly isolate rare and antigen-specific binders. Here we show the encapsulation of two million primary B cells into picoliter-sized droplets, where their cognate V genes are fused in frame to form a library of scFv cassettes. We used this approach to construct natively-paired phage-display libraries from healthy donors and drove selection towards cross-reactive antibodies targeting influenza hemagglutinin. Within four weeks we progressed from B cell isolation to a panel of unique monoclonal antibodies, including seven that displayed broad reactivity to different clinically-relevant influenza hemagglutinin subtypes. Most isolated antibody sequences were not detected by next-generation sequencing of the paired repertoire, illustrating how this method can isolate extremely rare leads not likely found by existing technologies.

11:35  Sponsored Presentation (Opportunity Available)

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

NEW TARGETS AND STRATEGIES IN IMMUNOTHERAPY

13:00  Chairperson’s Remarks
Mitchell Ho, PhD, Chief, Antibody Therapy Section, Laboratory of Molecular Biology, National Cancer Institute, NIH

We sequenced over a quarter million natively-paired, immunoglobulin (IgG) heavy and light chains from the activated B cells of patients having effective anti-cancer responses and used both sequence and repertoire feature analyses to select specific IgG’s for recombinant expression and characterization. Remarkably, antibodies from patients across several cancer types bound to non-autologous human-derived tumor tissues at a high rate, consistent with recognition of public tumor antigens. Some antibodies caused regression of, and durable immunity toward, established tumors in mouse cancer models, with activity greater than that of an anti-PD-1 inhibitor, and these have provided leads for early development. This reverse translation approach, starting from effective anti-tumor responses in patients, establishes a discovery strategy for novel cancer therapies and targets.
13:35 Targeting the Intracellular Proteome: Antibodies with T-Cell Receptor-Like Specificity towards the MHC-Peptide Complex

Yoram Reiter, PhD, Professor and Head of the Laboratory of Molecular Immunology, Faculty of Biology, Technion-Israel Institute of Technology

We have generated unique recombinant antibodies that mimic the fine specificity of the T-cell receptor and recognize tumor and viral specific class I peptide-MHC complexes, as well as class II complexes associated with autoimmunity and inflammation. The molecular feature of these molecules/approaches and their in vitro and in vivo activities will be described. The future development of these approaches as new modalities to immunotherapy, bridging antibody and T lymphocyte attack on cancer cells, will be discussed in the context of their development path to clinical trials humans. The use of these novel molecules to study basic questions of tolerance will be described as well, demonstrating the bridge between basic and translational immunological research.

14:05 Targeting p53 in Cancer Using T-Cell Receptor Mimic Antibodies

Demin Li, MBBS, MSc, PhD, University Research Lecturer, Senior Research Fellow, Nuffield Division of Clinical Laboratory Sciences, Radcliffe Department of Medicine, University of Oxford

Dysregulated tumour suppressor p53 presents in over half of all malignancies and is an attractive target for immunotherapy. We developed an antibody that recognises a p53-derived peptide presented by human major histocompatibility complex HLA-A*0201. The antibody recognises a wide range of cancers, induces cancer cell death in vitro and delays tumour growth in vivo without any detectable toxicity. Antibodies of such may represent promising new agents for future cancer immunotherapy.

14:35 CAR-Expressing NK-Cell-Based Immunotherapy for Cancer Retargeting

Prof. Dr. Ulrike Köhl, Head of Fraunhofer Institute of Cellular Therapeutics and Immunology (IZI); Director, Institute of Clinical Immunology, University and University Hospital of Leipzig; and Director, Institute of Cellular Therapeutics, GMP Development Unit and Cellular Therapy Centre, Hannover Medical School (MHH)

Based on both our previous clinical phase I/II trials with allogeneic NK cells and our experience in manufacturing of CAR expressing T cells, we are working on CAR expressing NK cells for cancer retargeting as an “off the shelf product”. Results on next generation CAR NK cells to improve cytotoxicity against leukemia and tumors with the possibility to lower side effects will be presented.

15:05 A Novel Multi-Specific Antibody Targeting PD-L1-Overexpressing Cancers that Stimulates Antigen-Committed CD8+ T Cells through Concomitant Engagement of a T Cell Costimulatory Receptor

Stefan Warmuth, PhD, Director CMC, Numab Innovation AG

To maximize potency and improve the safety of ICM combination approaches, we designed a multi-specific molecule bearing two ICM domains that depletes PD-L1-overexpressing cancer cells via selective recruitment and stimulation of tumor-reactive effector T cells in the tumor microenvironment. The multi-specific antibody format potently blocks PD-L1/PD-1 signaling and elicits further T cell activation through its costimulatory domain solely in the presence of cells that overexpress PD-L1.

15:35 End of Summit
Optimisation & Developability

Moving the Right Molecules Forward

Recommended Short Course*
SC4: Mutation and Selection Strategies beyond Affinity Optimisation
Separate registration required. Click here for details.

MONDAY 12 NOVEMBER

12:00 Conference Registration

MOLECULAR INSIGHTS DURING DEVELOPABILITY SCREENING

13:30 Organizer's Welcome
Mimi Langley, Senior Conference Director, Cambridge Healthtech Institute

13:35 Chairperson's Opening Remarks
Lars Linden, PhD, Head, Protein Biochemistry, Biologics-Research, Cell and Protein Science, Bayer AG

13:45 New Insights into the Mechanics of Antibody Pharmacokinetics
Hubert Kettenberger, PhD, Senior Principal Scientist, Large Molecule Research, Roche Innovation Center Munich
Therapeutic antibodies with nearly identical Fc domains may show >10-fold differences in clearance. We systematically identified properties of the Fv domain that can cause atypical pharmacokinetic behavior. Using protein engineering, we created Fab mutants with defined biophysical properties and tested them in biochemical PK prediction assays and in vivo clearance. Our results may pave the way for predicting and improving in vivo PK based on biophysical properties and biochemical assay data.

14:15 Unspecific Binding and Self Interaction during Developability
Benjamin Hackner, PhD, Scientist, Physico Chemical Analytics, Protein Sciences & CMC, MorphoSys AG
Self-interaction and unspecific binding are important parameters to assess during developability of mAbs. We will demonstrate with a case study how self-interaction can be linked to high concentration liquid formulations and unspecific binding.

14:45 Multi-Parameter Ultra-High-Throughput Antibody Developability Screening by Mammalian Display
Mike Dyson, PhD, CTO and Co-Founder, IONTAS Ltd.
Using directed integration of antibody genes by CRISPR/Cas9 or TALE nucleases, we have constructed large libraries of monoclonal stable cell lines. IgG-formatted antibodies are displayed on the cell surface permitting selection from the library of clones encoding desirable affinity, specificity, species cross-reactivity and “developability” properties. Two case studies will be presented where antibodies with well documented poor biophysical characteristics were modelled to identify surface hydrophobic and positive charge patches, and mammalian display used to select for antibodies with a superior developability profile.

15:15 Prediction of Protein-Protein Binding Sites and Epitope Mapping
Nels Thorsteinson, Scientific Services Manager, Biologics, Chemical Computing Group
We present a method for identifying important interaction sites in protein interfaces and carrying out epitope mapping using MOE software. A case study is presented in which hydrogen-deuterium exchange data are used to extract key interactions from calculations performed on an ensemble of interacting chain models.

15:30 Sponsored Presentation (Opportunity Available)

15:45 Networking Refreshment Break

PLENARY KEYNOTE SESSION

16:15 Moderator's Opening Remarks
Janine Schuurman, PhD, Corporate Vice President, Research & Innovation, Genmab BV

16:20 Bicycles and Bicycle Drug Conjugates
Sir Gregory Winter, PhD, FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics
Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles’ unique properties have been used to develop Bicycle Drug Conjugates® (BDCs); a novel toxin delivery platform which greatly improves toxin loading into tumour tissues. A BDC is expected to enter clinical trial in Q1 2018.

17:20 Paracrine Delivery: Therapeutic Biomolecules Produced in Situ
Andreas G. Plückthun, PhD, Professor and Director, Department of Biochemistry, University of Zürich
Cancer will have to be fought with cocktails of therapeutics acting locally, which may have to include therapeutic antibodies against receptors, checkpoint inhibitors, as well as cytokines to modify the tumor microenvironment. We have recently developed a technology of using non-replicative adenovirus carrying no viral genes, engineered to target desired cells and also to be shielded from the immune response, as a vehicle for simultaneous delivery of multiple genes of therapeutic proteins, produced and secreted by the infected cells.

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

19:30 End of Day
11:45 Purification Technologies to Tackle Complex Therapeutic Proteins during Lead Selection
Philipp Amsler, MSc, Functional Lead, Integrated Biologics Profiling, Novartis Institutes for BioMedical Research

Lead selection of therapeutic proteins requires careful characterization of a variety of molecule properties to reduce the risk for encountering unexpected obstacles during technical development. The developability assessment concept applied at Novartis combines information about expression, aggregation propensity, process fit, stability, physicochemical properties, and other parameters of potential candidates. The presentation will provide an overview of the concept and focus on examples for different purification approaches enabling the production and characterization of complex protein formats.

12:15 Avidity Kills Cancer – The Biophysical Analysis of Bispecific Antibodies with the SwitchSENSE® Biosensor
Ulrich Rant, PhD, CEO, Dynamic Biosensors GmbH

09:05 Efficient Identification of mAb Therapeutics with Optimal Developability
Fang Yi, PhD, Principal Scientist, Biologics Discovery Sciences, Janssen Biotechapeutics, Johnson & Johnson

We share our strategies of implementing a matrix of high throughput orthogonal biophysical screening assays during early mAb discovery to identify candidates with not only the high-potency and specificity towards their biological targets, but also desired “developability”, e.g. feasibility of the manufacturability, good solubility and stability, and absence of off-target binding. Such strategies help minimize the downstream optimization efforts, leading to efficient lead selection with optimal functional and biophysical properties.

09:35 KEYNOTE PRESENTATION: Developability Strategies to Support Fast to FTIH Studies
Mike Molloy, MSc, Director, Analytical and Characterisation, Biopharm Process Research, GlaxoSmithKline

Two key deliverables for a successful path to First time in Human (FTIH) studies are the selection of a quality molecule and a stable cell line. This presentation will give an insight into how a combination of biophysical characterisation and accelerated stress delivers a much better understanding of product attributes during the discovery phase of drug development. This workflow is used for screening novel lead panel molecules with respect to their developability, ensuring that the right molecule is progressed to cell line development.

13:15 Luncheon Presentation I to be Announced

13:15 Avidity Kills Cancer – The Biophysical Analysis of Bispecific Antibodies with the SwitchSENSE® Biosensor
Ulrich Rant, PhD, CEO, Dynamic Biosensors GmbH

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

RATIONAL APPROACHES TO IMPROVE BIOLOGICS DESIGN, DEVELOPABILITY AND FORMULATION

14:15 Chairperson’s Remarks
Mike Molloy, MSc, Director, Analytical and Characterisation, Biopharm Process Research, GlaxoSmithKline

14:20 Optimising Developability – Learning from Experimental Data
Lars Linden, PhD, Head, Protein Biochemistry, Biologics-Research, Cell and Protein Science, Bayer AG

This presentation will discuss how to address developability early on in lead discovery and later in lead optimization phase. We will feed in experimental data and machine learning concepts, and bring in examples showcasing predictivity of higher throughput in vitro methods.

14:50 Rational Structure Guided Approaches to Biologics Design & Optimization
Surjit Dixit, PhD, Vice President, Technology, Zymeworks, Inc.

Our growing understanding of disease biology and the need for personalized medicine is driving the design and development of fit for purpose, multispecific, multifunctional therapeutics. Protein engineering of biologics provides the opportunity to create such tailored therapeutic candidates and test their functional relevance. The presentation will highlight opportunities for rational engineering in the early stages of therapeutic design and its impact on developability of the drug candidates.

15:20 The CAMSOL Method of Rational Design of Protein Solubility
Michele Vendruscolo, PhD, Professor, Chemistry, University of Cambridge

CamSol is an in silico method developed for the rational design of mAbs developability. This method can provide accurate evaluations of key parameters of...
mAbs by replacing *in vitro* screening assays that are more demanding in both time and resources. CamSol thus enables the prediction of late-stage failures in early discovery phases.

15:50 **High Affinity Guinea Pig mAbs Development: Application to Small Molecules Detection with a Multiplex Label-Free Platform**

Yannick NIZET, CSO, Monoclonal Antibody Manufacturing Center, Synabs

16:00 **Using Molecular Modelling Tools to Optimize Ligand Presentation in Target Secretion Inhibitors (TSI)**

Teresa Silva Barata, PhD, Senior Scientist, Product Design and Characterization, Neurology R&D, Ipsen Bioinnovation

Botulinum neurotoxins provide effective treatment for a wide range of neuromuscular and autonomic conditions, although their inherent toxicity limits use. Recombinant strategies allow development of next-generation BoNTs with new binding domains that provide novel and differentiated cell targeting and specificity characteristics and potentially lower toxicity. Here, molecular modelling tools are utilized to evaluate different engineering strategies for the presentation of a ligand targeting nociceptive neurons. Characterization of molecular interactions, together with molecular dynamics simulations, is leading to a rational and optimized approach for new TSI design and development.

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

17:00 **Rational Design of Monoclonal Antibodies with High Developability Potential**

Adriana-Michelle Wolf Pérez, MSc, PhD Student, Large Protein Biophysics, Novo Nordisk

We will present an *in silico* predictor assisted rational design method. This method can be applied for the rational design of developable antibodies, for the re-engineering of troublesome lead candidates, and for the early screening and ranking of variant libraries. Consequently, the method potentially increases the chances of a faster identification of lead candidates with high developability potential.

17:30 **End of Optimisation & Developability**
**5th Annual Analytical Characterisation of Biotherapeutics**

**Harnessing Technologies to Speed Innovation**

**WEDNESDAY 14 NOVEMBER**

07:45 **Registration and Morning Coffee**

**CHARACTERISING NEW AND COMPLEX MOLECULES**

08:30 **Chairperson’s Remarks**
Bernice Yeung, PhD, Global Head of Characterization, Analytical Development, Shire

08:35 **Developing, Qualifying and Validating Analytical Methods for Novel Biologics**
Declan Lowney, MSc, Associate Director, Analytical Development, Janssen R&D

The presentation will cover the analytical strategies deployed for the characterization of novel biologics and the analytical approaches taken for release, stability and characterisation.

09:05 **Multi Attribute Method and Native Intact Mass Spectrometry for Characterization of Quality Attributes during Pharmaceutical Development of mAb Mixtures**
Dan Bach Kristensen, PhD, Principal Scientist, Analytical Development, Symphogen A/S

Symphogen develops anti-cancer mAb mixtures, which are inherently complex and difficult to characterize using conventional technologies (e.g. methods relying exclusively on chromatographic resolution). To address product complexity and meet regulatory demands, Symphogen is looking increasingly to mass spectrometry for qualitative and quantitative control of critical quality attributes (CQAs). Case studies employing LC MS (Multiple-Attribute Method, MAM) and native mass spectrometry for characterization and control of CQAs during biopharmaceutical development will be presented.

09:35 **Identification and Quantitation of Duobody® Bispecific IgG1 Using Mass Spectrometry and Automated Data Processing and Analysis Workflow**
Ewald van den Bremer, PhD, Senior Scientist, Analytical Sciences, Genmab B.V.

The characterization of bispecific antibodies (BsAbs) by mass spectrometry (MS) offers several advantages over traditional chromatographic techniques (e.g. HIC, CEX). MS provides unambiguous identification and relevant quantitative information, and combined with automated data processing and analysis, it can be employed in a high-throughput environment. We present a software solution and the related workflows that enabled us to accelerate BsAb research batch characterization and release, achieving high quality results and significant time and cost savings.

10:05 **Reproducible LC/MS in Biopharma: A New Paradigm**
John Gebler, PhD, Director, Biopharma Business Development, Pharmaceutical Business, Waters Corporation

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

11:15 **KEYNOTE PRESENTATION: Integrating Analytical Strategies into a Comprehensive Development Strategy**
Thomas Spitznagel, PhD, Senior Vice President, Biopharmaceutical Development & Manufacturing, MacroGenics

Appropriately selected and developed analytics are critical to ensure process development and manufacturing are effectively implemented. Phase appropriate strategies and approaches to developing analytical release, characterization, and in-process methods will be presented that balance speed, risk, and thoroughness. A variety of case studies across different protein platforms will be used to illustrate examples that ensure the overall development strategy is supported by the appropriate set of analytical tools.

11:45 **Cutting-Edge Analytical and Structural Methods for the Characterization of Antibodies and Antibody-Drug Conjugates**
Elsa Wagner-Rousset, PhD, Senior Scientist, NBEs, Analytical Chemistry, Centre d’Immunologie Pierre Fabre

mAbs and ADCs are one of the fastest growing classes of oncology therapeutics. Their development and optimization rely on improving their analytical characterization by assessing critical quality attributes (CQAs) such as sequence liabilities, drug load distribution, drug to antibody ratio and residual small molecular drugs. Therefore, early-developability assessment requires state-of-the-art analytical methods, such as native and ion mobility mass spectrometry (MS), 2D liquid chromatography and capillary electrophoresis coupled to MS.

12:15 **Product and Process Characterisation of Novel High-Potency Neurotoxin Therapeutics**
David Spencer, MSc, Characterization Manager, Ipsen

Distinct molecular attributes can critically modulate the physicochemical and pharmacological properties of protein biotherapeutics. Due to their highly potent nature, and resultant low dose, toxin-based therapeutics present some unique analytical challenges. Case studies will be presented where insight into quality attributes and key degradation pathways has been gained using novel, highly sensitive analytical characterisation techniques. Application of this knowledge to determine toxin manufacturing critical process parameters will also be discussed.

12:45 **Array-Based SPR Imaging as a Powerful Tool at Multiple Stages in Candidate Selection Cascades**
Alex van der Kooi, Manager Interaction Laboratory, IBIS Technologies

An immunization campaign often results in hundreds to thousands of lead candidates. A number of tests is applied to narrow down the best possible candidate(s). In this presentation we demonstrate that the IBIS MX96, an array-based SPR imaging platform, can be used at multiple stages in such a screening cascade.
13:00 Recent Advances in the Use of Capillary Electrophoresis for Biopharmaceutical Analysis
Jim Thorn, Senior Manager, Marketing & Applications Separations, SCIEX
We will present a case study of the rapid and complete characterization of the NIST mAb. Then, we will present the identification of biopharmaceutical modifications by the connection of CE to MS, and we will preview the acceleration of cell line development and process control through high throughput glycan screening.

13:15 Luncheon Presentation I: A Quick Check of Protein Quality that will Improve Biotherapeutic Candidate Purification/Characterization Workflow
Peter Fung, Senior Manager, Product Marketing, Marketing, NanoTemper Technologies
Starting with material of questionable quality for protein purification and characterization leads to irreproducible or ambiguous results. Transitioning between upstream and downstream workflows can be challenging for bioprocessing researchers, especially when the quality of the sample material is not known. We offer a new platform that identifies sample quality and relative functionality in minutes complementing and guiding bioprocessing workflows-making go/no go decisions easy and quick-saving time, effort and producing more consistent results.

13:45 Luncheon Presentation II (Sponsorship Opportunity Available)

14:15 Session Break

14:30 Chairperson's Remarks
Mario Lebendiker, PhD, Head, Protein Purification Facility, Wolfson Centre for Applied Structural Biology, Hebrew University of Jerusalem

14:35 Structure-Function Characterization of Sulfated Glycans in Recombinant Idursulfase
Bernice Yeung, PhD, Global Head of Characterization, Analytical Development, Shire Recombinant Idursulfase is used in enzyme replacement therapy for treatment of Hunter Syndrome. Characterization of Idursulfase has been performed to understand its structure-function relationships. In this highly glycosylated protein, it has been recognized that phosphorylated glycans are critical for facilitating cellular uptake of Idursulfase, while sialylated glycans are needed for pharmacokinetic effects. The discovery of sulfated glycans in Idursulfase has led to unexpected understanding of the role of glycosylation on its function.

15:05 HOS in QC Environment - Could Native Peptide Mapping Support/Replace Bioassay for Stability Monitoring of Biopharmaceuticals?
Annick Gervais, PhD, Director, Physico-Chemical Method Development, Analytical Sciences Biologicals, UCB
Higher Order Structure is one of the critical quality attributes to be controlled for therapeutic proteins. Current HOS techniques are hardly amenable to QC. The potential of a novel peptide mapping method for routine monitoring of HOS will be presented. This presentation will show how promising this QC-friendly method is to understand the link between structure (HOS) and function (biological activity) and the degradation pathways under different stress conditions.

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

16:15 Characterization of Complex Glycosylation Patterns for Biopharmaceuticals
Urs Lohrig, PhD, Labhead AL1, Global Drug Development / Technical, Research & Development, Novartis
Glycosylation remains a major challenge when probing the molecular structure of biopharmaceuticals. Tools for the in-depth characterization of N- and O-glycosylations have been developed over the years and were employed on various levels within the industry. Here, we present approaches including hyphenated LC/MS on various levels to tackle the complexity of glycan modifications within biosimilar characterization workflows. This enables a suitable depth of knowledge for manufacturing process development as well as supporting final biosimilarity evaluation.

16:45 Characterization of Variants of a Clinical Antibody Candidate Using Alternative and Novel Separation Methods
David Eisen, PhD, Scientist, Technical R&D, Technical Development Biosimilars, Novartis
This talk focuses on the characterization of charged variants of an analytically challenging monoclonal antibody candidate. We enriched the charged protein variants for analytical testing using OFFGEL electrophoresis. By applying specific RP-UPLC-MS and wide-pore HILIC-UPLC-MS methods, we could characterize these variants on intact, subunit and peptide level with enhanced resolution. These analyses helped to elucidate the degradation mechanism and criticality of an aspartate isomerization site in the variable domain of the antibody.

17:15 Presentation to be Announced

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 15 NOVEMBER

08:00 Registration and Morning Coffee

08:30 Chairperson's Remarks
Dan Bach Kristensen, PhD, Principal Scientist, Analytical Development, Symphogen A/S

08:35 A New Application of Multi Angle Light Scattering Coupled to Ion Exchange Chromatography (IEX-MALS) for Protein Characterization
Mario Lebendiker, PhD, Head, Protein Purification Facility, Wolfson Centre for Applied Structural Biology, Hebrew University of Jerusalem
We present here a new analytical tool for protein characterization that combines the high resolution ion exchange (IEX) chromatography method with multi-angle light scattering (MALS). The limited resolution of SEC interferes in some cases with the accurate analysis that can be achieved by MALS. Here we show that combining MALs with the higher resolution separation technique IEX (IEX-MALS) allows a precise analysis of samples that cannot be resolved by SEC-MALS. We conclude that IEX-MALS is a valuable technique for proteins that have limited analysis achieved with SEC-MALS.
09:05 Multiple Attribute Monitoring – Optimization of Automated Sample Preparation
Anja Pfenninger, PhD, Lab Head, Mass Spectrometry, Bioanalytics/Biopharmaceutical Development, Sanofi
Automated sample preparation of tryptic digests using a liquid-handling roboter is key for successful multiple-attribute monitoring in medium-throughput mode (100-200 samples per week). The optimization procedure will be discussed with regards to different aspects such as digest quality, costs of goods, speed and reproducibility.

09:35 Energetic Epitope Mapping of an Antibody/Interleukin-23 Interaction
Lumelle A. Schneeweis, PhD, Protein Science, Molecular Discovery Technologies, Bristol-Myers Squibb
Identification of the energetic epitope of the hot-spot residues which dominate the binding affinity of an antibody supports mechanistic interpretation, antibody optimization, and intellectual property claims. Complementary mass spectrometry, computational analysis, mutagenesis, and binding analytics provide a clear picture of the discontinuous interfacial hot-spot epitope on interleukin-23 (IL-23) that dominates its binding affinity for an anti-IL-23 antibody.

10:05 Next Steps in Biophysical Characterization and Screening: RPC/IEX-MALS and HT-SLS
Daniel Some, PhD, Principal Scientist, Marketing, Wyatt Technology Corp
SEC-MALS and high-throughput DLS (HT-DLS) are widely implemented across biopharma to characterize molar mass, aggregation, oligomerization and fragmentation, and to screen candidates and formulations for aggregation and stability. Recent extensions of light scattering will be presented: a light-scattering plate reader that measures both dynamic and static light scattering, to determine size, molar mass, KD, A2, thermal stability and viscosity; and the use of multi-angle light scattering with reversed-phase and ion-exchange chromatography.

11:45 Establishing High Throughput, Low Protein Consuming Biophysical Platform for Biologics Characterization
Alexey Rak, PhD, Head, Bio Structure and Biophysics Department, Integrated Drug Discovery, Sanofi
The presentation will cover new biophysical applications for biologic characterization using 1) Second Harmonic Generation (SHG); 2) Nano Differential Scanning Fluorimetry (nano-DSF); and 3) Micro Scale Thermophoresis (MST). It will also discuss the kinetics for thermal stability and activation energy barrier determination for biologics stability assessment, as well as present long-term stability prediction by computational biophysical approaches.

10:35 Coffee Break in the Exhibit Hall with Poster Viewing
11:15 Highly Glycosylated Therapeutic Proteins Neorecormon® and Micera*: Novel Methods for Sample Generation, Structural and Functional Characterization
Alexander Buettner, PhD, Scientist, Analytical Development and Quality Control, Pharma Technical Development Europe, Roche Diagnostics GmbH
NeoRecormon® and Micera® are therapeutic proteins for the treatment of anaemia and contain highly complex glycans. Glycan variety in combination with presence of multiple glycosylation sites makes CQA assessment cumbersome. We have been developing and applying sample generation techniques as well as structural and functional analysis methods to examine structure function relationships in this complex situation. The talk will address selected topics from these fields and present results of structure function case studies.

Recommended Short Course*
SC6: Fast Modelling of Protein and Nucleic Acid Structure and Dynamics - A Hands-On Introduction to MacroMoleculeBuilder (MMB)
*Sponsorship Opportunity Available. Click here for details.
**THURSDAY 15 NOVEMBER**

**13:00** Registration

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

**MECHANISMS OF AND IMPLICATIONS FOR PARTICLE FORMATION**

**14:00** Chairperson's Opening Remarks

**Christian Schoneich, PhD, Professor, Pharmaceutical Chemistry, University of Kansas**

**14:05** Regulatory Considerations for Impurity Characterization and Control for Biological Products

**Audrey Jia, PhD, Principal Consultant, DataRevive LLC and exFDA Senior CMC Reviewer**

Impurity characterization and impact to the product quality is important for both novel biologic and biosimilar development. To what extent the impurity needs to be characterized and analyzed to satisfy the regulatory need will be discussed.

**14:35** Factors Influencing Biotherapeutic mAb Aggregation

**Linda Yi, PhD, Senior Scientist, Analytical Development, Biogen**

Aggregation has been identified as one of the major degradation pathways that may affect safety, quality and efficacy of therapeutic mAbs. Aggregate present in mAb products can be complex, varying by size, type and origin, with underlying mechanisms not always being well-understood. This presentation will provide an overview of the factors that may influence biotherapeutic mAb aggregation. A case study will follow on impact of a chemical modification catalyzed by metals on aggregation of mAbs.

**15:05** Get Peace of Mind with Quick and Reliable Protein Quality Checks

**Dina Finan, PhD, Marketing Manager, Analytics Marketing, Unchained Labs**

There are many good reasons to quickly assess the quality of protein samples prior to downstream analysis, such as comparing batches of purified material, changing formulation conditions, or checking the integrity of frozen samples after thawing. Physical or chemical stress, like agitation or oxidation, can also lead to protein aggregation. We will discuss methods for doing painless quality checks, enabling you to save time and ensure the homogeneity of your samples.

**15:35** Networking Refreshment Break

**16:30** Weak, Promiscuous IgG Self- and Hetero-Association: Implications for Aggregation and Viscosity

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

The interactions between seven fluorescently labelled tracer IgG mAbs differing in V and C regions were detected and characterized by analytical ultracentrifugation. All interactions were found to be attractive, variable in strength, affected by both the variable and constant regions, but indiscriminate with respect to IgG subclass. Furthermore, weak attractive interactions were observed for all the mAbs with freshly purified human poly-IgG. The universality of the weak interactions suggests that they may contribute to effector function cooperativity in the normal immune response, and could be important contributors to viscosity.

**17:00** End of Day

**FRIDAY 16 NOVEMBER**

**08:00** Registration and Morning Coffee

**AGGREGATE DETECTION, QUANTIFICATION AND CONTROL**

**08:30** Chairperson's Remarks

**Joël Richard, PhD, Head, Technical & Pharmaceutical Operations, MedinCell**

**08:35** Detecting and Separating Sub-Visible Protein Aggregates from Other Particulates

**Alain Pluen, PhD, FHEA, Lecturer, Director, BSc Pharma Science, Division of Pharmacy and Optometry, School of Health Sciences, University of Manchester**

**09:05** A New Alternative to Conventional Aggregate Quantitation and Sizing

**Oliver Bannach, PhD, CEO, Attyloid GmbH**

According to a recent FDA guideline, subvisible aggregates ranging from 0.1-1 µm are of special concern regarding immunogenicity of biologicals. The FDA further emphasizes the need for quantitative methods covering this size range. sFIDA fills this gap by quantitating aggregates from 10 nm to 50 µm. sFIDA is a
novel platform technology for quantitation and sizing of protein aggregates. The technology combines the selectivity of immunological assays with the sensitivity of high-resolution fluorescence microscopy.

09:35 Scale-Down Models for Freezing/Thawing Process to Control Aggregation
Karoline Bechhold-Peters, PhD, Senior Strategy and Technology Leader, Biologics Technical Development & Manufacturing, Novartis Pharma AG

10:05 Networking Coffee Break

10:35 Development Strategy of Fibril-Prone Peptide Therapeutics: Aggregation Kinetics, Predictive Methods, and Detection Methods
Jingtao Zhang, PhD, Principal Scientist, Pharmaceutical Sciences, MSD

Peptide aggregation such as fibrillation presents significant challenges for DS and DP development of peptide therapeutics. Different development criteria and control strategy is required for fibril development in contrast to protein aggregation. Approaches to close gaps in these areas will be shared in the presentation, which includes the investigation on the aggregation kinetics of a fibril-prone peptide, the projection of physical stability shelf-life, and the development of highly sensitive characterization methods for fibrils.

11:05 Capreomycin Inhibits the Initiation of Amyloid Fibrillation and Suppresses Amyloid Induced Cell Toxicity
Rizwan Khan, PhD, Professor, Interdisciplinary Biotechnology Unit, Aligarh Muslim University

Protein aggregation and amyloid fibrillation are responsible for several serious pathological conditions (like type II diabetes, Alzheimer’s and Parkinson’s diseases, etc.) and protein drugs ineffectiveness. Therefore, a molecule that can inhibit the amyloid fibrillation and potentially clear amyloid fibrils is of great therapeutic value. In this manuscript, we investigated the antiAmyloidogenic, fibril disaggregating, as well as cell protective effect of an anti-tuberculosis drug, Capreomycin (CN).

11:35 New Tools to Anticipate and Prevent Protein Aggregation Undergoing Freeze-Thaw
Miguel Rodrigues, Professor, Co-Founder, SmartFreez

11:50 Sponsored Presentation (Opportunity Available)

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

PREDICTIONS OF AGGREGATION PROPENSITY

13:00 Chairperson’s Remarks
Thomas Laue, PhD, Professor Emeritus, Biochemistry and Molecular Biology; Director, Biomolecular Interaction Technologies Center (BITC), University of New Hampshire

13:05 Using Chemical Denaturants to Improve Predictions of Biopharmaceutical Aggregation during Storage
Robin Curtis, PhD, Senior Lecturer, Chemical Engineering and Analytical Science, University of Manchester

Here we show how to account for the high concentration of denaturants in the data analysis, which if unaccounted for, could lead to data misinterpretation. We then correlate light scattering measurements of five monoclonal antibodies at high denaturant concentration with their shelf stability. The results indicate there is a window of denaturant concentration over which the self association behaviour provides an indicator for the aggregation propensity upon storage.

13:35 Prediction of Aggregation Propensity at Early Development Stage Using Orthogonal Characterization Methods
Joël Richard, PhD, Head, Technical & Pharmaceutical Operations, MedinCell

In the perspective of accelerating early stage protein formulation development, it has become key to anticipate and predict formulation, storage and processing conditions that will lead to aggregation. To anticipate aggregation propensity, evaluate aggregation rate under critical conditions and mitigate associated immunogenicity risks, it is proposed to focus on the very early steps of aggregation, often involving higher order structure (HOS) alterations and loss of colloidal stability, using a set of orthogonal characterization techniques.

14:05 Using Physics-Based Simulations to Understand the Determinants of Viscosity in Concentrated Antibody Solutions
Saeed Izadi, PhD, Scientist, Early Stage Pharmaceutical Development, Genentech, Inc.

We have developed a physics-based multi-scale coarse-grained approach to explore how high viscosity can emerge from weak self-interactions. Key developments that enabled this approach are discussed, including our novel strategies to preserve electrostatic fields and hydrophobicity features. Our method improves on currently available approaches, evidenced by its accuracy when compared against experimental data, along with providing unexpected insights into the problem that enable consideration of mitigation strategies before material is available for testing.

DEGRADATION MONITORING FOR STABILITY AND FORMULATION DEVELOPMENT

14:35 Stability of Protein Disulfides: Sensitive Targets for Oxidation and Light-Induced Degradation
Christian Schoneich, PhD, Professor, Pharmaceutical Chemistry, University of Kansas

Protein disulfides are important for the structural integrity of proteins. Nevertheless, they are sensitive targets for multiple pathways of protein degradation, where specific degradation products have been detected in immunogenic protein samples. Hence, a thorough characterization of disulfide degradation pathways of biotherapeutics presents an important task. Recently, we detected about 60 different degradation products resulting from the light-induced degradation of a small protein, human growth hormone, and significantly more products may be expected from the degradation of monoclonal antibodies.

15:05 Quantification and Degradation Monitoring of PS80 in One Single Analysis Using QDa Mass Detector
Pierre Guibal, PhD, Deputy Head, Analytical Development, BioAnalytics, Sanofi

Different methods already exist for PS80 monitoring, but to our knowledge, no method is able to quantify intact PS80 and monitor its potential degradation.
15:35 **Protein-Excipient Interactions Evaluated via NMR Studies in Polysorbate-Based Multi-Dose Protein Formulations: Influence on Antimicrobial Efficacy and Potential Study Approach**

*Riccardo Torosantucci, PhD, Lab Head, Formulation Development, Pharmaceutical Development Biologics, Sanofi-Aventis Deutschland GmbH*

Preservatives are excipients needed in biopharmaceutical multi-dose formulations to prevent microbial growth; however, they are known to interact with non-ionic surfactants like polysorbate and potentially with the active pharmaceutical ingredient (API). In the current study those interactions were successfully quantified via NMR and correlated to the antimicrobial activity of the formulations. NMR represents therefore a powerful tool to support formulation development of multi-dose formulations.

16:05 **End of Summit**
Targeting the Tumour Microenvironment
Factors Influencing the Therapeutic Response

Recommended Short Course*
SC3: Introduction to the Tumour Microenvironment and Response to Cancer Immunotherapy
*Separate registration required. Click here for details.

MONDAY 12 NOVEMBER

12:00 Conference Registration

APPROACHES TO TARGET THE TUMOUR STROMA

13:30 Organizer’s Welcome
Nicole Lyscom, PhD, Senior Conference Director, Cambridge Healthtech Institute

13:35 Chairperson’s Opening Remarks
Denise L. Faustman, MD, PhD, Director, Immunobiology, Massachusetts General Hospital; Associate Professor, Medicine, Harvard Medical School

13:45 Novel Approaches to Target the Tumor Stroma for Cancer Immunotherapy
Christina Claus, PhD, Senior Scientist, Oncology, Immunotherapy, pRED, Roche Innovation Center, Zurich
This presentation will examine the prevalence of FAP expression in tumors and the design of our FAP-IL2v and FAP-4-1BBL fusion proteins including the preclinical mechanism of action, and their application in combination therapy.

14:15 Impact of Cytokine Fusion Proteins Delivered to the Tumour Microenvironment
Dario Neri, PhD, Professor, Biomacromolecules, Chemistry and Applied Biosciences, ETH Zürich
Certain pro-inflammatory cytokines (e.g., IL2, IL12, TNF) can potently activate the immune system, but are often toxic at low doses, preventing escalation to therapeutically active regimens. The fusion of suitable cytokine payloads to tumor-homing antibodies leads to a dramatic increase in therapeutic index. In this lecture, I will present preclinical and clinical results, obtained in collaboration with Philogen.

14:45 Selective IL-2 Immunotherapy to Fuel the Anti-Tumor Immune Response
Onur Boyman, MD, Professor and Chair, Immunology University Hospital Zurich, University of Zurich
Following the impact of immune checkpoint inhibitors, novel immunotherapies are entering clinical testing in patients with advanced cancer, including interleukin-2 (IL-2)-based approaches. But what are the mechanisms of action, benefits, and differences of IL-2-based immunotherapies in comparison to immune checkpoint inhibitors? This presentation will discuss these aspects of IL-2 immunotherapy by presenting data on selective and improved IL-2 formulations.

15:15 Abcam’s Custom Services Capabilities – from Development to Commercialization
Jamie Campbell, Head of Custom Services, Custom Manufacturing, Abcam
Abcam’s comprehensive approach to developing antibodies against challenging targets leverages three antibody discovery platforms: RabMAb®, NGS-based antibody discovery, and phage display, used in combination with comprehensive assay cascades. We partner with biopharma and diagnostic companies to develop antibodies as key reagents in drug discovery, in vitro diagnostics and therapeutics.

15:30 Sponsored Presentation (Opportunity Available)

15:45 Networking Refreshment Break

PLENARY KEYNOTE SESSION

16:15 Moderator’s Opening Remarks
Janine Schuurman, PhD, Corporate Vice President, Research & Innovation, Genmab BV

16:20 Bicycles and Bicycle Drug Conjugates
Sir Gregory Winter, PhD, FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics
Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles’ unique properties have been used to develop Bicycle Drug Conjugates™ (BDCs), a novel toxin delivery platform which greatly improves toxin loading into tumour tissues. A BDC is expected to enter clinical trial in Q1 2018.

17:20 Paracrine Delivery: Therapeutic Biomolecules Produced in Situ
Andreas G. Plückthun, PhD, Professor and Director, Department of Biochemistry, University of Zürich
Cancer will have to be fought with cocktails of therapeutics acting locally, which may have to include therapeutic antibodies against receptors, checkpoint inhibitors, as well as cytokines to modify the tumor microenvironment. We have recently developed a technology of using non-replicative adenovirus carrying no viral genes, engineered to target desired cells and also to be shielded from the immune response, as a vehicle for simultaneous delivery of multiple genes of therapeutic proteins, produced and secreted by the infected cells.

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

19:30 End of Day
10:30 Coffee Break in the Exhibit Hall with Poster Viewing

ANTAGONISTIC APPROACHES

11:15 KEYNOTE PRESENTATION: TNFR2 Antagonism: It Doesn’t Get Any Better - A Treg and Oncogene Targeted Therapy

Denise L. Faustman, MD, PhD, Director, Immunobiology, Massachusetts General Hospital
Associate Professor, Medicine, Harvard Medical School
Tumor necrosis factor receptor-2 (TNFR2) is a signaling molecule found on the surface of the most potent regulatory T-cells; signaling through TNFR2 proliferates cells through NF-κB. TNFR2 is also abundantly expressed on the surface of many human tumors as oncogene. We propose that blocking TNFR2 selectively targets abundant TNFR2+ tumor-infiltrating Tregs and directly kill TNFR2-expressing tumors. With multi-year efforts we have created TNFR2 antagonistic antibodies with tumor microenvironment specificity.

11:45 A-TIGIT Antagonist Antibody EOS884448 Shows Dual Mechanism of Action by Restoration of T-Cell Effector Functions and Preferential Depletion of Treg

Gregory Driessens, PhD, Project Leader & Head, in vivo Pharmacology, iTeos Therapeutics
TIGIT is a co-inhibitory receptor expressed by lymphoid populations. Antagonist anti-TIGIT antibodies have the potential to restore effector functions of T and NK cells by blocking TIGIT-ligand interaction and by depleting Treg that express high TIGIT level. This presentation will focus on the clinical development of EOS884448 a new antagonist anti-TIGIT Ab that induces potent monotherapy antitumor activity through different mechanisms of action and offers strong therapeutic potential in clinic.

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

IMPACT OF CHECKPOINT INHIBITORS

14:15 Chairperson's Remarks

Mark Cragg, PhD, Professor, Experimental Cancer Biology, Antibody & Vaccine Group, University of Southampton

14:20 Targeting Immune Checkpoints in Cancer: Mechanistic Insights

Frederick Arce Vargas, MD, PhD, MRCS, Group Leader, Translational Research, Autolus
Preclinical data in mice models has suggested that the mechanism of action of antibodies targeting co-stimulatory and co-inhibitory molecules in T-cells might extend beyond engagement of blockade of these receptors, relying upon their additional capacity to deplete regulatory T-cells through antibody-dependent cell-mediated cytotoxicity. There is evidence that human Fc gamma receptors also...
mediate this mechanism in the case of anti-CTLA-4 and anti-CD25 antibodies. This evidence supports the importance of understanding the immune landscape in the tumour microenvironment for the design of the next generation of immune regulatory antibodies.

14:50 Broad Impact of anti-PD-L1 on the Tumour Microenvironment
Yan Qu, PhD, Senior Principal Scientist, Rinat Pfizer

15:20 Development of Therapeutic Antibodies Targeting Suppressive Immune Cells in the Tumor Microenvironment to Boost Effector Cell Anti-Tumor Activity
Pascal Merchiers, PhD, Vice President, R&D, Tusk Therapeutics Ltd.
Tumors are masters in downregulating the immune response that aims at eliminating them. As such it is critical in immune therapy to target the negative suppressor cells driving the latter process. Tusk Therapeutics is developing antibodies that can effectively reduce the levels of these regulatory cells and enable the activation of effector cells. During this talk the preclinical proof-of-concept and development of these antibodies will be discussed.

15:50 Sponsored Presentation (Opportunity Available)

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

ADVANCES IN THE CLINIC / IMPACT OF ONCOYTIC VIRUSES AND VECTOR VACCINES ON IMMUNE MODULATION

17:00 Clinical Advances with Entinostat HDAC Inhibitors in Metastatic Breast Cancer
Michael L. Meyers, MD, PhD, CMO, Syndax Pharmaceuticals, Inc.

17:30 Studies with the Oncolytic Virus VSV-GP, Cancer Vaccines and Immune-Modulation: The Yin and the Yang
Philipp Mueller, PhD, Principal Scientist, Cancer Immunology & Immune Modulation, Boehringer Ingelheim Pharma GmbH & Co. KG
The talk will provide a short introduction to the MoA of oncolytic virotherapies, selective replication of the oncolytic virus VSV-GP in tumor cells, tumor cell lysis and reshaping of the tumor microenvironment. It will further outline the effectiveness of VSV-GP as an IO enabler in the poorly “T-cell inflamed” tumour space for a broad range of cancers and highlight VSV-GP as a non-mutagenic virus, which can be armed with transgenes and synergizes with other (non)-IO therapies.

18:00 Targeting Immunotherapy to the Tumour Microenvironment Using Bispecific Antibodies
Len Seymour, PhD, Professor, Gene Therapies, Oncology, University of Oxford
Oncolytic viruses replicate selectively within cancer cells and kill them, amplifying themselves selectively within tumour tissue. They can be ‘armed’ to produce specific biologics (such as bispecific T-cell engager antibodies, BiTEs) and secrete them into the tumour microenvironment, where the BiTEs can activate endogenous T-cells to kill chosen target cells. This paper will discuss using BiTEs that target tumour cells and also tumour-associated fibroblasts for reversal of tumour-related immunosuppression.
WEDNESDAY 14 NOVEMBER

07:45 Registration and Morning Coffee

08:30 Chairperson's Remarks
John Maher, FRCPath, PhD, Consultant & Senior Lecturer, Immunology, Cancer Studies, King's College London

08:35 T4 Pan-ERB-Targeted CAR T-Cell Immunotherapy of Head and Neck Cancer: Phase I Trial Results
John Maher, FRCPath, PhD, Consultant & Senior Lecturer, Immunology, Cancer Studies, King's College London

T4 immunotherapy comprises T-cells that have been engineered to co-express (i) T1E28β, a CD28+CD3ζ CAR that engages 8 of 9 ErbB homo- and heterodimers and (ii) 4αβ, a chimeric cytokine receptor consisting of the IL-4Rα ectodomain coupled to the IL-2Rβ endodomain. To de-risk T4 immunotherapy, a dose-escalation intra-tumoral Phase I clinical trial was commenced in SChN patients, without lymphodepletion. An update on the trial will be provided.

09:05 The Next Generation of CAR T-Cells
Hinrich Abken, PhD, Professor, Genetics & Immunology, Center for Molecular Medicine Cologne, University of Cologne

Chimeric antigen receptor (CAR) modified T cells substantially reduced the tumor burden in early phase trials and induced spectacular and lasting remissions. We discuss recent developments in the fourth generation of CAR T cells, so-called TRUCKs, which release an inducible IL-12 and/or IL-18 upon CAR engagement in the targeted tumor lesion and present a new CAR format to shape the T cell maturation in a specific fashion.

09:35 NKG2D CAR T-Cell Therapy: Developing an Autologous and Allogeneic CAR T Approach Exploiting the Targeting Capacity of the Innate Immune System
David Gilham, PhD, Vice President, R&D, Ceylad

The ability of the Natural Killer activatory receptor NKG2D to bind eight different ligands that are frequently over-expressed in tumors makes this receptor an attractive candidate for CAR T cell development. Our initial observations of clinical response in patients with relapsed/refractory Acute Myeloid Leukemia after treatment with CYAD-01, a CAR T cell employing NKG2D for targeting, provides support for the potential for this approach. Our clinical plans to fully explore NKG2D involve autologous approaches and also allogeneic CAR T approaches that do not involve gene editing methodologies and these will be discussed.

10:05 Target Specificity Screening of CAR T-Cells Using Human Cell Microarray Technology
Mark Aspinall-O'Dea, EMEA, Business Development Manager, Retrogenix Limited

Human cell microarray screening enables the discovery of both primary cell surface receptors as well as potential off-targets for a variety of biologics including: peptides, antibodies, proteins, CART 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 for antibodies, scFvs and CART T cells to aid safety assessment and provide key data to support IND submissions.

10:15 Imaging CAR T-Cells
Sophie Papa, PhD, Senior Lecturer and Honorary Consultant Medical Oncologist, King's College London

Clinical translation of CAR/TCR T-cell therapy would be enhanced if we could reliably trace the behavior in vivo of the cell product after infusion. Ideally, this non-invasive assessment of T-cell biodistribution would utilise a non-immunogenic reporter that mediates specific uptake of an inexpensive, non-toxic and clinically established imaging tracer. Here we demonstrate the utility of the human sodium iodide symporter for temporal and spatial monitoring of CAR T-cell behavior.

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

11:15 Targeting the Tumour Vasculature with CAR T-Cells
Steven P. Lee, PhD, Senior Cancer Research Fellow and Training Lead for the Birmingham CRUK Cancer Centre, Institute of Immunology and Immunotherapy, University of Birmingham

To improve CAR T-cell therapy for solid tumours, rather than targeting malignant cells directly, we are developing CARs to target markers on the tumour vasculature. Having identified the C-type lectin CLEC14A to be selectively overexpressed on tumour vasculature, we have generated CARs targeting this marker that are safe and effective at inhibiting tumour growth in three mouse models of cancer. We are currently developing the approach for a Phase I trial.

11:45 Targeting the Tumour Vasculature with CAR T-Cells
Sophie Papa, PhD, Senior Lecturer and Honorary Consultant Medical Oncologist, King's College London

Clinical translation of CAR/TCR T-cell therapy would be enhanced if we could reliably trace the behavior in vivo of the cell product after infusion. Ideally, this non-invasive assessment of T-cell biodistribution would utilise a non-immunogenic reporter that mediates specific uptake of an inexpensive, non-toxic and clinically established imaging tracer. Here we demonstrate the utility of the human sodium iodide symporter for temporal and spatial monitoring of CAR T-cell behavior.

12:15 Resistance to Chimeric Antigen Receptor T-Cells for Hematological Malignancies
Marco Ruella, MD, Clinical Instructor, Associate Director, Dr. June's Laboratory, Center for Cellular Immunotherapies (CCI), Perelman School of Medicine, University of Pennsylvania

Anti-CD19 chimeric antigen receptor T cells (CART19) is now an FDA-approved drug for relapsed leukemia and lymphoma. The approval by the FDA of the first adoptive T cell therapy, the UPenn/Novartis CART19 (CTL019), represents a huge achievement for cancer treatment and paves the way to the use of the CART technology in other cancers and in combination with other agents. However, a significant subset of patients treated with CART19 still does not respond or relapses. In his talk Dr. Ruella will present novel findings in the mechanism of CART19 resistance and show recent data on the development of CART combination strategies to overcome resistance.
12:45 Preclinical Selection of Optimal TCR Candidates for Cancer Immunotherapy
Claudia Wagner, PhD, Associate Director, Immunology, Immatics Biotechnologies GmbH
TCR-based immunotherapy is emerging as a promising alternative to CAR-T approaches, especially for solid cancers. Our proprietary TCR platform generates TCRs highly specific for XPRESIDENT®-validated tumor antigens. We use unique information from the large XPRESIDENT® collection of healthy tissues and tumor biopsies for the selection of efficient and safe TCR candidates.

13:00 Sponsored Presentation (Opportunity Available)

13:15 Luncheon Presentation I to be Announced

13:45 Luncheon Presentation II (Sponsorship Opportunity Available)

14:15 Session Break

UNCONVENTIONAL APPROACHES TO TCR ENGINEERING

14:30 Chairperson's Remarks
Andrew Sewell, PhD, Distinguished Research Professor and Wellcome Trust Senior Investigator, Infection & Immunity, Cardiff University School of Medicine

14:35 KEYNOTE PRESENTATION: The ImmTAC Platform: How Far We Have Come and Where We Are Going
Bent K. Jakobsen, PhD, CSO, Immunocore Ltd.
Immune mobilizing monoclonal TCRs against cancer (ImmTAC™) molecules are a novel class of immunotherapy agent comprised of a soluble T cell receptor (TCR) fused to a T-cell redirecting scFv anti-CD3. ImmTAC molecules offer distinct advantages over antibody- and cell-based formats, including access to a much larger pool of antigens in a soluble platform. The lead ImmTAC molecule, IMCgp100, has demonstrated encouraging preliminary anti-tumour activity in patients with metastatic uveal melanoma.

15:05 Genetic Engineering of Therapeutic T-Cells
Hans J. Stauss, MD, PhD, Director & Professor, Tumor Immunology, Infection & Immunity & Transplantation, Royal Free Hampstead NHS Trust
Effective gene transfer platforms can redirect the specificity of patient T-cells using chimeric antigen receptors (CARs) or T-cell receptors (TCRs). In this presentation, we will demonstrate that optimal TCR expression in engineered T-cells is essential for optimal antigen-specific function. We will combine TCR transfer with the engineering of T-cell effector function and show that this combination approach provides best cancer immunity in a murine model.

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

OPTIMIZING ADOPTIVE IMMUNOTHERAPY

16:15 Adoptive Cell Therapy-Based on TILs in the Era of Check Point Inhibitors
Marco Donia, MD, PhD, Staff Physician and Scientist, Medical Oncology, Herlev Hospital
TIL ACT approach can mediate complete and durable responses in 10%-20% of patients with metastatic melanoma, and can also yield clinical responses in other selected types of solid tumors. The presentation will include data on predictive markers for response, the role of neo-epitopes, immune escape mechanisms, as well as data on TIL ACT in anti-PD1 refractory patients and TIL ACT in combination with check point inhibitors.

16:45 New Broadly Expressed Cancer Targets from Successful TIL Therapy
Andrew Sewell, PhD, Distinguished Research Professor and Wellcome Trust Senior Investigator, Infection & Immunity, Cardiff University School of Medicine
We have developed two new techniques that allow rapid determination of the ligand recognised by any ‘orphan’ T-cell clone. These techniques have enabled discovery of novel cancer-associated epitopes that are present on the surface of most cancers.

16:50 PANEL DISCUSSION: CELLULAR THERAPY VS. SOLUBLE (ANTIBODY AND TCR)

17:15 Moderator
Moderator: Andrew Sewell, PhD, Distinguished Research Professor and Wellcome Trust Senior Investigator, Infection & Immunity, Cardiff University School of Medicine

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 15 NOVEMBER

08:00 Registration and Morning Coffee

IMPROVING SAFETY AND EFFICACY OF CAR T THERAPY

08:30 Chairperson's Remarks

08:35 Safety Challenges of T-Cell Therapies: The Balance between Efficacy and Safety
Michaela Sharpe, PhD, Head of Nonclinical Safety and Immunotherapy Strategy, Cell and Gene Therapy Catapult
Gene engineered T-cell therapies have the potential to revolutionize the treatment of cancer. The power of these treatments is linked with a distinct set of toxicities both predicted and unpredicted. As these therapies begin to reach more patients, it is critical to develop the nonclinical tools to adequately determine the mechanisms driving these toxicities, to assess the safety risks of candidate products, and to develop strategies for safety management.

09:05 Targeting the T-Cell Receptor β-Chain Constant Region for Immunotherapy of T-Cell Malignancies
Paul Maciocia, PhD, Clinical Training Fellow/BRC Clinical Lecturer in Haematology, Research Department of Haematology, Faculty of Medical Sciences, University College London
T-cell cancers have a poor prognosis with few effective treatments available. We developed a novel immunotherapy based on targeting T-cell receptor β-chain constant domain 1 (TRBC1) or 2 (TRBC2). While normal T-cells contain both TRBC1+ and TRBC2+ compartments, malignancies are restricted to only one. We engineered anti-TRBC1 CAR T-cells, which killed normal and malignant TRBC1+, but not TRBC2+, T-cells in vitro and in vivo. Thus, anti-TRBC immunotherapy could eradicate a T-cell cancer while preserving T-cell immunity.

09:35 CAR T-Cells – What’s Next? From Personalized to “Off the Shelf” CARs
Anat Globerson Levin, PhD, Senior Researcher & Immunology Lab Manager, Immunology Research Lab, Tel-Aviv Sourasky Medical Center
CAR (chimeric antibody receptors) T-cell therapy, pioneered in our lab, is a powerful tool for cancer treatment. This approach has proven very effective in clinical trials in leukemia and lymphoma patients and has recently gained FDA approval to treat certain types of large B-cell lymphoma. Today, the major challenge in the CAR T-cell field is to prevent ‘off-tumor on-target’ toxicity, namely, the risk of damage to the patient’s healthy tissue which expresses the target antigen of the selected CAR. Furthermore, the manufacturing of CAR T-cells under GMP is a focal point for this promising therapeutic modality. As personalized therapies, autologous cell-based therapies pose a distinct set of manufacturing challenges. Protocols must be developed to reduce the number of CAR T-cells needed for a therapeutic effect and treating patients with allogeneic CAR T-cells can facilitate the procedures needed for manufacturing and make CAR T-cell therapy more available for patients. Here, we will present our solution for these three obstacles. We took advantage of the surface expression of several antigens that are widely expressed on multiple myeloma cells and are poorly expressed by hematopoietic stem cells, and generated CAR T-cells with dual specificity, expressing two complementary CARs (double CARs) for the specific and effective treatment of MM and to overcome the ‘off-tumor on-target’ toxicity. We will also present the optimization of CAR T-cell treatments in order to minimize the number of cells administered. Finally, we will present our solution for “Off the Shelf” CARs.
Inaugural

Agonist Immunotherapy Targets and Combination Therapies

Accelerating T-Cell Response

THURSDAY 15 NOVEMBER

13:00 Registration

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

IL2, TNFR-SF, and STING SIGNALING

14:00 Chairperson's Opening Remarks
Patrick Mayes, PhD, Executive Director, Head of I-O Biotherapeutics, Incyte

14:05 Interleukin-2: Releasing an Immune System Brake to Attack Tumors
Daniel Christ, PhD, Associate Professor, Director, Centre for Targeted Therapy, Garvan Institute of Medical Research

Interleukin-2 is an established therapeutic agent used for cancer immunotherapy. It is generally believed that treatment efficacy is mediated by CD8+ and NK cell activity, and considerable efforts have focused on generating IL-2 variants that expand these subsets systemically. Here we describe a second and unexpected mechanism, namely the selective depletion of CD25+ CD4+ regulatory T-cells (Tregs), as a major determinant of antitumour activity. Our results outline mechanisms of action and provide important guidance for the development of next-generation cytokine therapeutics.

14:35 Extrinsic Phagocyte-Dependent STING Signaling Dictates the Immunogenicity of Dying Cells
Jeonghyun Ahn, PhD, Research Asst Prof, Cell Biology, University of Miami

15:05 Sponsored Presentation (Opportunity Available)

15:35 Networking Refreshment Break

16:00 HERA: Engineering Next-Generation TNFR-SF Agonists for Cancer Immunotherapy
Oliver Hill, PhD, Vice President, Molecular Biology/Protein Engineering, Apogenix AG

The HERA technology platform developed by Apogenix is based on trivalent but single-chain molecular mimics of the TNF-SF Receptor binding domains (scTNFSF-RBDs) fused to a dimerization scaffold. Being hexavalent by design, the HERA fusion proteins are potent TNF-SF agonists on their own and do not need secondary crosslinking events for their activity. The underlying engineering concept as well as selected in vitro and in vivo data obtained with HERA-CD40L, HERA-CD27L and HERA-GITRL will be presented.

16:30 Agonistic Activation of TNFR-SF Receptors by HexaBody IgG-induced Oligomerization
Rob de Jong, PhD, Assistant Director, Protein Chemistry & CMC, Genmab BV

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
*Separate registration required. Click here for details.

FRIDAY 16 NOVEMBER

08:00 Registration and Morning Coffee

08:35 KEYNOTE PRESENTATION: NKTR-214: Cytokine Engineering to Access the IL-2 Pathway
Jonathan Zalevsky, PhD, Senior Vice President, Research, CSO, Nektar Therapeutics

NKTR-214 is a CD-122-biased agonist that targets the IL-2 pathway to provide sustained signaling through the heterodimeric IL-2 receptor pathway (IL-2Rβγ). NKTR-214 preferentially activates and expands NK and effector CD8+ T cells over T-regulatory cells in the tumor microenvironment. In addition, NKTR-214 promotes an invigorated immune phenotype and drives cell surface expression of costimulatory molecules, such as ICOS, and coinhibitory receptors, such as PD-1 on the surface of newly proliferating lymphocytes. The immune replenishing mechanism of action of NKTR-214 makes it an ideal combination partner with multiple immune oncology mechanisms.

08:50 Chairperson's Remarks
Daniel Christ, PhD, Associate Professor, Director, Centre for Targeted Therapy, Garvan Institute of Medical Research

09:05 ATOR-1017 – An Agonistic Tumor Directed Fc-y Receptor Cross Linking Dependent CD137 Antibody
Anna Säll, PhD, Scientist, Alligator Bioscience

ATOR-1017 is an agonistic CD137 IgG4 antibody with a unique functional profile compared to the 4-1BB antibodies currently in clinical development. The functional activity depends on cross-linking mediated by Fcy receptors, which directs the immune activation to the tumor area and reduces the risk of inducing systemic immune activation and liver toxicity. ATOR-1017 is currently in preclinical development and clinical trials will start in the second half of 2019.
Online exhibit opportunities
Register by 5 October
& SAVE up to €200

09:35 Tumor-Targeted DARPin® Drug Candidates for Tumor-Restricted Immune Cell Co-Activation
Christian Reichen, PhD, Senior Scientist Lead Generation, Protein Engineering, Molecular Partners AG
Dose-limiting toxicity can hamper effective dosing and combination with chemokine inhibitors and other immune stimulating drugs. By using the DARPin® toolbox, we have developed a set of multi-specific molecules that enable tumor-restricted immune cell activation, thereby largely reducing the risk of systemic side effects. Data from the preclinical development of tumor-restricted agonists will be presented on MP0310, a 4-1BB/FAP bispecific DARPin drug candidate promoting CD8+ T cell expansion in a strictly FAP-dependent manner. FAP is highly expressed in human tumor stroma cells.

10:05 Networking Coffee Break

10:35 Multispecific and Multivalent Antibodies as OX40 Agonists
Bryan Glaser, PhD, Vice President, Research, Invenra Inc.
OX40 agonists have demonstrated significant therapeutic potential in preclinical models; however, their efficacy in clinical trials is minimal. We hypothesize the efficacy in humans is limited by insufficient crosslinking in the tumor microenvironment. Thus, we aimed for bishaptic antibody to directly crosslink OX40 and successfully developed soluble agonists, which are potent in the absence additional crosslinker. This strategy together with high-throughput bispecific antibody screening is applicable to agonist discovery for a wide range of receptors.

11:05 What's Next for GITR and OX40 Agonists?
Patrick Mayes, PhD, Executive Director, Head of I-O Biotherapeutics, Incyte
A discussion of combination approaches for GITR and OX40 agonist antibodies in cancer. Integration of tumor biomarker analyses in response to agonist antibody treatment to inform upon GITR and OX40 combinations.

11:35 Sponsored Presentation (Opportunity Available)

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

NOVEL AGONISTS AND COMBINATION THERAPIES

13:00 Chairperson’s Remarks
Jonathan Zalevsky, PhD, Senior Vice President, Resesarch, CSO, Nektar Therapeutics

13:05 CB307, a Novel T-Cell Agonist Humabody Therapeutic for PSMA-Positive Tumours
James Legg, PhD, Vice President, R&D, Crescendo Biologics

13:35 AcTakines: A Novel Class of Cancer Immunotherapeutics
Erik Depla, PhD, Director, Biology, Orionis Biosciences
Type I IFN-derived AcTakines targeting dendritic cells displayed strong antitumor activity in murine melanoma, breast carcinoma, and lymphoma models and against human lymphoma in humanized mice without detectable toxic side effects. Combined with immune checkpoint blockade or chemotherapy, complete tumor regression and long-lasting tumor immunity were observed. Our findings indicate that AcTakines targeting to dendritic cells provide a novel class of highly efficient, safe, and broad-spectrum cancer immunotherapeutics.

14:05 Chemotherapy Combinations to Enhance Tumor Response to Agonist Antibodies
Allison Betof Warner, MD, PhD, Medical Oncology Fellow, Memorial Sloan Kettering Cancer Center
Stimulation of glucocorticoid-induced tumor necrosis factor receptor (GITR) has been shown to enhance antitumor immunity by stimulating effector CD4+ and CD8+ T cells and attenuating suppression and depleting by CD4+Foxp3+ regulatory T cells (Treg). However, GITR monotherapy does not effectively control tumor growth. I will discuss our data showing that cyclophosphamide (CTX), a cytotoxic chemotherapeutic agent with key immunomodulatory properties, can enhance the potency of GITR engagement anti-tumor effects.

14:35 Tumor-Targeted Combination of TNFSF Agonists and IL-15 for Cancer Immunotherapy
Dafne Muller, PhD, Group Leader, Institute of Cell Biology and Immunology, University of Stuttgart
Costimulatory members of the TNF-superfamily and IL-15 have shown great potential to support the generation and development of an antitumor immune response. In order to improve the efficacy of such molecules at the tumor site, we designed different formats of bi- and trifunctional antibody-fusion proteins, focusing on tumor-targeted presentation and combined mode of action of diverse immunomodulatory molecules, demonstrating enhanced immune responsiveness in vitro and antitumor activity in a mouse model in vivo.

15:05 Oncorus Oncolytic HSV, a Platform for Combination Immunotherapy
Christophe Queva, PhD, CSO, Oncorus
Oncorus is developing the next generation HSV-based oncolytic virus with enhanced potency for tumor cell killing and recruitment of the immune system. Our innovative miR-attenuation strategy enables robust viral replication in tumor cells, while preventing replication in healthy tissue. Oncorus’ oHSV are armed with multiple immunomodulatory payloads to synergistically increase recruitment and effector function of immune cells, thus harnessing the full potential of OVs to evoke an abscoap immune response.

15:35 End of Summit
Systems Engineering and Synthetic Biology

Expanding the Protein Engineering and Production Toolbox

**Recommended Short Course**

SC1: Transient Protein Expression: A Key Tool to Enable Rapid Protein Engineering

*Separate registration required. Click [here](#) for details.

**MONDAY 12 NOVEMBER**

12:00 Conference Registration

13:30 Organizer’s Welcome
Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

13:35 Chairperson’s Opening Remarks
Dominic Esposito, PhD, Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research

13:45 Expanding the Synthetic Biology Toolbox for CHO Cell Factories
Nuša Pristovšek, Postdoctoral Researcher, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark

14:35 Expanding the Synthetic Biology Toolbox for CHO Cell Factories
Chinese hamster ovary (CHO) cells are widely used in the biopharmaceutical industry as a host for the production of complex therapeutic proteins. Thus, efficient synthetic biology tools to improve CHO cell factories are of great interest. Here, our latest development of these tools will be demonstrated. Together with high-throughput technologies and systems biology approaches, synthetic biology can pave the way for accelerated generation of desirable CHO cell factories with predicted culture performance.

14:15 CRISPR-Cas Implementation and Novel Expression Tools for Non-Conventional Yeasts
Thomas Vogl, PhD, Researcher, Department of Computer Science and Applied Mathematics & Department of Molecular Cell Biology, Weizmann Institute of Science

The setup of efficient CRISPR/Cas systems and the toolbox of advanced CRISPR-related applications will be illustrated by the example of the methylothrophic yeast *Pichia pastoris* (doi:10.1016/j.biotechadv.2018.01.006). Furthermore, synthetic biology and metabolic engineering experiments frequently require the fine-tuning of gene expression to balance and optimize protein levels of regulators or metabolic enzymes. Here also novel strategies for the transcriptional fine-tuning of gene co-expression will be presented.

14:45 Engineering the *Trichoplusia ni* Insect Cell Line Tni-FNL to Improve Recombinant Protein Production
Dominic Esposito, PhD, Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research

Tni-FNL is a fully sequenced insect cell line which is capable of outproducing many other *T. ni* cell lines in recombinant protein production. We describe ongoing systems biology efforts to better understand how this cell line functions and to improve characteristics related to higher protein yield and quality.

15:15 Sponsored Presentation (Opportunity Available)

15:45 Networking Refreshment Break

**PLENARY KEYNOTE SESSION**

16:15 Moderator’s Opening Remarks
Janine Schuurman, PhD, Corporate Vice President, Research & Innovation, Genmab BV

16:20 Bicycles and Bicycle Drug Conjugates
Sir Gregory Winter, PhD, FRS, Master, Trinity College and Co-Founder and Director, Bicycle Therapeutics

Bicycles® are a novel therapeutic class of constrained bicyclic peptides that combine antibody-like affinity and selectivity with small molecule-like tissue penetration, tunable exposure and chemical synthesis. They have potential in many indications, including oncology, where Bicycles’ unique properties have been used to develop Bicycle Drug Conjugates™ (BDCs); a novel toxin delivery platform which greatly improves toxin loading into tumour tissues. A BDC is expected to enter clinical trial in Q1 2018.

17:20 Paracrine Delivery: Therapeutic Biomolecules Produced in Situ
Andreas G. Plückthun, PhD, Professor and Director, Department of Biochemistry, University of Zürich

Cancer will have to be fought with cocktails of therapeutics acting locally, which may have to include therapeutic antibodies against receptors, checkpoint inhibitors, as well as cytokines to modify the tumor microenvironment. We have recently developed a technology of using non-replicative adenovirus carrying no viral genes, engineered to target desired cells and also to be shielded from the immune response, as a vehicle for simultaneous delivery of multiple genes of therapeutic proteins, produced and secreted by the infected cells.

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

19:30 End of Day

**TUESDAY 13 NOVEMBER**

07:45 Registration and Morning Coffee
08:30 Chairperson's Remarks
Fernando López-Gallego, PhD, ARAID Tenured Scientist, Institute of Synthetic Chemistry, University of Zaragoza

08:35 Cloning-Free Template DNA Preparation for a Wheat Germ Cell-Free System with Short 3’-UTR
Yasuo Tada, PhD, Professor, Center for Gene Research, Nagoya University

09:05 Expanding One-Pot Cell-Free Protein Synthesis and Immobilization for On-Demand Manufacturing of Biomaterials
Fernando López-Gallego, PhD, ARAID Tenured Scientist, Institute of Synthetic Chemistry, University of Zaragoza

09:35 Problem-Solving Breakout Discussions*
*See website for details.

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

11:15 Cell-Free Protein Synthesis from Resting versus Ultra-Fast Growing Cells: Findings from Systems Biology
Martin Siemann-Herzberg, PhD, Professor, Biotechnology, Institute of Biochemical Engineering, University of Stuttgart

11:45 Minimal Cell: Cell-Free Protein Synthesis in Micro-Compartment
Lei Kai, PhD, Group Leader, Department of Cellular and Molecular Biophysics, Max Planck Institute of Biochemistry

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

ENGINEERING SYSTEMS-SCALE STRATEGIES

14:15 Chairperson's Remarks
Arnaud Poterszman, PhD, Research Director, Integrated Structural Biology, IGBMC (CNRS/INSERM/UdS)

14:20 Design of Intracellular Inhibitors – A Platform for Target Validation and Drug Development
Andreas Ernst, PhD, Group Leader, Institute of Clinical Pharmacology, Goethe University Frankfurt

14:50 Top-Down and Bottom-Up Strategies for Production of Human Multi-Protein Complexes
Arnaud Poterszman, PhD, Research Director, Integrated Structural Biology, IGBMC (CNRS/INSERM/UdS)

Macromolecular complexes are vital cornerstones of most, if not all, biological processes in cells. We illustrate how the CRISPR/Cas9 editing technology allows us to label and isolate native protein assemblies from their natural cellular environment and the potential of the baculovirus expression vector system for reconstitution of multi-subunit complexes. As model systems, we use transcription regulators such as pTefb, nuclear receptors or the 10 subunits transcription factor TFIH.

15:20 Engineering the Evolution of Bacteria for Protein Production
Morten Nørholm, PhD, Principal Investigator & Senior Scientist, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark

Microorganisms have for centuries shown great capacity to produce useful materials. However, they are also naturally intolerant to dedicating all resources to a specialized metabolic task and inherently prone to evade stress and evolve new properties. We have explored natural and synthetic evolution of bacteria for production of pharmaceutical proteins and industrial enzymes.

15:50 Sponsored Presentation (Opportunity Available)

16:20 Refreshment Break in the Exhibit Hall with Poster Viewing
17:00 KEYNOTE PRESENTATION: From Systems Biology to Systems Biologics
Sachdev Sidhu, PhD, Professor, Molecular Genetics, The Donnelly Centre, University of Toronto
We have established a platform to combine large-scale systems biology approaches with the discovery and development of new antibody drugs, and to develop efficient, systems-scale strategies to target intracellular signaling networks at the protein level with ubiquitin variants and other scaffolds. This efficient pipeline connects basic research to translational science in a new model for drug development, which we have termed “Systems Biologics”.

17:30 CLOSING PANEL DISCUSSION: Tools for Expanding the Protein Engineering and Production Toolbox
Moderator:
Tsafi Danieli, PhD, Director, BioGiv Incubator & Head, Protein Expression Facility, Wolfson Centre for Applied Structural Biology, Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem
Panelists:
Richard Altman, MS, Scientist, Protein Technologies, Amgen
Nicola Burgess-Brown, PhD, Principal Investigator, Biotechnology, Structural Genomics Consortium (SGC), University of Oxford
Henry C. Chiou, PhD, Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific
Dominic Esposito, PhD, Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research
Mario Lebendiker, PhD, Head, Protein Purification Facility, Wolfson Centre for Applied Structural Biology, Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem
Bjørn Voldborg, MSc, Director, CHO Cell Line Development, The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark

18:30 End of Systems Engineering and Synthetic Biology
Optimising Expression Platforms

Employing Cell Factories for the Production of Therapeutic Proteins

WEDNESDAY 14 NOVEMBER

07:45 Registration and Morning Coffee

08:30 Chairperson's Remarks
Richard Altman, MS, Scientist, Protein Technologies, Amgen

08:35 KEYNOTE PRESENTATION: Transient Protein (Gene) Expression: From R&D towards Pharmaceutical Manufacturing
Florian M. Wurm, Dr. rer. nat., Professor Emeritus, Swiss Federal Institute of Technology Lausanne (EPFL); Founder, Chairman, ExcellGene SA

09:05 Stable versus Transient Gene Expression: A Case Study on Antibody Glycosylation
Cleo Kontoravdi, PhD, Reader, Biosystems Engineering, Department of Chemical Engineering, Imperial College London

09:35 How Do We Assemble an Effective and Efficient Protein Production Toolbox?
Richard Altman, MS, Scientist, Protein Technologies, Amgen

10:05 Selexis’ SUREscan and SUREsignature: Technologies for Assessment of Cell Line Integrity and Clonality
Igor Fisch, CEO, Selexis SA

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

11:15 Tracking the Evolution of Transiently Transfected Individual Cells in a Microfluidic Platform
Sébastien Sart, PhD, Research Associate, Genome and Genetics – Laboratory of Physical Microfluidics and Bioengineering, Institut Pasteur; Laboratoire d'Hydrodynamique, École Polytechnique

11:45 Discovery of Novel Enhancers for Antibody Expression by Transcriptomics-Based Pathway Analysis
Markus Neubauer, PhD, Head, Cell Culture Research, Pharma Research & Development, Roche Innovation Center Munich

12:15 High-Throughput Antigen and Antibody Production at the IPI
James Love, PhD, COO, Institute for Protein Innovation, Harvard Institutes of Medicine

Selexis’ SUREscan utilizes NGS technologies and proprietary bioinformatics to comprehensively assess the genomic architecture of Selexis-generated cell lines. SUREsignature is a unique, genome-wide collection of genetic markers that establishes cell line clonality to a probability significance not previously achievable and determines cell line-specific barcodes for better master cell bank quality control. These technologies minimize risk and accelerate biologics development by allowing for optimal clone selection and monitoring.

In this case study, we explored the differences in CHO cell metabolism, antibody productivity and N-linked glycosylation between stable and transient gene expression at physiological temperature and under mild hypothermia. For each system, we identified bottlenecks for improving antibody quality and have attempted to address them using cell and process engineering.

A robust, flexible transient protein production facility provides critical support to drug discovery efforts. We review the ongoing evolution of our protein production endeavors focusing on two critical components. The first is the strategic assembly of mammalian expression “tools” that gives us a toolbox capable of expressing diverse and challenging candidate proteins. The second is the harmonization of the entire protein production process thereby reducing turnaround times and increasing throughput.

In order to generate open-source monoclonal antibodies against every extracellular and secreted protein in humans, we have developed expression platforms capable of generating high-quality antigens and antibodies in HT format. Optimized transient transfection is performed via automated processes at 1ml and 30ml scales, and semi-automated for larger scales in HEK and CHO cells. Novel DNA preparation, protein purification and characterization platforms have been implemented to support the expression pipeline.
12:45 Scaling Up and Scaling Out: Pushing the Boundaries of Transient Protein Production
Ian Wilkinson, CSO, Research and Development, Absolute Antibody Ltd.
Whilst transient yields have improved drastically in the last decade, scalable systems are time-consuming and expensive 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.

13:00 Value Adding Microbial-Based Solutions for the GMP-Production of Recombinant Proteins
Nicole Peuker, PhD, Principal Expert USP Development, BioProcess Development, Wacker Biotech GmbH
Wacker Biotech, known as the microbial CDMO, handles several GMP production sites in Europe with capacities to deliver multiple hundred grams of drug substance per batch. We will present case studies for our innovative and cost-saving E. coli technologies for the production of difficult-to-make biopharmaceuticals.

13:15 Luncheon Presentation I to be Announced

13:45 Luncheon Presentation II: Accelerating Timelines by Integrating Cell Line Development and Manufacturing Programs
Simon Keen, Head, Cell Line Development, Biology, Abzena

14:15 Session Break
To overcome this issue, we developed an advanced transient expression system consisting in the synergistic association of a novel CHO chemically defined medium and a powerful transfection reagent.

Martin Gamer, PhD, Associate Director, Early Stage Bioprocess Development, Boehringer Ingelheim Pharma GmbH & Co. KG

The increasing number of engineered, often antibody-derived molecule formats entering into biopharmaceutical development poses significant challenges on the generation of high-yielding CHO cell factories. My talk highlights the most recent advances at Boehringer Ingelheim to improve cell line development of DTE proteins. Our toolbox comprises in silico methods to assess molecule developability leading to tailored development, a rationally designed novel host cell line ensuring high performances, robustness and scalability as well as innovative genetic elements and screening tools to select for outstanding CHO production cell lines.

Phillip Wright, PhD, Faculty Pro-Vice-Chancellor, Faculty of Science, Agriculture & Engineering, Newcastle University

Transgenic expression in CHO cells is commonly used to rapidly produce antibodies but is unfortunately limited by transfection efficiency and inherent productivity. To overcome this issue, we developed an advanced transient expression system consisting in the synergetic association of a novel CHO chemically defined medium and a powerful transfection reagent.

Mathieu PORTE, Senior Scientist, Bioproduction, Polyplus-transfection

The SGC promotes research advancement through our open access policy, and in the absence of IP. Globally, we have solved more than 2000 human protein structures and 10 novel integral membrane proteins (IMPs). Although we have made a significant contribution to structural biology and protein production for functional studies, IMPs and protein-protein complexes still remain a challenge to produce. Here, I present our established approaches for eukaryotic expression and screening IMPs using baculovirus/insect cells and BacMam technology.

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

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 premium-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.

Meelis Kadaja, PhD, MBA, Director, Business Development, Icosagen

The objective of the Human Secretome Project is to produce and screen all human secreted proteins to unlock biology leading to new hypotheses and target discovery. Over 1,000 secreted proteins have been expressed and purified using a mammalian expression system and screened in a number of cell-based phenotypic assays. The results of this work have revealed differential activities of protein family members in different biological contexts and provided some learning on successes and failures of recombinant expression of secreted proteins.

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

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

Through extensive systems biology-based cell line engineering, we have engineered CHO cells for the production of therapeutically relevant proteins that were previously not possible to produce using CHO cells.

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

Streamlining Processes

THURSDAY 15 NOVEMBER

13:00 Registration

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

INNOVATING PURIFICATION PROCESSES

14:00 Chairperson’s Opening Remarks

Dorota Antos, PhD, Professor, Chemical and Process Engineering, Rzeszow University of Technology

14:05 KEYNOTE PRESENTATION: How Problems of Protein Purification Are Being Addressed across Structural Laboratories in Europe: Insights from the European Research Infrastructure Consortium

Ray Owens, PhD, Professor, Molecular Biology and Head, Oxford Protein Production Facility, University of Oxford

Technology developments to streamline the production of proteins for structural biology have been largely driven by the demands of structural proteomics. However, the purification of increasingly complex proteins and protein assemblies has challenged traditional high-throughput structural proteomic workflows. The response of a number of academic centres in Instruct, a distributed European Research Infrastructure Consortium (www.structuralbiology.eu) will be reviewed and common trends highlighted.

14:35 Simplification of Purification Strategies for Mammalian Proteins from Single Targets to High-Throughput Projects Using an Enhanced Biochemical Code

David O’Connell, PhD, Lecturer, Biotherapeutics, Biomolecular & Biomedical Science, University College Dublin

We are investigating the sequences of amino acids and their associated post-translational modifications that confer superior transport characteristics upon secreted proteins to move through and across gradients. With one eye on creating new protein engineering design principles, we are aiming to understand the elements of encoded behaviour of proteins including IgG, cytokines, interferons and the very many proteins that make up our secretome using a high-throughput expression and interrogation model in HEK293. Establishing high-throughput expression, purification and transport assays will be described.

15:00 Overcoming Limitations of Conventional Tag Systems – Strep-Tactin®XT Applications

Dennis Karthaus, MSc, 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 mammalian expression systems (e.g. Expi) and is well suited for downstream applications like SPR.

15:20 Sponsored Presentation (Opportunity Available)

15:35 Networking Refreshment Break

HARNESSING THE POWER OF SMALL

16:00 Purification of Fabs from E. coli Cell Lysates – A Tricky Endeavour

Oliver Spadiut, PhD, Assistant Professor, Chemical, Environmental and Biological Engineering, Integrated Bioprocess Development, Technische Universität Wien (TU Wien)

In my presentation, I will highlight the challenges when purifying added value molecules, like Fabs, from E. coli cell lysates and compare different strategies to do so. Our group’s new feeding approach allows expression of complex products as soluble and active protein. Cell viability and growth can be prolonged by this approach which leads to higher overall yields and thus lower production costs. Our platform technology accelerates bioprocess development and yields higher product titers in E. coli.

16:30 Protein Purification and Detection with Nanobodies

Ulrich Rothbauer, PhD, Professor, Pharmaceutical Biotechnology, Natural and Medical Sciences Institute, University of Tübingen

Nanobodies are attractive tools for protein purification, detection and analysis as they are small, highly stable, and are easily producible thereby offering an unlimited supply of consistent binding molecules. Recent advances in identification of target-specific nanobodies from synthetic gene libraries makes these tools broadly available. Here, we present our latest progress in nanobody generation, functionalization and application for protein purification and detection.

17:00 End of Day

17:30 Dinner Short Course Registration*

17:30 – 20:30 Dinner Short Courses

Recommended Short Course*

SC9: Optimising Protein Purification Strategies in Advance: Getting Your Plan Right

*Separate registration required. Click here for details.
FRIDAY 16 NOVEMBER

08:00 Registration and Morning Coffee

08:30 Chairperson's Remarks

Maximilian Hartl, PhD, Senior Scientist, Roche Pharma Research & Early Development (pRED), Large Molecule Research, Roche Innovation Center Munich

08:35 Structural Biology of Membrane Proteins: Expression Tricks, and to Solubilize or Not to Solubilize

Dirk Linke, PhD, Professor, Genetics and Evolutionary Biology, Biosciences, University of Oslo

In recent work, we have designed expression systems for bacterial outer membrane and surface proteins. These can be used to express and purify, e.g., important vaccine candidates for bacterial diseases, but also for studying membrane protein structure directly in the membrane with solid-state NMR methods.

09:05 Adaptive Automated Membrane Protein Purification Using AkTA Avant

Jonas Lee, PhD, Scientist, Protein Technologies, Amgen, Inc.

Transmembrane proteins are key targets in drug discovery. However, they are difficult to purify due to complex buffer requirements to solubilize. We use various high-throughput methods to screen for best detergent conditions followed by innovative methods to purify multiple targets in different buffer conditions automatically.

09:35 Nanoparticles to Stabilize Membrane Proteins in a Lipid Environment

Jens Frauenfeld, PhD, CEO, Salipro Biotech AB

More than 60% of all current drugs target membrane proteins. However, membrane proteins are very unstable, which is a major challenge for the pharmaceutical industry. Here we present the latest results on a novel system to stabilize membrane proteins using Salipro nanoparticles. Salipro nanoparticles stabilize membrane proteins in a lipid environment that allows them to work in detergent-free buffer systems.

10:05 Networking Coffee Break

10:35 Potential of Centrifugal Partition Chromatography for the Separation of Proteins

Mirjana Minceva, PhD, Assistant Professor, Biothermodynamics, Life and Food Sciences Weihenstephan, Technische Universität München

Centrifugal partition chromatography (CPC) is a solid support-free chromatography method in which both stationary and mobile phase are liquid. This technology combines advantages of liquid-liquid extraction and chromatography, such as high loading capacity, high recovery and high resolution. Moreover, as a result of the liquid nature of the stationary phase, problems associated with column packing are avoided. CPC can be used with aqueous two-phase systems (ATPS) providing a mild environment for the separation of proteins. In this talk, the potential of CPC will be demonstrated for the separation of model mixture of proteins.

11:05 Tailor Made Affinity Adsorbents for Selective Capture and Recovery

Ana Cecília Roque, PhD, Principal Investigator and Associate Professor, Sciences and Technology, University Nova of Lisbon

Biological and chemical libraries containing a high diversity or designed to fit a target biopharmaceutical, are powerful tools to develop robust peptidomimetics based on different scaffold molecules. The scaffold molecules range from small synthetic ligands, to artificial β-hairpin peptides and small protein domains produced chemically. We study the potential of these scaffold affinity reagents to find binding partners against several targets (e.g. recombinant proteins, phosphorylated peptides, and virus-like particles), and to develop mild and selective affinity-based purification processes.

11:35 Membrane Technology to Significantly Improve Binding Capacity and Speed

William Barrett, PhD, Chromatography, Gore & Associates

Traditional protein purification processes may be time-consuming, causing slow-downs in the screening process. The GORE™ Protein Capture Device with Protein A eliminates those constraints by combining a high dynamic binding capacity of ~30mg/mL at 20 seconds residence time (3.0mL/min). The membrane-based pre-packed column may help produce a more highly-concentrated elution pool in less time and may help increase productivity by eliminating the need for additional downstream concentration steps.

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

*See website for details.

IMPROVING AND SCALING UP PURIFICATION PROCESSES

13:00 Chairperson's Remarks

Ulrich Rothbauer, PhD, Professor, Pharmaceutical Biotechnology, Natural and Medical Sciences Institute, University of Tübingen

13:05 Process Development of the Antibody-Drug Conjugate (ADC)

SYD985 – A Case Study

Xiaoan Li, PhD, Senior Scientist, Downstream Processing, Synthon Biopharmaceuticals BV

SYD985 is an antibody-drug conjugate (ADC) based on trastuzumab and a cleavable linker-duocarmycin payload. A case study will be presented in which a hydrophobic interaction chromatography (HIC) purification process was developed allowing removal of the undesired antibody species together with unbound linker-drug. It was possible to elute the product (SYD985) using mild conditions without requirement for any organic solvent. The HIC purification step was scaled up demonstrating consistency and robustness.

13:35 New Formats, New Experiences - DSP Feedback for Carefully Selecting a Molecule for Development

Maximilian Hartl, PhD, Senior Scientist, Roche Pharma Research & Early Development (pRED), Large Molecule Research, Roche Innovation Center Munich

Biopharmaceuticals evolved from copying natural molecules to tailor-made, highly engineered drugs with disease specific action modes. The impressive ideas of our molecule designers often result in promising early in vivo data that challenge technical-scale drug development. In this talk, we show examples of non-predicted challenges we faced during purification of novel drugs. We present solutions and feedback from purification for the selection process of next-generation drugs.
14:05 The Effect of New Stabilizers in Downstream mAb Process Intermediates

Irina Ramos, PhD, Downstream Process Scientist, MedImmune, Inc.

The stability of downstream process intermediates is extremely important to define fit-to-plant parameters and keep product quality attributes within the acceptance criteria. Here we present the impact of adding small novel organic molecules, designed to stabilize a protein's molecular structure, in the context of important downstream steps. In this work, we used a monoclonal antibody (mAb) that showed (1) aggregation during viral inactivation at low pH conditions and (2) low flux throughput during viral filtration. Both steps are traditionally part of the downstream process platform used in mAbs as dedicated virus reduction steps and contribute to the virus safety for mAb-based medicines. Our analysis identifies novel protein stabilizers that can significantly improve mAb process intermediates stability and manufacturing throughput.

14:35 Pitfalls in Design and Scaling Up Protein Chromatography

Dorota Antos, PhD, Professor, Chemical and Process Engineering, Rzeszow University of Technology

Because of the complexity of thermodynamic, kinetic, and hydrodynamic effects accompanying protein chromatography, design and scaling up of the process is often impossible without understanding underlying adsorption mechanism. Specific effects that can occur in protein chromatography will be discussed. The phenomena of band deformation due to mass transport resistances, protein unfolding, sample solvent effect, and dispersion in extra column volumes will be illustrated. The solvent gradient and temperature mediated separations will be considered.

15:05 Monoclonal Antibody Reduction and Re-Oxidation by Copper Sulfate during Manufacturing and Impact on Product Quality

Green Guihang Zhang, PhD, Associate Director, Large Molecule Purification Development, Global Product and Process Development, Incyte Corporation

Significant disulfide bond reduction of an IgG1 monoclonal antibody was observed during the late stage of the CHO cell culture in manufacturing, leading to the batch failure due to significant amount of low molecular weight species and aggregates. Two methods of copper sulfate spiking were investigated to prevent and reverse the product disulfide bond reduction during manufacturing. Both methods could re-oxidize the reduced product and prevent further reduction throughout the manufacturing process.

15:35 End of Summit
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.

Instructor:
G. Jonah Rainey, PhD, Executive Director, Head of Antibody Research, MabVax Therapeutics Holdings, Inc.
WEDNESDAY 14 NOVEMBER

07:45 Registration and Morning Coffee

ENGAGEMENT OF NK CELLS / CHECKPOINT INHIBITORS IN COMBINATION

08:30 Chairperson’s Remarks
Marina Bacac, PhD, Head, Cancer Immunotherapy, Roche Innovation Center Zurich

08:35 Multi-Specific Antibody Technology Engaging NK Cells in Oncology
Laurent Gauthier, PhD, Senior Director, Research and Development, Innate Pharma

We report the design and generation of new multi-specific antibodies which selectively recruit NK cells against tumour targets (NKCE). NKCEs bind to NKp46 on NK cells and can potentially co-engage other activating receptors like CD16 to induce tumor target killing. NKCEs show good developability profile, anti-tumour activity in vitro and in vivo preclinical models and provide new therapeutic options for cancer treatment.

09:05 ATOR-1015, a Next-Generation, Bispecific CTLA-4 x OX40 Targeting Antibody for Tumor Directed Immunotherapy of Cancer
Christina Furebring, PhD, Senior Vice President, Research, Alligator Bioscience AB

ATOR-1015 is a next-generation CTLA-4 x OX40 bispecific immune activating antibody developed for tumor-directed immunotherapy. ATOR-1015 binds both targets simultaneously, promoting cell-cell interactions expected to enhance the immuno-stimulating effect of the compound. The mode of action of ATOR-1015 is a combination of regulatory T-cell (Treg) depletion and effector T-cell activation. ATOR-1015 is currently in preclinical development and clinical trials will start in the second half of 2018.

09:35 Development of an Agonist Redirected Checkpoint, SIRPa-Fc-CD40L, for Cancer Immunotherapy
George Fromm, PhD, VP, R&D, Shattuck Labs

We will present the generation of a novel, two-sided human fusion protein incorporating the extra cellular domains of SIRPs and CD40L. SL-172154 binds both CD47 and CD40 with high affinity, activates CD40 signaling in the absence of Fc receptor cross-linking, outperforms CD47 and CD40 antibodies in multiple tumor models and was safe in non-human primates. SL-172154 will enter the clinic in 2019 in multiple indications.

10:05 Development and Application of MOA-Based Reporter Bioassays for Immunotherapy Drug Development
Mei Cong, Director, Custom Assay Services, Promega Corporation

Having a functional bioassay that is MOA-based, accurate, precise, robust and reproducible is critical for the development of antibody-based biologics. We have developed reporter bioassays that meet these criteria for a broad range of antibody modalities including Fc effector function, immune checkpoint modulation, bispecific antibody engagement, cytokine modulation, and others. Here we will present the latest technology advancements and demonstrate how these bioassays can be used for a broad range of applications.
therapeutically relevant targets such as PD-L1 and LAG-3. We have shown that the Affimer scaffold can be formatted as in-line fusions, to the Fc domain or a full antibody to create bispecific molecules are able to engage both target antigens.

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

14:15 Session Break

COMBINATION THERAPIES / T-CELL ENGAGEMENT (CONT.)

14:30 Chairperson's Remarks

Eric Smith, PhD, Director, Bispecific Antibodies, Regeneron

14:35 Targeting B-Cell Malignancies with a CD3 Bispecific Antibody - Preclinical Evaluation of DuoBody-CD3xCD20

Ida Hiemstra, PhD, Lead Scientist, Translational Research, Genmab B.V.

An overview will be presented of preclinical data identifying DuoBody-CD3xCD20 as the most potent B-cell-targeting CD3 bispecific antibody in an in vitro functional screen covering a comprehensive panel of B cell targets. DuoBody-CD3xCD20 induced potent T cell activation and cytokotoxic activity in the presence of malignant B-cells in vitro and in vivo. The capacity of DuoBody-CD3xCD20 to deplete B cells from blood and lymphoid organs, after intravenous or subcutaneous administration, was assessed in cynomolgus monkeys as part of the non-clinical safety studies. A clinical study evaluating the DuoBody-CD3xCD20 is currently enrolling.

15:05 APVO436: A CD3 Engager with Low Cytokine Release Profile Targeting CD123 for AML

Catherine J McMahan, PhD, Senior Director, Pharmacology and Cell Sciences Research and Non-Clinical Development, Aptevo Therapeutics

APVO436 is a CD123 x CD3 bispecific ADAPTIR antibody designed to treat AML. It contains an Fc region for extended half-life and has bivalent binding to both the tumor target and CD3. APVO436 was optimized for manufacturability, specificity and low levels of cytokine release compared to other bispecific formats. APVO436 induces robust proliferation of T-cells and tumor target lysis in vitro and in vivo xenograft models.

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

IMMUNOSTIMULATORY CYTOKINES FOR TUMOUR TARGETING AND CONTROL OF TOXICITY

16:15 Engineering Bispecific Cytokine-Fc Fusions to Create Safer and More Effective Immuno-Oncology Therapies

David Syzmkowski, PhD, Vice President, Cell Biology, Xencor

Immunostimulatory cytokines such as IL-2 and IL-15, while extremely potent, suffer from poor tolerability and rapid clearance, limiting their potential as cancer treatments. Using our clinically-validated bispecific Fc domain, we generated a heterodimeric IL15/IL15Ra-Fc with reduced potency and longer half-life. IL15/IL15Ra-Fc demonstrates improved exposure and stimulates multiple effector-cell responses in mice and monkeys. Such cytokine-Fc biologics may possess better tolerability and improved efficacy with less-frequent dosing than recombinant cytokines.

16:45 Immunostimulatory Properties of a Novel IL-15-Based Tumor-Targeted Immunocytokine

Anika Jäkel, PhD, Director, Preclinical Pharmacology & Cancer Immunology, Glycotope GmbH

Interleukin-15 (IL-15), a potent stimulator of NK and CD8 T-cells, is considered to be one of the most encouraging immunotherapeutics for cancer treatment. We created novel IL-15-based immunocytokines with different potencies and Fc effector functions binding to a tumor-specific carbohydrate antigen to potentiate tumor targeting. By applying a comprehensive screening approach considering PK, PD and cytokine profile, we seek to identify a promising lead candidate suitable for mono or combinatorial therapy of solid tumors.

17:15 Development of Novel Interleukin-2 Variants for Immunotherapy of Cancer and Autoimmune Diseases

Ekkehard Moessner, PhD, Head, Protein Engineering, Large Molecules Research, Roche Innovation Center Zurich

The development of interleukin-2 muteins throughout the preclinical development will be described, for two different approaches. In one approach the IL-2 will be used for cancer immunotherapy, and in the other the IL-2 is engineered for applications in autoimmune diseases.

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

18:45 Problem-Solving Breakout Discussions*  
*See website for details.

19:45 End of Day

THURSDAY 15 NOVEMBER

08:00 Registration and Morning Coffee

BISPECIFICS IN THE CLINIC

08:30 Chairperson's Remarks

David Syzmkowski, PhD, Vice President, Cell Biology, Xencor

08:35 Update on BiTE® Antibody Constructs Currently in Clinical Development

Virginie Nägele, PhD, Senior Scientist BiTE Technology Amgen Research (Munich) GmbH

The BiTE® technology is a clinically explored approach targeting malignant cells by T-cells with blinatumomab being the first bispecific T-cell engager (BiTE) approved for the treatment of patients with relapsed or refractory B-precursor acute lymphoblastic leukemia (B-ALL) in the US. More recently, blinatumomab has also received accelerated approval for the treatment of B-ALL minimal residual disease. This presentation will give an update on the current clinical development of BiTE antibody constructs at Amgen focusing on hematologic malignancies like acute myeloid leukemia and multiple myeloma, and on solid tumor indications.

09:05 DVD-Ig Platform: Clinical Lessons and Future Directions

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

Several DVD-Ig molecules have been tested in preclinical models and in clinic for...
autoimmune and oncology indications. Emerging data suggests that the DVD-Ig format per se is not immunogenic. However, target biology may play an important role in anti-drug antibody response (ADA, immunogenicity). Lessons learned from these studies may be broadly applicable and will be discussed.

09:35 **Development of a Potent Anti-Cancer Bispecific Antibody Targeting VEGF and DLL4**

Weon-Kyoo You, PhD, Head, R&D, Vice President, ABL Bio, Inc.

Simultaneous blockade of VEGF/VEGFR and DLL4/Notch signaling pathways is known to lead potent inhibition of tumor progression. In this presentation, we will talk about ABL Bio’s bispecific antibody platforms and development processes of the most advanced asset, a bispecific antibody targeting VEGF and DLL4 (ABL001) which is currently ongoing a phase 1 clinical study. We will cover an overview of preclinical data as well as interim clinical data of ABL001.

10:05 **SMAB: a Novel Bispecific Antibody Platform for Therapeutic Development**

Janice Jin, Head, Project Management Center, Project Management Department, GenScript

Urgent demands for new therapeutic strategies, such as novel modalities are raised during explosive growth of therapeutic antibody drugs. In this presentation, we will introduce GenScript proprietary SMAB bispecific antibody platform which minimizes the immunogenicity and manufacture concerns of current bispecific antibody platforms while enabling bi-valent and multi-valent therapeutics.

10:20 **Sponsored Presentation (Opportunity Available)**

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

DESIGN TO PROOF-OF-CONCEPT

11:15 **Case Study on New Product: Biology and Proof-of-Concept**

Mihriban Tuna, PhD, Vice President, Drug Discovery, F-star

11:45 **Tumor-Localized T-Cell Co-Stimulation Using Antibody-Anticalin Fusion Proteins: From Flexible Design to Proof-of-Concept and Beyond**

Marina Pavlidou, PhD, Project Leader, Discovery, Pieris Pharmaceuticals GmbH

We describe the generation of bispecific molecules by fusing T-cell targeting Anticalin proteins to tumor targeting antibodies. We show superior potency of the bispecific over the combination of building blocks and the combination of benchmark molecules. The activity of the bispecific is dependent on the expression of the tumor target showing the potential of providing a tumor localized activation of the immune system with high efficacy and reduced peripheral toxicity.

12:15 **Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own**
This presentation describes our approach to developing immune-oncology therapeutics, in particular Humabody VH products, small highly adaptable multi-functional proteins which can be developed into differentiated therapeutics with excellent characteristics for tumour targeting. It includes the development of a Biparatopic PD-1 inhibitor showing efficacy in a Pembrolizumab insensitive in vivo model, a Bispecific PD-1, LAG3 inhibitor and a targeted IO approach in which T-cell co-stimulation is focused away from the periphery and into the tumour microenvironment.

14:05 KEYNOTE PRESENTATION: Novel T Cell Engagers for Targeted Recruitment of Effector Cells to Tumors
Yoram Reiter, PhD, Head, Molecular Immunology, Technion-Israel Institute of Technology
We have developed a new class of recombinant chimerical molecule that serve as T cell engagers to re-direct potent immune effector functions to specifically kill tumor cells. These T cell engagers are based on the genetic fusion of antibody fragments, specific for tumor cell surface antigens to monomeric HLA molecules that carry immunodominant peptides that can recall potent effector T cells. The molecular feature of these molecules/approaches and their in vitro and in vivo activities will be described.

14:35 Engineering of a T-Cell Dependent Bispecific to Broaden the Therapeutic Index for Solid Tumors
Christoph Spiess, PhD, Senior Scientist, Antibody Engineering, Genentech, Inc.
I will present the engineering of the bispecific to achieve selective binding to tumor cells and provide data demonstrating improved tumour infiltration in vitro and in vivo and preclinical safety.

15:05 Presentation to be Announced

15:35 Networking Refreshment Break

16:00 Creating a Novel T-Cell Engaging Bispecific Antibody Platform: Fine Tuning Anti-Tumor Activity with Sequence-Based Discovery and Machine Learning
Nathan Trinklein, PhD, Vice President, Teneobio
Using a multiple myeloma tumor cell line along with primary human PBMCs, we demonstrate a spectrum of in vitro tumor cell killing activity with varied levels of cytokine release using our bispecific molecules with diverse CD3 binding activities. In summary, we have created a T-cell engaging bispecific antibody platform with tuned T-cell agonism that can be used to optimize the therapeutic index for a variety of tumor antigens.

16:30 Developing Humabody VH Therapeutics for Immuno-Oncology
James Legg, PhD, Vice President, R&D, Crescendo Biologies
Enhanced Targeting and Functionality

17:00 End of Day

FRIDAY 16 NOVEMBER

08:00 Registration and Morning Coffee

FC ENGINEERING FOR ENHANCED PRODUCT PROPERTIES AND FOR BRAIN DELIVERY

08:30 Chairperson's Remarks
Martin Bader, PhD, Head, Biochemical and Analytical Research, Pharma Research and Early Development Roche

08:35 Glyco-Optimization of Antibodies Targeting Immune Checkpoint Molecules: Case Studies of an Agonist and an Antagonist
Christoph Goletz, PhD, Associate Director, Preclinical Pharmacology & Cancer Immunology, Glycopte GmbH
Glyco-engineering is an established strategy to improve tumor antigen-targeting antibodies, e.g. anti-CD20, anti-EGFR, regarding their ADCC activity. In two case studies of an agonistic anti-CD40 and an antagonistic anti-PD-L1 antibody, we show that glyco-optimization can also be applied to enhance activity of antibodies targeting immune checkpoint molecules.

09:05 Development of a Novel Fc Heterodimerization Technology
Fabian Richter, PhD, Post-Doc, Biomedical Engineering, Cell Biology and Immunology, University of Stuttgart
The innovative heterodimerization technology “Fc1k” (Fc-one-kappa) was created and used for the generation of monovalent as well as polyvalent and multi-specific antibody-like molecules. We demonstrated the applicability in a monovalent Fv...
Fc1k format, used for cytokine receptor blockade and in a bispecific scFv2-Fc1k molecule, simultaneously targeting two antigens. This novel platform technique provides for covalent heterodimerization of immunoglobulin domains, based on fully human and naturally occurring sequences.

**09:35 Identification of a PD-L1 Binding Fcab: A Potent Inhibitor of Immunosuppressive Signals**

*Jose Munoz Olaya, PhD, Principal Scientist, Drug Discovery, F-star*

Checkpoint inhibitors have been very popular and successful targets in the field of immuno-oncology. Here we describe the isolation of an Fcab, an antibody Fc domain modified to bind to a target, specific to PD-L1. The Fcab exhibits high affinity to human PD-L1 that translates into strong potency in cell-based functional assays. An anti-murine surrogate molecule, with similar potency, also exhibits activity in an MC38 syngeneic tumour model. This activity is improved when the Fcab is paired with Fabs targeting other immune checkpoint regulators.

**10:05 Networking Coffee Break**

**10:35 Antibody Transport Vehicle (ATV): A Novel Brain Delivery Platform**

*Mark S. Dennis, PhD, Fellow, Denali Therapeutics*

The Antibody Transport Vehicle (ATV) enables the delivery of large molecule therapeutics to the brain for the treatment of neurological diseases. The ATV platform contains an engineered Fc domain that binds the transferrin receptor and utilizes receptor-mediated transcytosis to cross the BBB. Transport in nonhuman primates was assessed by the inhibition of β-secretase 1 (BACE1) in brain which was robustly inhibited by ATV:BACE1 leading to a sustained reduction in amyloid beta levels.

**11:05 Turning Affibody Molecules into Efficient Peptide Binders by Dimerization**

*John Lofblom, PhD, Associate Professor, Engineering Sciences in Chemistry, Biotechnology and Health, KTH Royal Institute of Technology*

Affibody molecules are small three-helical affinity proteins. Generating binders for the amyloid beta peptide yielded a variant with 20-pM affinity, and with a tunnel-like cavity. Engineered binders for other peptides show similar structural rearrangements and mode of binding, indicating that the new dimeric scaffold is well suited for such molecular recognitions.

**11:35 Industrializing IO Therapeutic Discovery Platforms: Multispecifics, Engineered TCRs and CARs**

*Maria Wendt, PhD, Head, Science 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.

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

*See website for more details.*

**TECHNOLOGIES FOR DISCOVERY AND SCREENING, CMC, TARGETING, POTENCY AND LOW RISK OF TOX**

**13:00 Chairperson’s Remarks**

*Mark S. Dennis, PhD, Fellow, Denali Therapeutics*

**13:05 Case Studies on How Digital and Automated Solutions Transform the Discovery and Development of Next-Generation Antibodies**

*Martin Bader, PhD, Head, Biochemical and Analytical Research, Pharma Research and Early Development, Roche*

We systematically introduced automated and digital solutions along our antibody discovery and development chain. A number of examples will be highlighted that demonstrate how automation and data science speed up 1) developability predictions to enable fast selection of clinical leads, 2) automation during functional characterization, and 3) machine learning during cell line selection and bioprocess modeling. As a consequence, output during the antibody discovery and development phase increases substantially.

**13:35 Talk Title to be Announced**

**14:05 Redefinition of ErbB2/3 Tumor Targeting: How to Design Truly Potent Bispecific and Biparatopic Agents**

*Rastislav Tamaskovic, PhD, Head, TC Facility, Senior Scientist, Biochemistry, University of Zurich*

Due to adaptiveness of oncogenic networks, tumors readily develop resistance against targeted therapies. Recently, we have described major compensatory routes, which become activated in therapy of ErbB2-positive cancer - and developed a new class of bispecific and biparatopic anti-ErbB2/3 targeting agents endowed with capabilities to overcome the adaptive resistance. Analogously, we build a new platform for tumor RTK fingerprinting aimed at identification of prospective therapeutic leads and truly synergistic combination therapies.

**14:35 Productive Common Light Chain Libraries Yield Diverse Panels of High Affinity Bispecific Antibodies**

*Thomas Van Blarcom, PhD, Associate Research Fellow, Protein Engineering, Pfizer, Inc.*

Here we describe the design of a synthetic human antibody library based on common light chains to generate antibodies with biochemical and biophysical properties that are indistinguishable to traditional therapeutic monoclonal antibodies. We used this library to generate diverse panels of well-behaved, high affinity antibodies toward a variety of epitopes across multiple antigens including mouse 4-1BB in order to investigate the therapeutic potential of biparatopic bispecific antibodies.

**15:05 DuoBody Technology: A Versatile Platform for Bispecific Antibody Discovery and Development**

*Rick Hibbert, MBA, PhD, Assistant Director, Protein Production and Chemistry, Genmab B.V.*

The DuoBody® platform represents a versatile, elegant and robust technology for generating bispecific antibodies. The post-production process is based on controlled Fab-arm exchange and yields bispecific antibodies that retain the...
molecular structure and quality attributes of therapeutic IgGs. The process is robust, high-throughput compatible and shows linear scalability from bench to manufacturing scale. This presentation will highlight recent insights in the preclinical and CMC development of DuoBody products.

15:35 **End of Summit**
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